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ORIGINAL ARTICLE OPEN ACCESS

Efficacy of Doxylamine and Pyridoxine during Pregnancy Induced Nausea and Vomiting

Tinni Rani Paul*[1], Khan Md. Muzammel Hossain[2], Shukdeb Paul[3], Amirun Nahar[4], Estiak Ahmed[5], Farah Diba Chowdhury[6]

Abstract

Introduction: *Nausea and vomiting in pregnancy (NVP) is the most common medical condition of pregnancy causes a significant clinical, psychological and economic burden. Therefore, it is very important to treat this condition appropriately and effectively. The combination of Doxylamine and Pyridoxine is recommended as first-line therapy for nausea and vomiting in pregnancy.* **Objectives:** *To observe the therapeutic efficacy of combined Doxylamine and Pyridoxine for treatment of nausea and vomiting in pregnancy.* **Materials and Methods:** *An observational study was conducted on patients with nausea and vomiting in pregnancy attended the Model Family planning clinic in the Department of Obstetrics and Gynaecology, Sylhet MAG Osmani Medical College Hospital, Sylhet during the period from January 2019 to December 2019. A total 90 patients with clinically meaningful nausea vomiting (Pregnancy-Unique Quantification of Emesis [PUQE] score > 6) were selected and given 2-4 tablets each containing combined Doxylamine succinate 10 mg and Pyridoxine hydrochloride 10 mg based on a pre-specified titration protocol response to symptoms by respective physician and PUQE score was recorded in all participants before initiation of treatment and at 8th day and 15th day of treatment. In course of follow up period 7 patients were dropped out and finally 83 patients were analyzed in this study.* **Result:** *The mean PUQE score was decreased from 10.27 ± 1.76 to 7.94 ± 1.75 at 8th day and to 5.35 ± 1.47 at 15th day of treatment was significant ($p<0.001$). The percentage reduction of PUQE score was 23.14% at 8th day and 46.91% at 15th day of treatment. The difference was significant ($p<0.001$).* **Conclusion:** *Combined Doxylamine-Pyridoxine is effective and well tolerated in the treatment of nausea and vomiting in pregnancy (NVP).*

Keywords: *Nausea, Vomiting, Pregnancy, Combined Doxylamine-Pyridoxine.*

Number of Tables: 03; Number of References: 21; Number of Correspondences: 04.

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Introduction:

Nausea is the unpleasant, painless sensation that may potentiate to vomit. Vomiting is an organized, autonomic response that ultimately results in the forceful expulsion of gastric contents through the mouth[1]. Nausea and vomiting of pregnancy (NVP) is the most common symptoms associated with pregnancy. The symptoms are usually worse in the morning, hence the name 'morning sickness', but it can occur throughout the day and night. Symptoms of NVP include nausea, retching and vomiting, usually appear between 4 and 9 weeks of pregnancy and subside between 12 and 16 weeks of pregnancy; however, about 15% of women, symptoms continue up to 20 weeks gestation and less than 10% of women suffer throughout their entire pregnancy[2].

Nausea and vomiting of pregnancy affect up to 90% of pregnant women[3,4]. NVP affects the health of both pregnant woman and her fetus. It can diminish the woman's quality of life and also contributes significantly to health care cost and time lost from work. The severity of NVP ranges from mild to severe by using the Pregnancy Unique Quantification of Emesis (PUQE) Score, severity of symptom are ranged between 3 (no symptom) to 15 (the worst symptoms). The most severe form of NVP is hyperemesis gravidarum (HG), affects between 0.3 and 2% of pregnant women[5].

The etiology of NVP is multi-factorial and still remains unknown. The hormonal changes during the first trimester of pregnancy include increase production of human chorionic gonadotropin hormone (hCG), oestrogen and progesterone. There is a temporal relationship between peak of hCG concentration and peak symptoms of NVP[6]. Numerous other factors such as psychiatric diseases, liver abnormalities, elevated cytokine levels, deficiencies in vitamin B_1, B_6 and also genetic predisposition have been suggested to contribute to the etiology of NVP[7-9].

Many non-pharmacological (Dietary and lifestyle modification) and pharmacological treatment regimens are available for treatment of NVP. Pharmacologic treatments include Antihistamines (Meclizine, Doxylamine), Dopamine antagonists (Metoclopramide, Domperidone), vitamin B6 (Pyridoxine), serotonin ($5HT_3$) antagonists (Ondansetron) or combinations of these substances[10].

The American College of Obstetricians and Gynecologists recommends combined Doxylamine and Pyridoxine as first-line agents when dietary and lifestyle changes is unsuccessful[11]. Antihistamines are commonly used during early pregnancy in the treatment of nausea and vomiting. Diphenhydramine, Dimenhydrinate, Meclizine and Doxylamine are first generation H1-receptor antagonists[12]. Doxylamine directly inhibit the action of histamine at the H1 receptor and indirectly affvestibular system and decreasing stimulation of the vomiting center. It has also inhibitory action on muscarinic receptor causing antiemetic activity[13].

Pyridoxine is a water-soluble vitamin, essential co-enzyme for the metabolism of amino acids, lipids and carbohydrates[14]. It is also a co-factor in γ-amino butyric acid (GABA) synthesis and GABA acting as the inhibitory neurotransmitter at Chemoreceptor trigger zone (CTZ) and suppresses vomiting[15]. The combination of Doxylamine and Pyridoxine, have a synergistic effect in the alleviation of NVP. In April 2013, the US Food and Drug Administration (FDA) approved combination of Doxylamine and Pyridoxine, for the treatment of NVP and considered as a Pregnancy Category A[16]. Several trials of combined Doxylamine and Pyridoxine shows improvement of NVP compared to placebo[17, 18].

So, this study is planned to assess the effectiveness of combined Doxylamine and Pyridoxine for the treatment of nausea and vomiting in pregnancy (NVP).

Materials and Methods:

This was an observational study conducted in the Department of Pharmacology and Therapeutics, Sylhet MAG Osmani Medical College, Sylhet in collaboration with Model Family planning clinic of Department of obstetrics and Gynaecology, Sylhet MAG Osmani Medical College Hospital, Sylhet during the period from 1st January 2019 to 31st December 2019. Patient's nausea with or without vomiting related to pregnancy, less than 16 weeks of gestation and clinically meaningful nausea and vomiting (PUQE score > 6) were included in this study. Women were excluded from the study if their nausea or vomiting predated the pregnancy, hyperemesis gravidarum (HG), medications taken in the past week that aggravate or alleviate nausea or vomiting, such as iron tablets, anti-emetics etc, others medical, surgical and gynecological causes of vomiting in pregnancy and history of allergy to the study medications. Convenient sampling method was applied to select sample.

Informed written consent was taken from the patient after detailed explanation of the process and purpose of the study. Clinical histories, physical examination, obstetrical evaluation and relevant investigation (USG of uterus for pregnancy profile or urine for pregnancy test) of the patient were done. After confirmed the diagnosis of NVP by respective gynaecologist, patients were asked to complete the Pregnancy-Unique Quantification of Emesis (PUQE) score at initial enrollment to grade the severity of nausea and vomiting experienced last 24 hours . The PUQE score incorporates the number of daily vomiting episodes, number of daily retching and length of daily nausea in hours, for an overall score of symptoms rated from 3 (no symptoms) to 15 (most severe). Scores of 4–6 denote mild, Scores of 7–12 denote moderate and scores of 13–15 denote severe NVP. Those with PUQE score > 6 were enrolled in this study[19].

In this way 90 patients with nausea and vomiting in pregnancy were selected. Before initiating treatment, age, estimated gestational age, BMI, current medications, gravidity and parity were recorded for each patient. The patients were prescribed combined Doxylamine succinate 10 mg and

Pyridoxine hydrochloride 10 mg two tablets orally at bedtime on Day 1. If this dose adequately control symptoms, continue taking two tablets daily at bed times. If symptoms persist into the afternoon of Day-2, take the usual dose of two tablets at bed time that night then take three tablets starting on Day-3 (one tablet in the morning and two tablets at bedtime). If three tablets adequately control symptoms, continue taking three tablets daily. Otherwise take four tablets starting on Day-4 (one tablet in the morning, one tablet in mid-afternoon and two tablets at bedtime) by attending gynaecologist. The maximum recommended dose is four tablets daily. The total period of study was 15 day consisting of 14 dosing days[20].

Patients were reevaluated on 8th and 15th day after initiating the drug regimen using PUQE score. All the collected data were compiled and analyzed using the Statistical Package for Social Science (SPSS) version 25.0. Quantitative data were expressed as mean and standard deviation and qualitative data were expressed in frequency and percentage. Analysis was done by repeated measure ANOVA and Z-test for proportion accordingly.

Result:

Total 90 pregnant women with NVP were enrolled and in course of follow up period 7 patients failed to complete study follow up visit were excluded from analysis. So, 83 patients were analyzed in this study.

Table-I: Distribution of the patients by baseline characteristics.

Parameters	Study group (n=83)
Age in years (Mean ± SD)	24.45 ± 4.39
Gestational age in weeks (Mean ± SD)	9.00 ± 2.62
Gravida	
Primigravida n (%)	25 (30.1)
Multigravida n (%)	58 (69.9)
BMI in Kg/M^2 (Mean ± SD)	20.14 ± 1.88

Table- II: showed the effects of Combined Doxylamine and Pyridoxine on the PUQE score in patients with NVP estimated at baseline, 8th and 15th day of treatment.

The mean PUQE score was 10.27 ± 1.76 before the initiation of treatment which decreased gradually to 7.94 ± 1.75 at 8th day and to 5.35 ± 1.47 at 15th day of treatment. The overall difference from the baseline to the end point of treatment was significant (F=843.620; df=2; p<0.001). Post hoc analysis revealed that PUQE score decreased significantly at 8th day (p<0.001) and at 15th day (p<0.001) of treatment from baseline; and between 8th and 15th day (p<0.001) of treatment.

Table-II: Effects of Combined Doxylamine-Pyridoxine on the PUQE score

PUQE Score (Mean ± SD)					
Study (n=83)	group	Baseline '0' day	At 8th day	At 15th day	*p value
		10.27 ± 1.76	7.94 ± 1.75	5.35 ± 1.47	p<0.001

* Repeated measure ANOVA.

Table-III: showed the percentage reduction in PUQE score estimated at 8th day and 15th day of treatment. The percentage reduction of PUQE score was 23.14 at 8th day and 46.91 at 15th day of treatment. Difference between 8th day and 15th day was statistically significant (Z=-3.314; p<0.001).

Table–III: Percentage reduction of PUQE score on combined Doxylamine-Pyridoxine treatment

Percentage reduction of PUQE score				
Study (n=83)	group	At 8th day	At 15th day	*p value
		23.14	46.91	p<0.001

*Z-test for proportion

Discussion:

In this study the age of the patients ranged from 18 to 38 years with the mean age of 24.45 ± 4.39 years. This result was consistent with the study of Koren et al., (2015) which reported the maternal age of 25.9 ± 6 years in combined Doxylamine-Pyridoxine treated group of NVP and 25.0 ± 5.7 years in placebo group; difference was not significant (p=0.23)[20].

In the present study the mean gestational age was 9.00 ± 2.62 weeks. This finding was concordant with the study of Koren et al., (2015) which reported the mean gestational age of patients with NVP was 9.3 ± 2.0 weeks in combined Doxylamine-Pyridoxine treated group and was 9.3 ± 1.8 weeks in placebo group; which was not significant (p=0.75)[20]. Oliveira et al., (2014) found the median gestational age of women with NVP was 8 (IQR, 7.1-8.9) weeks in Ondansetron group and 8.1 (IQR, 7.2-9.9) weeks in Doxylamine-Pyridoxine treated group; the difference was not statistically significant (p=0.54)[21].

In the current study 30.1% patients were primigravid and 69.9% patients were multigravida. This result was in line with the study of Koren et al., (2015) where they found 77.1% of patients with NVP treated with combined Doxylamine-Pyridoxine were multipara[20]. Oliveira et al., (2014) found median gravid was 2 (IQR, 1-3) in Ondansetron treated group and was same in combined Doxylamine-Pyridoxine group; the difference was not statistically significant (p>0.05)[21]. In the present study the mean BMI (Kg/M^2) was 20.14 ± 1.88. In this regards Koren et al., (2015) found the mean BMI of patients with NVP of combined Doxylamine-Pyridoxine treated group was 28.77 ± 7.60 Kg/M^2; whereas the mean BMI of patients with NVP of placebo treated group was 29.67 ± 11.20 Kg/M^2; difference was not significant (p=0.95)[20] .

This study showed the effect of combined Doxylamine and Pyridoxine on PUQE score in patients with NVP estimated at baseline, 8th and 15th day of treatment. The mean PUQE score was 10.27 ± 1.76 before the initiation of treatment which decreased gradually to 7.94 ± 1.75 at 8th day and to 5.35 ± 1.47 at 15th day of treatment. The overall difference from the baseline to the end point of treatment was significant (p<0.001) and the Post hoc results indicated significant

decrease at 8th day ($p<0.001$) and at 15th day ($p<0.001$) of treatment from baseline; and between 8th and 15th day ($p<0.001$) of treatment. In this aspects Koren et al., (2016) found that combined Doxylamine and Pyridoxine treatment lead decrease of PUQE score in NVP symptoms at end of treatment from baseline (PUQE score 9.0 ± 2.1 to 4.2 ± 1.9)[18]. In another study Koren et al., (2010) found that combined Doxylamine and Pyridoxine treatment lead to significantly greater improvement in NVP symptoms as compared with placebo (-4.8 ± 2.7 PUQE score vs -3.9 ± 2.6; $p=0.006$)[17].

This study revealed that the percentage reduction of PUQE score was 23.14 at 8th day and 46.91 at 15th day of treatment. The difference between 8th day and 15th day of treatment was significant ($p<0.001$). Koren et al., (2016) reported the percentage reduction of PUQE score was 44.4% at 5th day and 53.0% at 15th day of treatment in combined Doxylamine-Pyridoxine treated group[18].

This study was conducted in tertiary hospital and did not represent the actual situation of the country. Sample size was small and duration of treatment period was short.

Conclusion:

This study, concluded that combined Doxylamine-Pyridoxine up to 40 mg daily is effective in the treatment of nausea and vomiting in pregnancy with good safety profile.

A further study involving multicenter, large sample size should be conducted to evaluate the efficacy and safety of combined Doxylamine-Pyridoxine in the treatment of nausea and vomiting in pregnancy.

Conflict of Interest: None.

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ORIGINAL ARTICLE OPEN ACCESS

Morphological Parameters of Gallbladder are Correlated with Age

Farjana Mansura*[1], Kazi Abdullah Al Mamun[2], Abdullah Al Faisal[3], Mahmuda Khatun [4], Halima Akter Suchi[5]

Abstract

Introduction: *Gallbladder issues are prevalent globally, particularly in Bangladesh, and become more common with age. Diagnosis involves clinical assessment and confirmation through noninvasive and invasive methods. Understanding gallbladder features is crucial for effective investigation, diagnosis, and management.* ***Objectives:*** *To find out relation between morphological parameters of human gallbladder with age.* ***Materials and Methods:*** *This cross-sectional descriptive study was conducted in the Department of Anatomy in collaboration with the Department of Forensic Medicine, Sylhet MAG Osmani Medical College, Sylhet from January 2014 to December 2014. Fifty human postmortem gallbladders were selected. Dead bodies autopsied within 36 hours of death. Considerable signs of decomposition or decomposed dead body, presence of gross gallbladder disease and any history of poisoning cases were excluded. All the specimens were examined to detect the length, breadth, weight and thickness of the gallbladder; and length and diameter of cystic duct.* ***Results:*** The study included cadavers ranging in age from 11 to 55 years, with a mean age of 35.02 ± 19.98 years. Of the total, 29 (58.0%) were male, and 21 (42.0%) were female. The length and thickness of the gallbladder increased significantly with age, as did the length and diameter of the cystic duct. But the weight and breadth also change with age, although not significantly. ***Conclusion:*** The length and thickness of the gallbladder; the length and diameter of the cystic duct were varied with age; but no variation in weight and breadth.

Keywords: *Morphological parameters, gallbladder, age.*

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Introduction:

The gallbladder is a flask-shaped, blind-ending diverticulum attached to the common bile duct by the cystic duct. In life, it is grey-blue in colour and usually lies attached to the inferior surface of the right lobe of the liver by connective tissue. In the adult the gallbladder is between 7 and 10 cm long. It usually lies in a shallow fossa in the liver parenchyma covered by peritoneum continued from the liver surface. This attachment can vary widely. At one extreme the gallbladder may be almost completely buried within the liver surface, having no peritoneal covering (intraparenchymal pattern); at the other extreme it may hang from a short mesentery formed by the two layers of peritoneum separated only by connective tissue and a few small vessels (mesenteric pattern)[1].

The gallbladder stores bile up to 5 fold of its capacity and concentrates bile by absorbing water to a maximum 20 fold. Bile is secreted by the liver cells but most of it is normally stored in the gallbladder until needed. The maximum volume that the gallbladder can hold is only 30 to 60 milliliters[2,3].

The organ is divided into fundus, body and neck, the latter opening into the cystic duct. In dilated and pathological gall-bladders there is frequently a pouch present on the ventral aspect just proximal to

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the neck termed Hartmann's pouch in which gallstones may become lodged. The gall-bladder is supplied by the cystic artery (a branch usually of the right hepatic artery) which lies in the triangle made by the liver, the cystic duct and the common hepatic duct. Other vessels derived from the hepatic artery pass to the gall-bladder from its bed in the liver. Interestingly, small veins pass from the gall-bladder through its bed directly into tributaries of the right portal vein within the liver[4].

The gall-bladder wall and the sphincter of Oddi contain muscle, but there are only scattered muscle fibres throughout the remaining biliary duct system. The mucosa is lined throughout by columnar cells and bears mucus-secreting glands[4].

The gall-bladder and ducts are subject to numerous anatomical variations which are best understood by considering their embryological development. A diverticulum grows out from the ventral wall of the duodenum which differentiates into the hepatic ducts and the liver. Another diverticulum from the side of the hepatic duct bud forms the gall-bladder and cystic duct[4].

Some variations in biliary anatomy are (a) Along cystic duct joining the hepatic duct low down behind the duodenum. (b) Absence of the cystic duct—the gall-bladder opens directly into the common hepatic duct. (c) A double gall-bladder, the result of a rare bifid embryonic diverticulum from the hepatic duct. (d) The right hepatic artery crosses in front of the common hepatic duct; this occurs in 25 per cent of cases[4].

Liver and biliary diseases are the most common health problem throughout the world as well as in Bangladesh. The most common biliary diseases are cholelithiasis[5]. Gallstones afflict 10% to 20% of adult populations in developed countries. It is estimated that over 20,000,000 persons in the United States have gallstones (Crawford, 2005). Up to 25% of all Bangladeshi people have gallstones[5]. Cholecystitis is associated with cholelithiasis in 95% cases (Crawford, 2005)[6]. Gallstone formation is the most common disorder of the biliary tree and it is unusual for the gallbladder to be diseased in the absence of gall stone[7]. The commonest lesion observed is chronic cholecystitis (80%) followed by acute cholecystitis (9.3%) invasive carcinoma (7.3%) carcinoma in situ (0.6%) and dysplasia (0.6%)[8].

A traditional cholecystectomy is most commonly performed from the infundibulum to the fundus as no medical treatment is still available. Now a day's laparoscopic cholecystectomy replaces the open surgical method[5]. During operation surgeons have to identify the cystic duct and cystic artery properly before ligation. Uncontrolled bleeding from the cystic artery and its branches is a serious problem that may, increase the risk of intraoperative lesions to vital vascular and biliary structures[5]. The performance of a safe cholecystectomy depends on thorough knowledge about the normal anatomy and anatomical variations that may contribute to the occurrence of major postoperative complications.

Materials and Methods:

This cross-sectional descriptive study was conducted in the Department of Forensic Medicine in Sylhet M.A.G Osmani Medical College from 1st January 2014 to 31st December 2014 over a period of one year. Fifty dead bodies autopsied within 36 hours of death were included in this study. Bodies with considerable signs of decomposition, any gross gallbladder disease, any injury to the gallbladder or biliary tract area and any history of poisoning were excluded from this study. Data were collected by using pre-designed checklist prepared for the study. The questionnaires were pre-tested and face validated by consulting with experts.

A total 50 human gallbladder were collected from 50 cadavers, whose age limits were from 11-55 years, of both sexes. The specimens were divided into three groups by age according to Khan et al.[9] for the convenience of differentiating the changes if various histomorphological features of the gallbladder in relation to age. Group A consisted with 7 patients of age 11-20 years, Group B with 28 patients of age 21-40 years and Group C with 15 patients of age 41-55 year.

Fifty human gallbladders were collected from the unclaimed dead bodies autopsied in the Department of Forensic Medicine in Sylhet M.A.G Osmani Medical College, Sylhet during the period from January 2014 to December 2014 meeting the inclusion and exclusion criteria. Particulars of dead body was collected from police inquest report and chalan.

Dead body was kept in supine position on the mortuary table. A longitudinal midline incision was made from the tip of the ziphoid process to the upper border of the symphysis pubis encircling the umbilicus. Then a transverse incision was made from the ziphoid process to mid axillary line in both side. Another incision was made from the symphysis pubis to the anterior superior iliac spine along with inguinal line both side. Then skin and superficial fascia was retracted laterally. After cutting the rectus sheath and parietal peritoneum abdomen was opened. Then gallbladder was identified. Then gallbladder along with cystic duct was collected as block dissection with part of the liver and part of common hepatic duct. After removal from the body, unwanted tissues were cleared and gently washed out in normal saline and fixed with 10% formol saline. Then they were brought to the Department of Anatomy, Sylhet M.A.G Osmani Medical College, Sylhet.

Measurement of the parameters of gallbladder and cystic duct

Bile was removed by cutting one edge of the gallbladder. The interior of the gallbladder was washed and cleaned thoroughly and carefully. The surface of the gallbladder was dried with blotting paper. Then it was weighed by means of an analytical balance (Mega digital scale, made

in china) expressed in grams. Length of the gallbladder was measured from the neck of the gallbladder to the maximum convexity of the fundus using a thread and imposed it on a measuring scale expressed in centimeter. The breadth was measured at its maximum width in the body of the gallbladder using a thread and imposed it on a measuring scale expressed in centimeter. As the gallbladder was irregular in its shape, therefore, three readings were taken for each parameter and the average value was taken and recorded. After cutting from one edge the inner wall of the gallbladder was exposed and washed and cleaned thoroughly and carefully, then the thickness of the gallbladder i.e. wall thickness was measured at three points by using slide calipers expressed in millimeter and the average value was taken and recorded. The length of the cystic duct was measured from neck of the gallbladder to the junction of its to common hepatic duct by using a thread and imposed it on a measuring scale and the value was expressed in centimeter. The diameter of the cystic duct was measured by using a slide calipers and the value was expressed in millimeter.

Data were processed manually and analyzed with the help of SPSS (Statistical package for social sciences) Version 21.0. Quantitative data were expressed as mean and standard deviation; and comparison was done by unpaired t test between two groups and ANOVA test among three groups. A probability value (p) of less than 0.05 was considered statistical significant.

Prior to the commencement of the study, approval of the research protocol was obtained from the Ethical Committee of Sylhet M.A.G Osmani medical college, Sylhet.

Observations and Results

A total of 50 human postmortem gallbladders were studied in the present work. All the specimens were examined to detect the morphology of gallbladder, but only 18 specimens examined histologically. The outcome of the study was as follows:

Distribution of age of the cadaver

The age of the cadaver ranged from 11 to 55 years with the mean age of 35.02 (SD ± 19.98) years. Distribution of the cadaver by age group was shown in figure 1.

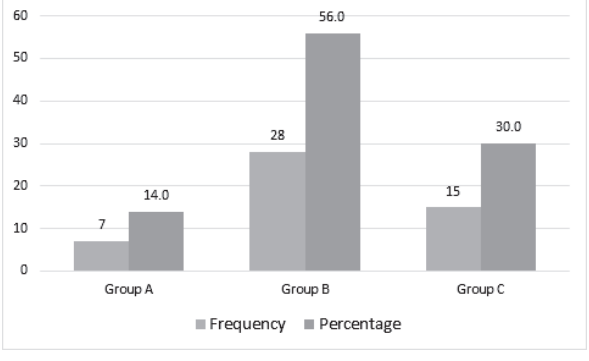

Figure-1: Distribution of the cadaver by age group (n=50)

In this study age Group-A (11-20 years) constituted 7 (14.0%) cases, age Group-B (21-40 years) constituted 28 (56.0%) cases and age Group-C (41-55 years) constituted 15 (30.0%) cases.

Distribution of the cadaver by sex

There were 29 (58.0%) male and 21 (42.0%) female with a ratio of male to female was 1.38:1. Distribution of the cadaver by sex was shown in figure 2.

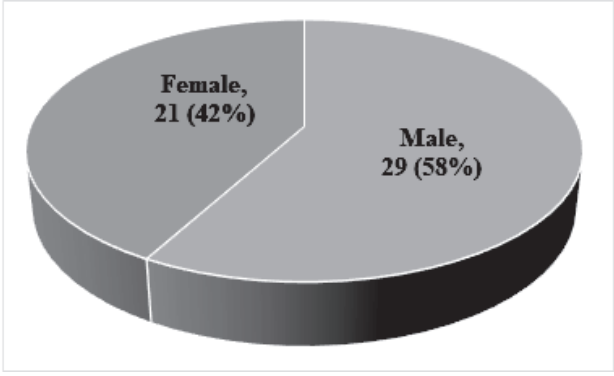

Figure-2: Distribution of the cadaver by sex (n=50)

Distribution of the parameters of gallbladder by different age group

The mean length of the gallbladder was 7.07 ± 0.55 cm in the age group of 11 to 20 years; 8.00 ± 0.88 cm in the age group of 21 to 40 years and 8.57 ± 1.05 cm in the age group of 41 to 55 years. The difference among the groups was statistically significant (F=6.622; p=0.003).

The mean weight of the gallbladder was 4.58 ± 1.39 gm in the age group of 11 to 20 years; 6.26 ± 2.12 gm in the age group of 21 to 40 years and 6.98 ± 2.51 gm in the age group of 41 to 55 years. The difference among the groups was statistically not significant (F=2.920; p=0.064).

The mean breadth of the gallbladder was 2.90 ± 0.45 cm in the age group of 11 to 20 years; 3.07 ± 0.43 cm in the age group of 21 to 40 years and 3.19 ± 0.44 cm in the age group of 41 to 55 years. The difference among the groups was statistically not significant (F=1.112; p=0.338).

The mean thickness of the gallbladder wall was 1.33 ± 0.16 mm in the age group of 11 to 20 years; 1.61 ± 0.14 mm in the age group of 21 to 40 years and 2.25 ± 0.35 mm in the age group of 41 to 55 years. The difference among the groups was statistically significant (F=52.845; p=0.0001).

Table I: Distribution of the parameters of cystic duct by different age group

Parameters of gallbladder	Total	Group-A (n=7)	Group-B (n=28)	Group-C (n=15)	p-value
Length (cm)	8.04±1.00	7.07±0.55	8.00±0.88	8.57±1.05	
	(6.5-10.5)	(6.5-8.0)	(7.0-10.0)	(7.0-10.5)	0.003
Weight (gm)	6.24±2.25	4.58±1.39	6.26±2.12	6.98±2.51	
	(2.0-9.88)	(2.80-6.76)	(2.40-9.23)	(2.00-9.88)	0.064
Breadth (cm)	3.08±0.48	2.90±0.45	3.07±0.43	3.19±0.44	
	(2.5-4.0)	(2.50-3.50)	(2.50-4.00)	(2.50-3.80)	0.338

Parameters of gallbladder	Total	Group-A (n=7)	Group-B (n=28)	Group-C (n=15)	p-value
Thickness of wall (mm)	1.76±0.40 (1.1-2.9)	1.33±0.16 (1.10-1.60)	1.61±0.15 (1.40-1.90)	2.25±0.35 (1.70-2.90)	0.0001

ANOVA test was done

Distribution of the parameters of cystic duct by different age group

The mean length of the cystic duct was 2.57 ± 0.31 cm in the age group of 11 to 20 years, 2.74 ± 0.21 cm in the age group of 21 to 40 years and 3.02 ± 0.22 cm in the age group of 41 to 55 years. The difference among the groups was statistically significant (F=11.178; p=0.001).

The mean diameter of the cystic duct was 2.54 ± 0.17 mm in the age group of 11 to 20 years; 3.12 ± 0.45 mm in the age group of 21 to 40 years and 3.22 ± 0.27 mm in the age group of 41 to 55 years. The difference among the groups was statistically significant (F=8.277; p=0.001).

Table II: Distribution of the parameters of cystic duct by different age group

Parameters of gallbladder	Total	Group-A (n=7)	Group-B (n=28)	Group-C (n=15)	p-value
Length (cm)	2.80±0.27 (2.0-3.5)	2.57±0.31 (2.00-2.90)	2.74±0.21 (2.30-3.20)	3.02±0.22 (2.70-3.50)	0.0001
Diameter (mm)	3.07±0.43 (2.1-3.8)	2.54±0.17 (2.30-2.80)	3.12±0.45 (2.10-3.80)	3.22±0.27 (2.80-3.60)	0.001

Discussion:

In this study the age of the cadaver ranged from 11 to 55 years with the mean age of (35.02 ± 19.98) years. In this regards Rahman and Anwar[5] found that age of the cadaver ranged from 20 to 65 years. Difference was may be due to inclusion of younger age in the present study.

This study also showed that age Group-A (11-20 years) constituted 7 (14.0%) cases, age Group-B (21-40 years) constituted 28 (56.0%) cases and age Group-C (41-55 years) constituted 15 (30.0%) cases. Similar findings were observed in the study of Nahar et al[10]. In the current study there were 29 (58.0%) male and 21 (42.0%) female with a ratio of male to female was 1.38:1. Nahar[11] also included similar sex distribution of cadavers that 39 (55.7%) male and 31 (44.3%) female cadaver with a ratio of male to female was 1.26:1 in her study.

In this study the length of the gallbladder ranged from 6.5 to 10.5 cm with the mean 8.04 ± 1.00 cm. This result was correlated with several other studies[12,13,14]. All these studies, the length of the gall bladder was 7 to 10 cm. Rahman et al.[15] found that the average length of the gall bladder was 6-7cm. In this study the mean length of the gallbladder was 7.07 ± 0.55 cm in the age group of 11 to 20 years; 8.00 ± 0.88 cm in the age group of 21 to 40 years and 8.57 ± 1.05 cm in the age group of 41 to 55 years. The difference among the groups was statistically significant (p=0.003). Nahar[11], found that the mean length of the gallbladder in male and female between group A and B (p<0.05) and group A and (p<0.01) were statistically significant.

In the present study the weight of the gallbladder ranged from 2.0 to 9.88 gm with the mean 6.24 ± 2.25 gm. This result was consistent with the study of Nahar[11] where the mean weight of the gallbladder was 6.37± 0.29 gm in male and 6.26 ± 0.03 gm in female in the age group of 10-20 years. The mean weight of the gallbladder was 4.58 ± 1.39 gm in the age group of 11 to 20 years; 6.26 ± 2.12 gm in the age group of 21 to 40 years and 6.98 ± 2.51 gm in the age group of 41 to 55 years. The difference among the groups was statistically not significant (p=0.064). This result was correlated with the study of Nahar[11], that the mean weight of the gallbladder in male and female among the groups was statistically not significant (p>0.05).

In the current study the breadth of the gallbladder ranged from 2.50 to 4.00 cm with the mean 3.08 ± 0.48 cm. Rahman et al.[15] found that the average breadth of the gall bladder was 2cm. Vakili and Pomfret[16] reported that the breadth of the gall bladder was 4 cm. Turner et al.[11] reported that the breadth of the gall bladder was 3-5 cm. Chari and Shah[13] found that the breadth of the gall bladder was 2-5 cm. In the present study the mean breadth of the gallbladder was 2.90 ± 0.45 cm in the age group of 11 to 20 years; 3.07 ± 0.43 cm in the age group of 21 to 40 years and 3.19 ± 0.44 cm in the age group of 41 to 55 years. The difference among the groups was statistically not significant (p=0.338). This result was supported by Nahar[11], that the mean breadth of the gallbladder of male and female was not statistically significant in any age group (p>0.50).

This study showed that the thickness of the gallbladder wall ranged from 1.10 to 2.90 mm with the mean 1.76 ± 0.40 mm. Majeski[17], found that the thickness of the adult gallbladder wall was 3mm. This finding is slightly higher than the present study. This variation is probably due to difference in geographical distribution and racial variation. In the current study the mean thickness of the gallbladder wall was 1.33 ± 0.16 mm in the age group of 11 to 20 years; 1.61 ± 0.14 mm in the age group of 21 to 40 years and 2.25 ± 0.35 mm in the age group of 41 to 55 years. The difference among the groups was statistically significant (p<0.001). Nahar[11], found that the difference in mean thickness of the gallbladder wall in male between group A and C (p<0.01) and group B and C (p<0.05) were statistically significant which correlated with the present study. Khan et al., (2012) found that the thickness of the gallbladder wall was 1.47+0.06 mm in group A (10-20 years), 1.57 ± 0.05 mm in group B (21-40 years) and 1.61 ± 0.04 mm in group C (41-70 years).

In this study the length of the cystic duct ranged from 2.00 to 3.50 cm with the mean 2.80 ± 0.27 cm. In this regards Standring[1], found the length of the cystic duct was 3-4 cm. Limthanakhom et al.[18] found that the mean length of the cystic duct was 1.42 cm. According to Sinnatamby[19], the length of the cystic duct is 2-3 cm and according to Moore et al. [14], the length of the cystic duct is 3-4 cm. In this study the mean length of the cystic duct was 2.57 ± 0.31 cm in the age group of 11 to 20

years; 2.74 ± 0.21 cm in the age group of 21 to 40 years and 3.02 ± 0.22 cm in the age group of 41 to 55 years. The difference among the groups was statistically significant (p=0.001). In this regards Nahar et al.[10] found that the mean length of the cystic duct between male and female was not statistically significant in any age group (p >0.50).

The diameter of the cystic duct ranged from 2.10 to 3.80 mm with the mean 3.07 ± 0.43 mm. This result was correlated with the study of Sinnatamby[19], where the diameter of the cystic duct was 2-3 mm. Nahar[11] found that the mean diameter of the cystic duct in male and female were 2.07 ± 0.56 mm and 2.20 ± 0.64 mm respectively in group B (21-40 year); and 2.73 ± 0.59 mm and 2.95 ± 0.60 mm respectively in group C (41-55 year). In the present study the mean diameter of the cystic duct was 2.54 ± 0.17 mm in the age group of 11 to 20 years; 3.12 ± 0.45 mm in the age group of 21 to 40 years and 3.22 ± 0.27 mm in the age group of 41 to 55 years. The difference among the groups was statistically significant (p=0.001). The difference in mean diameter of the cystic duct in male and female was statistically significant in between group A and C and group B and C (p <0.01) reported in the study of Nahar et al.[10].

Conclusion:

The length and thickness of the gallbladder, the length and diameter of the cystic duct were varied with age; but no variation in weight and breadth.

Conflict of Interests: None.

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ORIGINAL ARTICLE OPEN ACCESS

Pattern of Pesticide and Herbicide Poisoning Among People Admitted to Medicine Wards of a Tertiary Care Hospital

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Abstract

Introduction:*Acute poisoning has become a major public health problem accounting for significant morbidity and mortality around the globe[2]. According to WHO data, an estimated 193,460 people died worldwide in 2012 from unintentional acute poisoning. 84% of these deaths occurred in resource-lacking low- and middle income countries[3]. The toxicity of accessible poisons and the scarcity of adequate medical facilities for poisoning management is responsible for a such a high mortality rate in this region[4]. Acute pesticide poisoning usually occurs during agricultural use either by accidental exposure or by suicidal attempt, rarely as homicidal[2,5&8]. This study is designed to assess the patterns of pesticide & herbicide poisoning among rural & urban peoples admitted to medicine ward of a tertiary level hospital and to find out the sociodemographic characteristics of the respondents. So that the supply of these agents be properly regulated to prevent easy accessibility and misuse.* ***Materials and Methods:*** It was a hospital based cross-sectional observational study conducted at indoor Department of Medicine, Chittagong Medical College Hospital for six months period from 01/01/2019 to 31/06/2019. Ethical clearance was taken from ethical review committee of Chittagong Medical College and informed consent was obtained from each participants. Hundred patients above 12 years of age with a relevant history and clinical signs and symptoms of any type of pesticides and herbicides poisoning who fulfilled the selection criteria were selected consecutively for the study. Data was collected using a pretested, multi-structured questionnaire which comprised of questions to identify demographic data, type and circumstances of poisoning. ***Results:****Regarding motive of poisoning in our study 81% patient took pesticide & herbicide poisoning for suicide and 19% admitted with accidental case. This result is consistent with the study where most common reason of pesticide & herbicide poisoning was suicide (93.3%) [20]. A study performed at Rajshahi Medical College from January 1991 to December 1994 showed that out of those 405 cases of OPC poisoning 310 were suicidal (76.54%) and 95 were homicidal (23.45%) poisoning[28]. The present study revealed that factors responsible for the suicidal attempt were familial disharmony in 46% of cases, marital problems in 19%, financial problem in 16%, mental disorder in 3% and 11% due to other reasons. Shadequl-Islam et al. reported the motive of pesticide poisoning in their study that 45% of cases were due to familial disharmony, 15% unknown, 13.3% depression, 8.3% marital problems, 5% financial problems and 13.3% due to other reasons[26]. In most cases, the patient could access to the poison by self-purchasing from poison retailers.* ***Conclusion:*** *This study has indicated that young adults, males and socially underprivileged people are at a higher risk of pesticides and herbicides poisoning. This study showed pesticides & herbicides poisoning is the most common modes of suicidal deaths. Pesticides are mostly misused purposefully as an easy means for committing suicide. Early diagnosis and treatment is mandatory in order to minimize mortality from these potentially lethal compounds. It is recommended that the supply of pesticides be properly regulated to prevent easy accessibility and misuse.*

Key words: Pattern, Pesticide, Herbicide, Poisoning.

Number of Tables: 05; Number of References: 28; Number of Correspondences: 04.

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Introduction:

Death is the inevitable outcome of human life but unnatura[1] deaths whether suicidal, accidental or homicidal, causes a terrible waste of valuable human life and resources[1]. Acute poisoning has become a major public health problem accounting for significant

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morbidity and mortality around the globe[2]. According to WHO data, an estimated 193,460 people died worldwide in 2012 from unintentional acute poisoning. 84% of these deaths occurred in resource-lacking low- and middle-income countries[3]. Mortality due to self-poisoning is very low (0.5%-1%) in most industrialized countries while in the developing world, the rate is high (10%-20%). The toxicity of accessible poisons and the scarcity of adequate medical facilities for poisoning management is responsible for a such a high mortality rate in this region[4]. This is reflected by the fact that acute poisoning by various modalities, amount to a massive 300,000 deaths each year in the Asia Pacific region5. Much of this burden is borne by developing countries where more than 80% of cases are fatal pesticide poisoning related hospitalization[3]. Bangladesh is a developing tropical country in the South East Asia having seventy percent of its population dependent on agriculture directly or indirectly. In Bangladesh poisoning is an important health problem causing around 2000 deaths per year[7]. Acute pesticide poisoning usually occurs during agricultural use either by accidental exposure or by suicidal attempt, rarely as homicidal[2,5&8]. Pesticides are very easily available here having been used in agriculture, industries and for domestic purposes;[8] but these are extensively used in the agricultural field for the better outcome of cultivation[9]. But due to lack of training facilities to farmers, they spray excessive amount of harmful chemicals without taking any protective measures[10]. The consequences of the overuse of insecticides lead to ecological imbalance and environmental pollution. The poisoning agents differ regionally depending on easy availability of poisons, socio-economic condition status, educational level, awareness of our people. In tropical countries organophosphorus compounds are the commonly used agent[6].There is also increasing use of herbicides in agriculture for weeding control. Though most of the herbicides are less toxic but some are highly toxic (e.g. Paraquat). This study is designed to assess the patterns of pesticide & herbicide poisoning among rural & urban peoples admitted to medicine ward of a tertiary level hospital and to find out the socio-demographic characteristics of the respondents. So that the supply of these agents be properly regulated to prevent easy accessibility and misuse.

Materials and Methods:

It was a hospital based cross-sectional observational study conducted at indoor Department of Medicine, Chittagong Medical College Hospital for six months period from 01/01/2019 to 31/06/2019. Ethical clearance was taken from ethical review committee of Chittagong Medical College and informed consent was obtained from each participants. Hundred patients above 12 years of age with a relevant history and clinical signs and symptoms of any type of pesticides and herbicides poisoning who fulfilled the selection criteria were selected consecutively for the study. If pesticide poisoning is doubtful and patient not willing to participate are excluded from the study. Data was collected using a pretested, multi-structured questionnaire which comprised of questions to identify demographic data, type and circumstances of poisoning. Data was recorded, collected, organized and analyzed according to prescribed proforma.

Procedure of data analysis:

After collection of all the data, these were checked, verified for consistency and tabulated using the SPSS/PC 21 software. Statistical significance is set as 95% confidence level at 5% acceptable error level. Data were presented as proportion for discrete variables and as means±SD and/or medians with interquartile ranges for continuous variables. Differences in baseline characteristics was compared using both the student t-test and the Pearson chi square test. A p value of <0.05 was considered significant.

Ethical Implication:

Patients (subjects) and key relatives were clearly informed about the scope and limitations of the study. Informed written consent was obtained from the patients (subjects). Confidentiality of the patients (subjects) about personal information was strictly maintained. The study did no hazard to environment.

Result:

Table I: Demographic characteristics of the study subjects (n=100)

Age	Number	Percentage (%)
10-19 years	29	29.0
20-29 years	36	36.0
30-39 years	23	23.0
40-49 years	6	6.0
≥50 years	6	6.0
Sex		
Male	68	68.0
Female	32	32.0
Place of residence		
Urban	36	36.0
Rural	64	64.0
Occupation		
Govt. Employee	11	11.0
Non govt. employee	9	9.0
Business	17	17.0
House wife	26	26.0
Unemployed	28	28.0
Others	21	21.0

Age	Number	Percentage (%)
Educational qualification		
Illiterate	36	36.0
Below SSC	27	27.0
SSC	22	22.0
HSC	11	11.0
Graduate and above	4	4.0
Marital status		
Unmarried	33	31.0
Married	58	58.0
Separated	5	5.0
Divorced	2	2.0
Widow	1	1.0
Monthly family income		
<10000 taka	47	47.0
10000 to 20000 taka	34	34.0
20000-40000 taka	18	18.0
>40000 taka	12	12.

Most of the patients 36% were between 20-29 years followed by 29% from 10-19 years and 23% belongs to age group 30-39 years. Among these, 68% were male and 32% were female patients. Maximum number of poisoning patients was from rural area. Most of the patients were un employed and housewife. Majority of the patients are illiterate and below SSC level. Out of 100 patients 76% had monthly family income less than 10000 taka.

Table II: Patient status when coming to the hospital (n=100).

	Frequency	Percent
Conscious	82	82.0
Unconscious	18	18.0
Total	100	100.0

Most of patients 82% were conscious and 18% were unconscious.

Table III: Type of pesticide use (n=100).

	Frequency	Percent
Pesticides	89	89.0
Herbicides	11	11.0
Total	100	100.0

In majority of cases 89% were poisoning with pesticides and 11% were herbicides.

Table IV: Pattern of pesticide poisoning

	Frequency	Percent
Suicidal	81	81.0
Accidental	19	19.0
Total	100	100.0

Majority (81%) cases of poisoning were suicidal and 19% were accidental poisoning.

Table V: Factors responsible for this suicidal attempt (n=100)

	Frequency	Percent
Family disharmony	46	46.0
Marital disharmony	19	19.0
Unknown	5	5.0
Mental disorder	3	13.0
Financial problem	16	16.0
Others	11	11.0
Total	100	100.0

In majority of cases 46% were due to familial disharmony followed by marital problems and financial problems in 19%, 16% respectively.

Discussion:

Pesticide & herbicide poisoning is a common method of suicide attempt and less commonly accidental poisoning in Bangladesh. This study reflects that young peoples from 10 to 39 years are commonly affected 88% by pesticide & herbicide poisoning. Cha et al. reported 76% of OPC was 11-30 years of age group[13]. Sarkar in Rangpur Medical College Hospital also reported similar result. So this study is consistent with findings of other study carried out in Bangladesh[5]. Gyenwali et al. reported that the age of the patients with poisoning varied from 20 to 70 years with 65% of them between 21-30 age group and 58% belonged to lower socioeconomic status[12]. Among the studied patients, 68% were male and 32% were female. Male to female ratio is 2.1:1. Dewan et al. showed male to female ratio in pesticide & herbicide poisoning is 1.6:1[14]. Cha et al. showed male to female ratio 2.21:1[13]. Yadav et al. reported male to female ratio is 3.3:1[19]. So this study shows increasing trend of pesticide & herbicide poisoning in male and is consistent with other study.

This study shows majority (66%) were from rural area and (34%) from urban residence. This findings are in well contract with the findings of the other research works (Cha et al. also Nabih et al.)[13 & 17]. Pesticide poisoning rates were higher in rural areas, agricultural workers, and unemployed individuals and is the most common method of self-harm resulting in death in Sri Lanka[20] Taiwan[21] and China[22]. Numerous aspects of rural life, such as socioeconomic disadvantages, limited availability of and access to emergency medical services may contribute to the elevated rates of suicide in rural areas[23,24]. The present study showed majority of patients (58%) were unmarried. Marital status was reported in two studies and showed that most of the patients were unmarried (56.4%) [11,17]. Our study revealed Pesticide & herbicide poisoning was common among unemployed and housewife group 28% and 26% respectively. This findings consistent with Dewan et al.[12] Another study showed, 47% of patients were farmer, 16% student and 13% housewife[25]. Illiteracy observed in 36% cases in our study which is similar to other study[26].

In this study shows 89% were pesticides and 11% were herbicides. Previous studies showed that OPCs are the most common pesticides used for poisoning (89.8%). However, the reported frequencies ranged from 12% to 100% in different series[9,11,12,27]. Twelve-year statistics of national forensic science

laboratory of Nepal showed that among 1016 poisoning cases, the poisons used by 34% of cases were insecticides and by 4% of cases were rodenticides[18]. Among insecticides, OPCs were used by 71% of cases, pyrethroids by 13%, mixed insecticides (OPC + Pyrethroid) by 7%, carbamates by 5% and OCCs by 4%[11]. In Mysore (South India) pesticides were responsible for 39.5% of poisoning cases and frequency of different pesticides were OPCs in 71%, rodenticides in 13%, pyrethroids in 7%, carbamates in 6.5% and OCCs in 2.5% of cases[27]. Frequency of carbamate and rodenticides used in Bangladesh were almost identical with Nepal but that of OPC and pyrethroids were noticeably different from what in India and Nepal (~70%) as the rate of use of OPCs in Bangladesh is about 90% and for pyrethroids is less than 1%[18].Therefore, the findings of the study are in well agreement with the findings of the other research works (Cha et al. and Nabih et al. Yadav et al.) [13,17, 19]. Regarding motive of poisoning in our study 81% patient took pesticide & herbicide poisoning for suicide and 19% admitted with accidental case. This result is consistent with the study where most common reason of pesticide & herbicide poisoning was suicide (93.3%)[20]. A study performed at Rajshahi Medical College from January 1991 to December 1994 showed that out of those 405 cases of OPC poisoning 310 were suicidal (76.54%) and 95 were homicidal (23.45%) poisoning[28].

The present study revealed that factors responsible for the suicidal attempt were familial disharmony in 46% of cases, marital problems in 19%, financial problem in 16%, mental disorder in 3% and 11% due to other reasons. Shadequl-Islam et al. reported the motive of pesticide poisoning in their study that 45% of cases were due to familial disharmony, 15% unknown, 13.3% depression, 8.3% marital problems, 5% financial problems and 13.3% due to other reasons[26]. In most cases, the patient could access to the poison by self-purchasing from poison retailers.

Conclusion:

This study has indicated that young adults, males and socially underprivileged people are at a higher risk of pesticides and herbicides poisoning. This study showed pesticides & herbicides poisoning is the most common modes of suicidal deaths. Pesticides are mostly misused purposefully as an easy means for committing suicide. Early diagnosis and treatment is mandatory in order to minimize mortality from these potentially lethal compounds. It is recommended that the supply of pesticides be properly regulated to prevent easy accessibility and misuse.

Conflict of Interest: None.

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The Principal Investigator, Dr. Mohammad Abu Naser Siddique, oversaw all activities related to the conduct of the study and contributed to the study idea, discussion, and writing of the manuscript. Dr. Ummay Fatema Khatun contributed to the data collection. Dr. Imran Uddin Robel contributed to the literature review .We are very much grateful to Prfessor Dr. Md. Abdus Sattar, Head of the Department of Medicine, Chittagong Medical College for his guidance. We are also grateful to all indoor medical officers and assistant registrars of Medicine for their help in collecting data. All authors accepted the final version. All authors read and approved the final manuscript.

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ORIGINAL ARTICLE OPEN ACCESS

Bleeding Time and Clotting Time in Pre-eclampsia, Eclampsia and Normal Pregnancy

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Abstract

Introduction: *The most important cause of maternal and perinatal morbidity and mortality are hypertensive disorder (Preeclampsia and eclampsia). In preeclampsia and eclampsia there is hypercoagulable state which acts as a risk factor for thromboembolism and DIC.* ***Objective:*** *This study was carried out to compare the coagulation indices in normal pregnancy, preeclampsia and eclampsia.* ***Materials and Methods:*** *This cross sectional study was conducted in Dhaka Medical College from January to December' 2014 . Total 150 women aged 18 – 40 years were selected for this study. Among them 50 normal pregnant, 50 preeclamptic and 50 eclamptic women were selected as study group and age matched 50 healthy nonpregnant women were considered as control group. Bleeding time was estimated by Duke's method and clotting time was estimated by capillary tube method.* ***Results:*** *In this study bleeding time and clotting time were significantly higher in preeclamptic and eclamptic women than those of healthy nonpregnant women.* ***Conclusion:*** *From this study it can be concluded that bleeding time and clotting time are closely related with preeclampsia and eclampsia.*

Keywords: *Preeclampsia, platelet count, bleeding time, clotting time.*

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Introduction:

Preeclampsia is a pregnancy specific, idiopathic multisystem disorder characterized by the development of hypertension and proteinuria after the 20 weeks of gestation[1,2]. Worldwide, the incidence of preeclampsia ranges between 2-10% of pregnancies[3]. Preeclampsia when associated with convulsion known as eclampsia[3]. Eclampsia is clinically characterized by a chronic, gradual process that begins with the development of preeclampsia and results in generalized convulsions or coma. But, in approximately 15-20% of cases, the onset of eclampsia may be abrupt without previous evidence of preeclampsia[2]. Overall 10-15% of direct maternal mortality is associated with preeclampsia and eclampsia[4]. Preeclampsia creates a functional derangement of multiple organ system. Complications of preeclampsia include eclampsia, placental abruption, ascities, hepatic infarction and rupture, intra-abdominal bleeding, pulmonary edema and acute renal failure. Complications affecting the developing fetus include intrauterine growth retardation, prematurity, oligohydramnios, bronchopulmonary dysplasia and increased risk of perinatal death[2]. Pre-eclampsia is an important obstetric problem and is associated with a five-fold increase in perinatal mortality[5]. During normal pregnancy profound changes occur in the coagulation and fibrinolytic system of the mother causing a hypercoagulable state which accentuate in preeclampsia[6]. Coagulation abnormalities such as thrombocytopenia and decrease in some plasma clotting factors may develop in preeclampsia[7]. Coagulation abnormalities may cause life threatening condition like disseminated intravascular coagulation (DIC) and HELLP syndrome. Monitoring of coagulation parameters may help to overcome these complications[7]. Numerous studies observed coagulation abnormalities in preeclampsia and eclampsia. The level of anticoagulants such as antithrombin III,

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protein C and protein S are decreased in these groups. The clotting factors such as factor VIII and von Willebrand factors are elevated in preeclampsia and eclampsia. There is also increase in plasminogen activator inhibitor type 1(PAI-1) in preeclampsia. So preeclampsia is a highly thrombotic and procoagulant state[1]. Measurement of prothrombin time (PT), activated partial thromboplastin time (APTT), bleeding time (BT) and clotting time (CT) are the most commonly used laboratory tests in patients with a suspected abnormal coagulation.Several studies showed increase in BT and CT in severe preeclampsia and eclampsia[6,9]. Jambhulkar et al. (2001) performed a cross sectional study on 50 severe preeclamptic and 30 eclamptic patients and found normal BT and CT in these patients[8]. From the above studies, it has been revealed that increase bleeding time (BT) and clotting time (CT) act as a future risk for complications in preeclampsia and eclampsia. Several studies have done abroad to observe these parameters in these groups but their exact relationship with preeclampsia and eclampsia still debatable. As, there is less published data available regarding this topic in our country, the relationship among this parameter in the Bangladeshi preeclamptic and eclamptic is not precisely known. Furthermore, we need a data from which we can compare these parameters in our population.

Materials & Methods:

The present cross sectional analytic study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from January to December' 2014 . For this study, 150 women were selected as group B (50 normal pregnant women, 50 diagnosed preeclamptic women and 50 diagnosed eclamptic women) aged 18 to 40 years were selected as group B. Age matched 50 healthy nonpregnant women were considered as control group (group-A) for comparison. The subjects were selected from department of Obstetrics and Gynaecology, Dhaka Medical College Hospital and from personal contact in different areas of Dhaka city by simple random sampling. After selection the nature, purpose, benefit and risks of the study were explained in details. Informed written consent was taken from the participants. Before taking blood detailed family and medical history were taken and recorded in a prefixed data schedule. Bleeding time (BT) was estimated by Duke's method & clotting time (CT) was estimated by capillary tube method. In addition BMI was calculated and blood pressure was measured. Presence of proteinuria was determined by conventional heat coagulation test. Then interpretation of the heat coagulation test was done according to presence of turbidity in the urine as nil/trace (0), 1+, 2+, 3+ and 4+[16]. For statistical analysis one-way ANOVA test, Bonferroni test and Pearson's correlation co-efficient (r) test were performed as applicable using SPSS for windows version 22.

Result:

The mean systolic (159.8±19.2 mmHg) and diastolic (110.0±9.9 mmHg) blood pressure were significantly higher in preeclampsia compared to healthy non pregnant women (SBP112.2±7.1mmHg, DBP 73.0±6.1mmHg). Again the mean urinary protein level was significantly higher (1.34±1.72)gm/dL in preeclampsia compared to healthy non pregnant women (Table I).

Table 1: General Characteristics of the Subjects in Different Groups (n=100).

Parameters	Healthy nonpregnan women (n=50)	Normal pregnant (n=50)	Patients with preeclampsia (n=50)	Patients with Eclampsia (n=50)
Age (years)	28.24±4.63	26.74±3.93	26.86±5.33	25.88±5.99
BMI (kg/m^2)	26.17±2.58	27.54±5.50	27.72±3.5	27.97±1.85
SBP (mmHg)	112.2±7.1	118.0±9.5	159.8±19.2	180.2±19.6
DBP (mmHg)	73.0±6.1	75.0±6.8	110.0±9.9	125.0±15.5
Urinary protein level (gm/dL)	-	.013±0.043	1.34±1.72	1.82±1.98

Results are expressed as Mean ±SD; Figures in parentheses indicate range; One-way ANOVA test was performed to compare among groups; n = Number of subjects; *p<0.001, compared to control; BMI= Body mass index; SBP= Systolic blood pressure; DBP= Diastolic blood pressure

Statistical analysis

Groups	SBP (mmHg) (p value)	DBP (mmHg) (p value)	Urinary protein (gm/L) (p value)
A vs B_1 vs B_2 vs B_3	<0.001^s	<0.001^s	<0.001^s

Results are expressed as Mean ±SD. Figures in parentheses indicate range. One-way ANOVA test was performed to compare among four groups. n = Number of subjects; s = Significant; ns = Not significant. The test of significance was calculated and p values < 0.05 was accepted as level of significance.

Bleeding time and clotting time were higher in preeclampsia than healthy non pregnant women and the result was significant (Table II**).**

Table II: Bleeding time & clotting time of the Subjects in Different Groups (n=50)

Parameters	Healthy nonpregnant (n=50)	Healthy pregnant (n=50)	Preeclampsia (n=50)	Eclampsia (n=50)
BT (min)	3.48±0.45	3.94±0.67	5.28±0.59	5.76±0.55
CT (min)	5.68±0.48	5.98±0.48	7.01.±0.70	7.44±0.75

Results are expressed as Mean ±SD. Figures in parentheses indicate range. One-way ANOVA test was performed to compare between groups. Bonferroni test was performed to compare between groups. n = Number of subjects; Group A: Healthy adult non pregnant women (Control group); Group B_2: Women with preeclampsia (Study group).

Statistical analysis

Groups	Bleeding Time (min) (p value)	Clotting Time (min) (p value)
A vs B_1 vs B_2 vs B_3	<0.001^s	<0.001^s

Results are expressed as Mean ±SD. Figures in parentheses indicate range. One-way ANOVA test was performed to compare among four groups. n = Number of subjects; s = Significant; ns = Not significant. The test of significance was calculated and p values < 0.05 was accepted as level of significance.

Moreover in this study, increased bleeding time (>6min) and clotting time (CT) (>10min) were found in different percentages of preeclamptic , eclamptic women and normal pregnancy (Table III)

Table III: Distribution of the subjects by bleeding time & clotting time in study groups (n=50)

Parameters		Normal pregnancy	Preeclampsia	Eclampsia
Bleeding time	1-6 min	37(74%)	23(46%)	18(36%)
	> 6 min	13(26%)	27(54%)	32(64%)
Clotting time	6-10 min	32(64%)	21(42%)	16(32%)
	> 10 min	18(36%)	29(58%)	34(68%)

Results are expressed as frequency and percentage. n = Number of subjects; Group A: Healthy adult non pregnant women (Control group); Group B: Women with preeclampsia (Study group)

Discussion:

Preeclampsia is a poorly understood condition of human pregnancy, which can affect multiple organs and is a leading cause of maternal mortality worldwide[1]. Its exact pathophysiology is not yet fully understood[2]. Out of all hematological changes that occur in preeclampsia thrombocytopenia is the most common and the degree of thrombocytopenia increases with the severity of disease[3]. Preeclampsia and maternal mortality might be reduced through serial monitoring of platelet count as a part of antenatal check-up. The main aim of this study is to detect levels of some coagulation indices like bleeding time and clotting time in preeclampsia. Aref, Mazny & Mazny (2012) found no statistically significant difference in coagulation profile in preeclamptic women than that of healthy nonpregnant female[10]. In the present study, mean BT was higher in preeclamptic women than that of healthy nonpregnant female and the result was statistically significant (P<0.001). Almost similar type of result was found by Chauhan et al. 2014 where mean BT was also higher in preeclamptic women but the result was not statistically significant6. Bleeding time also showed an increasing trend from normal control to severe preeclampsia patients but the result was within normal range by Tadu, yerroju and Gudey[11]. Again, mean BT & CT were in normal range in all group of patients of pregnancy induced hypertension but CT was significantly higher in eclampsia group than preeclampsia & gestational hypertension[12]. Sameer et al. 2011 and Anjali, Garkal & Pratibha 2013 found prolonged BT & CT in preeclamptic and eclamptic women but the result was not statistically significant[13,14]. In the present study, mean CT was significantly prolonged (p < 0.001) in preeclamptic women than that of healthy nonpregnant female and the result was significant (P<0.001). Prolonged CT was also found by Namita et. al. 2022 but the result was not statistically signinificant. However, Chauhan et al. 2014 found no significant changes in CT in preeclamptic women.

Conclusion:

From the result of this study, it may be concluded that BT & CT are increased in preeclampsia, eclampsia and normal pregnancy than that of healthy nonpregnant women. Therefore, measurement of these parameters may reflect the severity of preeclampsia, eclampsia and helps to provide appropriate treatment to ensure a satisfactory outcome for mother and fetus.

Conflict of Interest: None.

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ORIGINAL ARTICLE OPEN ACCESS

Comparative Study of Paramedian and Midline Incision in Laparotomy for Peritonitis due to Non-traumatic Gastro-intestinal Tract Perforation

Md Zillur Rahman *[1], Md Aziz Ullah[2], Sadia Rahman[3], Soma Rahman[4]

Abstract

Introduction: *A prospective observational study was conducted to compare the paramedian incision with midline incision in gastro-intestinal tract perforation.* ***Objectives:*** *To identify better or superior incision which may reduce post operative mortality and morbidity after laparotomy.* ***Materials and Methods:*** *A prospective observational Hospital based study was conducted from January 2009 to June 2009 at department surgery of Shaheed Ziaur Medical College Hospital, Bogura. A total 100 patients of peritonitis due to non-traumatic gastro-intestinal tract perforation were taken for study. Sample were collected by Convenience (purposive) sampling method. Midline incision and Para median incisions were performed as per standard technique. The details of operations, post-operative complications and follow up to be recorded and analyzed.* ***Results:*** *Opening time and closing time in midline incision is significantly less than paramedian (P <0.001). Incidence of wound infection and incidence of wound dehiscence in our study in midline group was less compared to paramedian group buy it is not significant. All forms of dehiscence ranging from superficial dehiscence to burst abdomen were included. Incidence of incisional hernia was significantly higher in midline incision (P<0.05). Healing time was significantly lower in midline compared to Paramedian group (P<0.05).*
Conclusion: *It is concluded that midline incision is preferred compared to paramedian incision. Incidence of wound dehiscence and wound infection is less in midline incision.*

Keywords: *Paramedian, Midline incision, Laparotomy.*

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Introduction:

Non traumatic gastro intestinal tract perforation is one of the most common surgical emergencies. Non-traumatic perforation of the small bowel is a serious complication associated with high morbidity and mortality. Diseases that cause small bowel perforation vary in different areas of the world[1]. The most common cause of non-traumatic perforation of small intestine was typhoid (46.4%), followed by non-specific inflammation (39.2%), tuberculosis (12.8%) and malignant neoplasm (1.6%). Primary repair was the most frequent procedure (44.0%), followed by ileostomy (25.5%) and resection-anastomosis (19.3%)[2]. Insight into the management of non-traumatic perforation of the small intestine[3]. Gastrointestinal perforations constitute one of the commonest surgical emergencies encountered by surgeons[4]. In spite of advances in perioperative care, antimicrobial therapy, and intensive care support, perforation peritonitis still has high morbidity and mortality[5]. The spectrum of etiology of perforation in tropical countries is different from its western counterpart. In contrast to western countries where lower gastro-intestinal tract perforations predominate, upper gastro intestinal tract perforations constitute the majority of cases in India[6]. Common causes of non-traumatic gastro intestinal tract perforations in our country are perforation of gastric ulcer, perforation of duodenal ulcer, perforation of vermiform appendix, typhoid ulcer, tubercular ulcer and malignant ulcer perforation etc. A large number of patients are

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admitted in our hospital almost every day with non-traumatic gastro intestinal tract perforations and almost all of them need surgical intervention. Laparotomies of these patients are done by midline incision and sometimes by paramedian incision especially for duodenal ulcer perforation and other non-traumatic gastro intestinal tract perforation. Shaheed Ziaur Rahman Medical College Hospital, Bogura is the tertiary level hospital. It is the affordable modern hospital for the large number of poor people in this region. A large number of patients are admitted every day in different general surgical wards. Many patients admit with non-traumatic gastro intestinal tract perforations in different surgical units almost every day. Most of them are treated with emergency laparotomy either by midline or paramedian incision. Some surgeons here always do laparotomy for peritonitis by midline incision but some go through paramedian incision commonly for perforation of duodenal ulcer and other non-traumatic gastro intestinal tract perforation. Among these two incisions, we observed difference in opening and closing time, arbitrary amount of bleeding, surgeon's compliance, wound infection wound dehiscence, healing time, scar strength and incisional hernia. In general observation, midline incision bleeds less, less time consuming to open and close and can be readily enlarged when necessary. As less tissue planes are opened, so incidence of wound infection and subsequent wound dehiscence and other complications are also less. Although comfortable to open and close and to enlarge but approach to lesion is difficult to some extent especially in perforation of duodenal ulcer and other non-traumatic gastro intestinal tract perforation. Someone also complains for formation of weaker scar in midline incision and increased chance of subsequent incisional hernia. By comparison, paramedian incision bleeds more, more time consuming to open and close and less comfortable to enlarge when necessary. As more tissue planes are opened incidence of wound infection and subsequent wound dehiscence and other complications are also more. Of course, approach to lesion is more comfortable in perforation of duodenal ulcer and other non-traumatic gastro intestinal tract perforation. Due to stronger scar and multiple layers of tissue support, incidence of incisional hernia also less. Subsequently patient's mortality and morbidity rate also vary. So better or superior incision in laparotomy for peritonitis due to non-traumatic intestinal perforation should be identified. This study is a prospective study of 100 cases between January 2009 to June 2009 in department of General Surgery of Shaheed Ziaur Rahman Medical College Hospital, Bogura. Cases will be selected randomly form patients of 15 to 50 years of age group, admitted with non-traumatic gastro-intestinal tract perforation and undergone laparotomy. All patients will be properly resuscitated preoperatively and will be provided with same antibiotic. Thorough peritoneal toileting will be done with normal saline and povidone iodine solution and drain will be given in all patients. Same suture material will be used for repair of perforation and wound closure. Post operative physiotherapy will be given to all patients. In this study we will compare midline incision and paramedian incision in laparotomy for peritonitis due to non-traumatic gastro-intestinal tract perforation in context of opening and closure time, arbitrary amount of bleeding, surgeon's compliance, healing time, rate of wound infection, incidence of incisional hernia and incidence of chest complications. So, overall better or superior incision will be identified which may reduce post operative mortality and morbidity after laparotomy for peritonitis due to non-traumatic gastro-intestinal tract perforation.

Materials and Methods:

This prospective observational study was conducted from January 2009 to June 2009 at department surgery of Shaheed Ziaur Medical College Hospital, Bogura. Sample were collected by Convenience (purposive) sampling method. Total 100 Patients of peritonitis due to non-traumatic gastro-intestinal tract perforation who has under gone laparotomy in Shaheed Ziaur Rahman Medical College Hospital, Bogura between 15 to 50 years of age were selected for the study. Exclusion criteria were – patients with comorbid diseases and patients with traumatic perforation. Data was collected in pre-organized data collection sheet from patients fulfilling inclusion exclusion criteria with informed written consent. All findings will be recorded in prescribed data collection sheet including clinical history, physical examination and pre operative findings. Patient is prepared with all investigations for anesthesia and operation. With informed written consent for operation, patient is operated under general anesthesia. Operation notes including indication, procedure per operative and, preoperative findings are recorded. All findings including post operative follow up and outcome recorded in predesigned data collection shit. All cases will be numbered chronologically. Statistical analyses were carried out by using the Statistical Package for Social Sciences version 23.0 for Windows. The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Clearance was taken from ethical clearance committee of CuMCH prior to the study. Confidentiality of the data was strictly maintained.

Observations & Results:

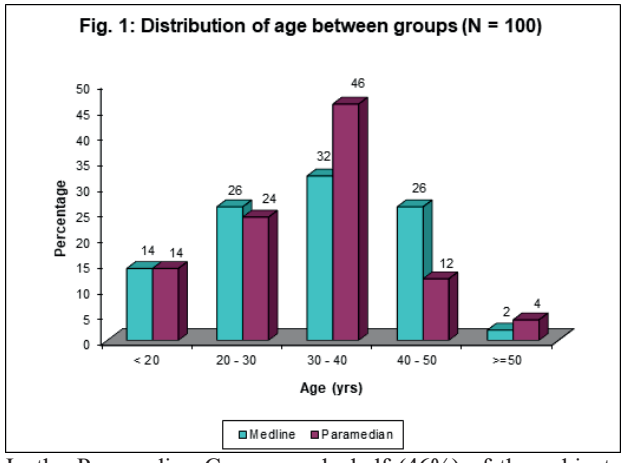
All the data were collected by a structured protocol. Result is summarized and analyzed by appropriate statistical methods. The result is then compared and discussed with the similar standard study in home and abroad. Finally, the study was concluded with specific findings, ideas and highlights. Out of total 100 patients selected for study, 50 were in Midline Group and 50 in Paramedian Group. The findings derived from data analysis are furnished below:

Table- I: Comparison of age between groups:

Age (years)	Group	
	Midline (n= 50)	Paramedian (n=50)
<20	7 (14.0) *	7 (14.0)
20-30	13 (26.0)	12 (24.0)
30-40	16 (32.0)	23 (46.0)
40-50	13 (26.0)	6 (12.0)
≥ 50	1 (2.0)	2 (4.0)
Mean ± SD	**32.38 ± 1.44**	**31.32 ± 1.41**
Range	15 - 50	15 - 50

* Values in the parentheses denote corresponding%

Table-I and Fig. I demonstrates that about one-third (32%) of the subjects in the Midline Group was between 30-40 years followed by 26% between 20-30 years, another 26% in the range 40-50 years and 14% below 20 years of age.



In the Paramedian Group nearly half (46%) of the subjects were in the 3rd decades of life, 26% were between 40 – 50 years, 24% between 20 – 30 years and 14% below 20 years of age. Very few subjects in both the groups were of 50 years and above. The lowest and highest ages in both Midline and Paramedian Groups were 15 and 50 years respectively. The mean ages of Midline and Paramedian Groups were 32.38 ± 1.44 and 30.56 ± 1.27 years respectively.

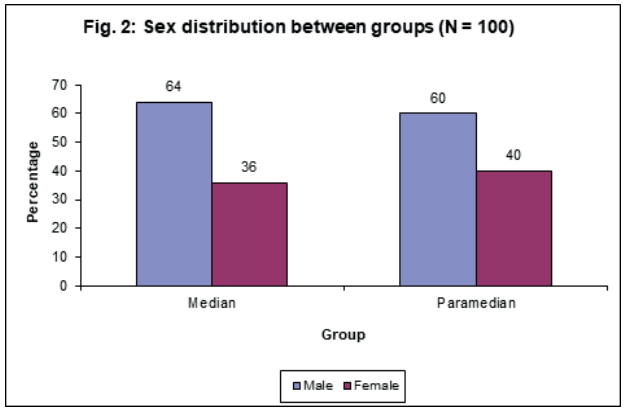


Table-II & Fig. 2 compare the distribution of sex between groups. In Midline Group 64% were males and in Paramedian Group 60% were males giving a male female ratio of roughly 3:2. The groups were almost identical with respect to sex.

Table- II: Showing comparison sex distribution between groups

Sex	Group	
	Midline (n= 50)	Paramedian (n=50)
Male	32(64.0)*	30(60.0)
Female	18(36.0)	20(40.0)

* Values in the parentheses denote corresponding %.

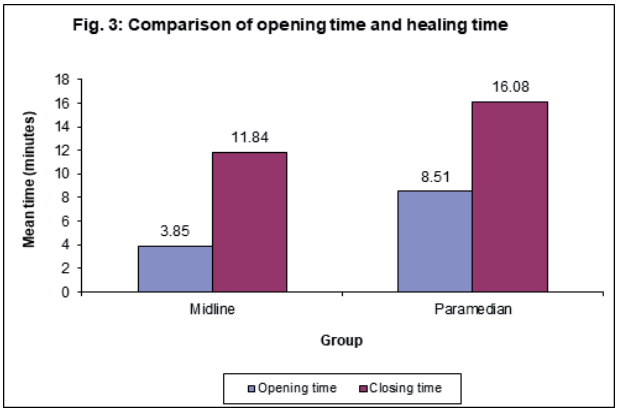


Table III demonstrates that both opening and closing time were significantly less in Midline Group compared to those in Paramedian Group (3.81 ± 1.01 vs. 8.51 ± 3.67 minutes, $p < 0.001$ and 11.84 ± 3.50 vs. 16.08 ± 3.37 minutes, $p < 0.001$ respectively).

Table-III: Comparison of opening and closing time between groups

Time	Group		p-value
	Midline (n= 50)	Paramedian (n=50)	
Opening time	3.81 ± 1.01	8.51 ± 3.67	<0.001
Closing time	11.84 ± 3.50	16.08 ± 3.37	<0.001

Data were analyzed using Student's t-test and were presented as mean ± SD.

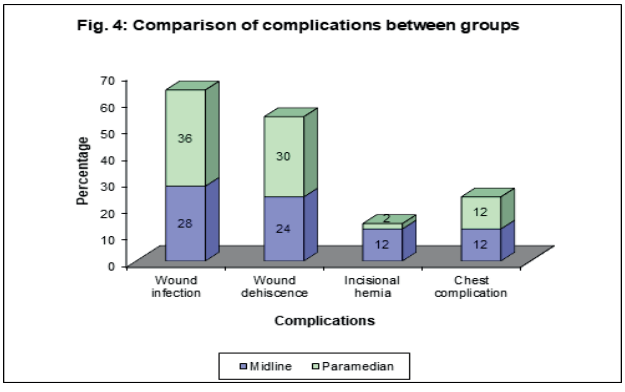


Fig. 4 & Table-IV show that incidence of incisional hernia was significantly higher in Midline Group (12%) than that in Paramedian Group (2%) ($p < 0.05$).

Table-IV: Comparison of complications between groups

Complications#	Group		p-value
	Midline (n= 50)	Paramedian (n=50)	
Wound infection	14(28.0) *	18(36.0)	0.260
Wound dehiscence	12(24.0)	15(30.0)	0.326
Incisional hernia	6(12.0)	1(2.0)	0.040S
Chest complication	6(12.0)	6(12.0)	0.620

* Values in the parentheses denote corresponding %.

All the variables, except incisional hernia, were analyzed using Chi-squared (x^2) Test and data were presented as n (%); the data of incisional hernia were analyzed with the help of Fisher's Exact Test. Level of significance was 0.05 and $p < 0.05$ was considered significant.

Incidence of wound infection and wound dehiscence are more in paramedian group.

Fig. 5 & Table V compares the outcome between groups. The healing time was observed to be significantly less in Midline Group than that in Paramedian Group (14.78 ± 1.10 vs. 18.16 ± 0.95 days, $p < 0.05$).

Fig. 5: Comparison healing time between groups

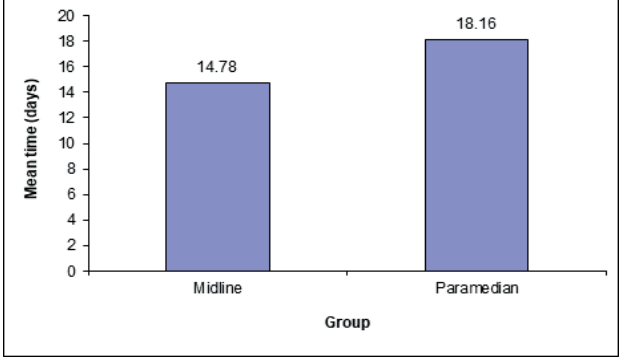


Table-V: Comparison of outcome between groups

Outcome	Group		p-value
	Midline (n= 50)	Paramedian (n=50)	
Healing time (days)	14.78 ± 1.10	18.16 ± 0.95	0.025

Data were analyzed using Student's t-test and were presented as mean ± SD.

Discussion:

Non traumatic gastro intestinal tract perforation is one of the most common causes of surgical emergency. A good number of patients are admitted almost every day in surgical wards with symptoms of acute abdomen. Almost all of them are treated by laparotomy either by midline or paramedian incision. Significant difference of outcome among these two incisions is observed. In this study, we compared 50 cases of midline group with 50 cases of paramedian group in terms of opening time, closing time, rate of wound infection, wound dehiscence, incisional hernia, chest complication, healing time, arbitrary amount of bleeding and surgeons' compliance. All patient had proper preoperative resuscitation, received same antibiotic (Ciprofloxacin + metronidazole), same suture materials was used in all case and thorough peritoneal toileting was done with normal saline plus Povidone iodine. Drain was given in all cases and all received post operative physiotherapy. Mean time taken for laparotomy or opening time in our study in midline incision was 3.81±1.01 minutes. This was close to findings of Keran SR, canolly EM[7] which was 4.37 minutes (7.5 second/cm^2). Mean opening time in paramedian group is 8.51 ± 3.67 minutes. Opening time in midline incision is significantly less than paramedian ($P < 0.001$). Mean time taken to close laparotomy wound or closing time in midline incision in our study is 11.84 ± 3.50 minutes and paramedian group that is 16.08 ± 3.37 minutes. Closing time were significantly less in midline group compared to paramedian group ($P < 0.001$). Incidence of wound infection in midline group was less (28%) compared to paramedian group 36% with P-0.260. Acta chir Sand[8]: Observed in 1980, 28.8% wound infection in dirty abdominal condition. According to Ann surg[9], rate of wound infection in dirty abdominal condition was 40%. Incidence of wound dehiscence in our study in midline group was 24% which is significantly less compared to paramedian group 30%, P-0.326. All forms of dehiscence ranging from superficial dehiscence to burst abdomen were included. Marwahs and Marwah N[10] observed 28% of incidence of wound dehiscence in midline laparotomy for peritonitis in a randomized clinical study of consecutive 50 cases. Talwars, Laddha BL[11], observed 37% wound dehiscence in paramedian laparotomy for typhoid Ulcer perforation. Incidence of incisional hernia in follow-up from after 2 months of operation to 1 year was 12% in midline group and 2% in paramedian group. Incidence of incisional hernia was significantly higher in midline incision ($P<0.05$). Ballon-Caneiro JM[12], observed 16% incidence of incisional hernia within 1-6 years in midline laparotomy. According to Br. J. surg[13], 0.37% incidence of incisional hernia in Para median laparotomy. According to JR Soc.med[14], Comparative study between midline and paramedian laparotomy reveals incidence of incisional hernia was 2 in midline and 20 in paramedian ($P<0.001$). Incidence of post-operative chest complication was similar in both groups (12%). Arbitrary amount of bleeding was more in paramedian incision than midline incision. Exact measurement of bleeding could not be done due to lac technical support in our hospital. Amount of bleeding was assessed arbitrarily from number of gauzes soaked and degree of soaking which was more in paramedian group than midline group. In observation by kerans SR, canolly EM[7] bleeding in laparotomy was

1.7ml/cm^2. Surgeon's compliance was better in paramedian group where approach to operation site was more comfortable than midline incision according to some surgeon. This difficulty was significantly over come by increasing length of incision for 2-3 cm, adequate muscle relaxation and good retraction. Healing time was assessed by post. Operative hospital stays. Mean post operative hospital stay in midline group was 14.78 ± 1.10 days and in Paramedian group that was 18.10 ± 0.95 days. Healing time was significantly lower in midline compared to Paramedian group ($P<0.05$). Talwars, Laddha BL[11], observed mean post operative hospital stay 16.8 days in typhoid ulcer perforation which is close to our observation. Increased post operative hospital stay in Paramedian group was due to increased incidence of wound infection and wound dehiscence and for subsequent management.

Conclusion:

It is concluded that midline incision is preferred compared to paramedian incision. Incidence of wound dehiscence and wound infection is less in midline incision. Per operative bleeding is also less. Regarding post operative hospital stay, paramedian incision observed longer hospital stay due to increased incidence of wound infection and wound dehiscence and for subsequent management.

Conflict of Interest: None.

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ORIGINAL ARTICLE OPEN ACCESS

Outcome of Myringoplasty with Temporal Fascia and With Sliced Tragal Cartilage Graft-A Comparative Study

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Abstract

Introduction: *Myringoplasty is the surgical procedure to repair tympanic membrane perforations and thereby improving hearing, providing a dry ear, and reducing susceptibility to infections. Although there are many kinds of techniques and graft materials used, no methods have proven indisputably superior to the other. Therefore, to find out the outcome of myringoplasty using temporal fascia and sliced tragal cartilage in chronic inactive mucosal otitis media was set as an objective of the study.* ***Materials and Methods:*** *This cross-sectional observational study was conducted at the department of Otolaryngology & Head-Neck surgery, Shaheed Suhrawardy Medical College Hospital (ShSMCH) for six months from July 2018 to December 2018, after acceptance of the protocol and approval from IRB. Patients attending in the ShSMCH with complaints of chronic inactive mucosal otitis media were approached for inclusion of the study and final selection were done in according to the selection criteria. Ethical issues were ensured properly throughout the study period and inclusion was confirmed following signing written informed consent. All patients were randomly allocated into two groups where one group were received myringoplasty with temporalis fascia graft and another group received sliced tragal cartilage. Total 50 patients (25 patients in each group) were included, and they were subjected to details history taking, physical examination and necessary investigations. The researcher conducted all the interview and collected data were recorded into a case record form for each patient. Data analysis was done by SPSS 17.* ***Results:*** *Of total, 50 study population, mean age of the 32.30±10.93 SD (years) with 58% male and 42% females respectively. No significant age and gender difference is noted across the group ($p>0.05$). Patients having temporal fascia graft had significantly higher proportion of graft uptake in comparison to patients having sliced tragal graft ($p<0.05$). Both groups of the patient improve significantly in term of hearing after operation ($p<0.05$ in each group) but comparison in between groups showed that the improvement was significantly higher in temporal fascia graft group ($p<0.001$).* ***Conclusion:*** *Myringoplasty with temporal fascia graft could be a better option than sliced tragal cartilage graft in our population. However, further larger study with longer follow up is necessary to finalize the comment.*

Keywords: *Myringoplasty, Temporal fascia, Tragal cartilage graft.*

Number of Tables: 06 ; Number of Figure:01 ; Number of References: 19; Number of Correspondences: 03.

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Introduction:

Chronic otitis media (COM) is the major community ear disorder in our country. It is the chronic inflammation of the middle ear cleft which is composed of eustachian tube, hypotympanum, mesotympanum, epitympanum, aditus and mastoid air cells and presents with recurrent ear discharge through tympanic perforation. Continuing mucosal infection of the middle ear by resistant organisms, continuing infection of the nasopharynx with secondary infection of the middle ear cleft and changes in the mucosa of the middle ear secondary to eustachian tube dysfunction may all

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contribute to the development of chronic otitis media. The diagnosis on COM implies a permanent abnormality of the pars tensa or flaccida, Various time related definitions have been applied to COM; however, generally a perforation for more than 3 months is deemed chronic[1]. In India, prevalence rate is 7.8% which is very high. In Bangladesh prevalence rate is 5.2%[2]. A study over 4260 subjects was conducted by Department of Otolaryngology and Head–Neck Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, World Health Organization, Dhaka, and Head–Neck Cancer Hospital and Institute, Dhaka, Bangladesh stated that 6.2 per cent had COM[3] (tubotympanic in 3.6 percent, atticoantral in 0.6 percent and dry perforation variety in 2.0 percent). Worldwide, there are nearly 65 to330 million sufferers. Risk factors for the chronic otitis media are early nasopharyngeal acquisition of otological pathogens due to high rate of cross-infection, more siblings under the age five, more crowded accommodation, higher number of siblings with a history of ear inflammation, age at first episode of acute otitis media, poorer nutritional status, reduced exposure to medical services and supportive therapies[4]. Otoscopy with the aid of a microscope is the 'gold standard' for the diagnosis of COM. History taking and investigations are an aid to management rather than to diagnosis. Pure tone audiometry assesses the magnitude of conductive hearing impairment due to the disease. The degree of air bone gap depends on- size of the perforation of tympanic membrane, erosion of the ossicular chain. Standard treatment of active mucosal COM is conservative management with aural toilet, topical antibiotics, systemic antibiotics, and advice. In case of inactive mucosal COM, other prerequisites are dry ear, good Eustachian tube function. Myringoplasty is the main stay of treatment for chronic otitis media of inactive mucosal disease. In a study the overall success rate of myringoplasty was 86 %. Posterior & inferior perforations had a 90% success rate for repair, compared to only 67% of anterior perforations[5]. The success rate of subtotal perforation closure (92.5%) was as good as the closure rate for small perforation (94.1%). But the poorer results were in younger patients. Vrabec et al[6] found better success with advancing age. This is due to lower incidence of upper airway infections and better eustachian tube function in later age and relative immaturity of the immune system in younger children. Caylon et al[7] found no statistical difference in the success rate between two sex groups. No significant difference was found when comparing the two surgical techniques of overlay and underlay; the success rate was 79.1% in the former & 82.3% in the later[8]. When hearing improvement was the main indication for surgery it was improved in 67%. A study was done by Mani Lal Aich et al[9] at Dhaka Medical College on 100 cases in 2009. The overall graft take rate was 84%. The mean preoperative and postoperative air conduction threshold in the successful cases were 35.2dB & 24.1dB respectively with a mean audiological improvement of 11.1dB & air bone gap improvement was 12.4dB. Various types of grafts are being used to repair the tympanic membrane. The most widely used graft in tympanoplasty is temporal fascia graft followed by cartilage, skin, vein graft, fat, perichondria etc. Temporal fascia graft is considered to be a better graft in terms of hearing outcome owing to its thinness and more pliable texture. Tragal cartilage with perichondrium fulfills all the required qualities of an ideal graft material namely low rejection rate, sufficient quantity, good tensile strength, conductive properties similar to that of tympanic membrane and easy availability. Fernandes from Newcastle, Australia published the technique of composite chondroperichondrial clip tympanoplasty using the tragal cartilage[10]. Tragal cartilage is a fibroelastic cartilage and being composed of collagen type II is also similar nature of the tympanic membrane, temporal muscle fascia consists primarily of collagen type I. Collagen type II has higher tensile strength than other types. Nowadays, several institutes preferred cartilage not only hard cases but also simple tympanic membrane perforations. A study was done by Mubarak M. Khan[11] at Department of Otorhinolaryngology, MIMER Medical College, Pune, India was performed on 223 cases by using slice tragal cartilage as graft during myringoplasty. The overall success rate was 98.20% in terms of perforation closure and airbone gap closure within 7.06 ± 3.39 dB. The success rates in the various age groups are as follows: 11 to 20 years, 97.67%; 21 to 40 years, 99.12%; and 41 to 60 years, 96.96%. So ultimate management for chronic mucosal otitis media is myringoplasty. To evaluate the outcome of the surgery postoperative graft, take rate and audiological assessment is essential.

Materials and Methods:

This cross-sectional observational study was conducted at the department of Otolaryngology & Head-Neck surgery, Shaheed Suhrawardy Medical College Hospital (ShSMCH) for six months from July 2018 to December 2018, after acceptance of the protocol and approval from IRB. Patients attending in the ShSMCH with complaints of chronic inactive mucosal otitis media were approached for inclusion of the study and final selection were done in according to the selection criteria. Ethical issues were ensured properly throughout the study period and inclusion was confirmed following signing written informed consent. All patients were randomly allocated into two groups where one group were received myringoplasty with temporalis fascia graft and another group received sliced tragal cartilage. Total 50 patients (25 patients in each group) were included, and they were subjected to details history taking, physical examination and necessary investigations. The researcher conducted all the interview and collected data were recorded into a case record form for each patient. Data analysis was done by SPSS 17.

Study procedure: This is a cross-sectional study which involve interviewing all patients and or his/her attendant who underwent myringoplasty by using temporal fascia and sliced

tragal cartilage in the Department of Otorhinolaryngology and Head Neck surgery, Shaheed Suhrawardy Medical College Hospital (ShSMCH), Dhaka. All patients were interviewed using a standard questionnaire. After admission history was taken and physical examination was done. Then all the investigations including pure tone audiometry and impedance audiometry were done. Then informed written consent was taken from the patient. The operation was performed under general anesthesia. A Per-operative microscopic examination was done. Incision site was infiltrated with two percent lignocaine with 1:200000 adrenaline in both cases. Temporalis fascia graft was harvested in the first group by a standard postauricular incision. The margin was freshened by a curved needle and the handle of the malleus was denuded. Graft was placed in underlay technique (under the remnant tympanic membrane medial to the handle of malleus) and gel foam was placed on either side of the graft. Sliced tragal cartilage was used as graft material in the second group. A horizontal incision was given at 2-3 mm below and behind the tip of tragus. Cartilage along with perichondrium was taken. Thin cartilage slices (with perichondrium) of 0.5 mm thickness were created with the Slice its cartilage slicer. Rosen incision was given transmeatally. The incision was made in the meatus from 12 to 6 o'clock on the posterior side, parallel to the tympanic annulus at a distance between 5 and 8 mm. At 12 and 6 o'clock the incision nearly joins the annulus. Margin freshening was done. Tympanomeatal flap was elevated. Sliced cartilage of 0.5mm was placed medial to the handle of the malleus. Gel foam was placed, and the flap was repositioned. Sofratulle packs were given in both cases. After the operation first follow up on 7th postoperative day, during which skin sutures were removed. The second follow-up visit will be done on the 2nd week, during which pack were removed. Assessment of graft uptake was done by using microscope in all visits of the patient. Graft uptakes were considered successful if there is no residual perforation seen after the end of follow up period at 6 weeks. After 12 weeks, a pure tone audiogram was done to evaluate the post-operative hearing status.

Results:

Fifty patients of chronic inactive otitis media were included in the final analysis. Among the respondents 50% underwent myringoplasty using temporal fascia graft and another 50% underwent myringoplasty using sliced tragal cartilage.

The mean age of 50 patients was 32.30±10.93 years, ranging from 16 to 58 years. Distribution was similar in both groups of patients (Table I).

Table-I: Distribution of respondents according to age (n=50)

Age group (years)	Temporal Fascia Graft	Sliced Tragal Cartilage Graft	Total
	N (%)	N (%)	N (%)
≤20	7 (28)	3 (12)	10 (20)
21-30	5 (20)	8 (32)	13 (26)
31-40	7 (28)	11 (44)	18 (36)
41-30	5 (20)	1 (4)	6 (12)
51-60	1 (4)	2 (8)	3 (6)

Among all patients, majority were male (58%) and 42% were female. Distribution was similar across groups (Table II).

Table II: Distribution of respondents according to sex (n=50)

Sex	Temporal Fascia Graft	Sliced Tragal Cartilage Graft	Total
	N (%)	N (%)	N (%)
Male	15 (60)	14 (56)	29 (58)
Female	10 (40)	11 (44)	21 (42)

74% of patients had hearing loss, 12% had tinnitus, 18% had vertigo and 10% had earache (Figure 1).

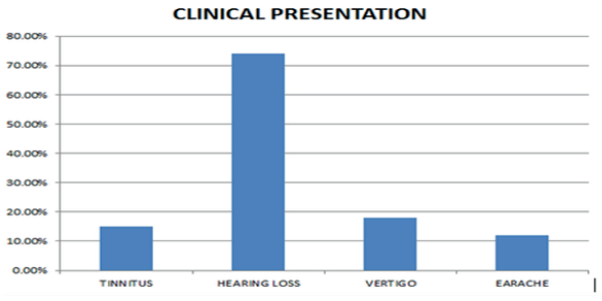

Figure 1: Clinical presentation of patients (n=50)

Majority 48% patients had inferior perforation, 28% had posterior perforation and 24% had anterior perforation. Majority 56% patients had medium sized perforation and 44% had small sized perforation. Patients were followed up in the 1st week, 2nd week and 12th week after surgery. Graft uptake was assessed after 6 weeks of treatment. Patients having temporal fascia graft had significantly higher proportion of graft uptake in comparison to patients having sliced tragal graft ($p<0.05$) (Table III).

Table III: Distribution of respondents according to graft uptake (n=50)

Graft uptake	Temporal Fascia Graft	Sliced Tragal Cartilage Graft	Total	P value
	N (%)	N (%)	N (%)	
Yes	22 (88)	15 (60)	37 (74)	0.024
No	3 (12)	10 (40)	13 (26)	

P value obtained by Chi-squared test

At admission mean Pure Tone Audiometry Air-Bone Gap (PTA-ABG) of all patients was 34.17±2.86, ranging from 30 to 40 (mild to moderate hearing impairment). Both surgical group had similar audiometry result at admission ($p>0.05$) (Table IV).

Table IV: PTA-ABG before surgery (n=50)

	Temporal Fascia Graft	Sliced Tragal Cartilage Graft	P value
ABG (dB)	**Mean±SD**	**Mean±SD**	
Small sized perforation	24.17±2.86	26.17±2.56	0.286
Medium sized perforation	32±3.15	34.17±3.02	0.304

P obtained by unpaired t test

Both temporal fascia graft and sliced tragal cartilage graft group of patients showed improvement in ABG 6 weeks after treatment (p<0.001) (Table V).

Table V: PTA-ABG result before and six weeks after myringoplasty (n=50)

Graft type		PTA-ABG (dB)		
		Before operation	6 Weeks after operation	P value
		Mean±SD	Mean±SD	
Temporal fascia graft	Small Sized Perforation	24.17±2.86	15±2.58	<0.001
	Medium Sized Perforation	32±3.15	20±3.13	<0.001
Sliced tragal cartilage graft	Small Sized Perforation	26.17±2.56	16±2.27	<0.001
	Medium Sized Perforation	34.17±3.02	22±3.29	<0.001

Audiometry results showed a 12.19±1.27 dB reduction in temporal fascia graft group and 6.55±.090 dB reduction in sliced tragal cartilage graft group. The improvement was significantly higher in temporal fascia graft group (p<0.001) (Table VI).

Table VI: Comparison of improvement in audiometry results between two surgical groups. (n=50)

	Temporal fascia graft		Sliced tragal cartilage graft		P value
	Mean±SD		Mean±SD		
Improvement in ABG	Small	Medium	Small	Medium	<0.001
	9.17±0.32	12±0.02	10.17±0.29	12.17±0.27	

P obtained by unpaired t test

Discussion:

Various graft materials including temporalis fascia, perichondrium, skin, vein, cartilage etc. have been used to repair the tympanic membrane perforation for a long time. There are variable results having merits and demerits of each graft material used in tympanoplasty. In this study sliced tragal cartilage and temporalis fascia were used as graft materials. In this study 50 patients of chronic inactive otitis media with small to medium sized perforation were surgically treated. Twenty-five patients were selected for repair with temporal fascia graft and another 25 with sliced tragal cartilage graft. The mean age of the patients studied was 32.30±10.93 years. Most patients were aged between 31 – 40 years (36%). Majority patients were male (58%) and 42% patients were female. Similarly, 54.76% patients were male and 45.23% where female were found in the study by Mazumder and colleagues[12]. Santoshi Kumari et al found that 58.4% male and 41.4% female in their study involving patients with otitis media[13]. In the study 74% of patients had hearing loss, 72% had tinnitus, 60% had aural fullness, 18% had vertigo and 32% had earache. In comparison Islam et al found hearing loss in 83.3% patients of otitis media in a rural setting, earache in 15.6%, vomiting in 5.2%, vertigo in 5.2% and tinnitus in 2.1% among others[14]. The present study found that 48% of patients had inferior perforation, 28% had posterior perforation and 24% had anterior perforation. This is similar to the findings of Naderpur et al.[15] They found central perforation in 56.7%, posterior perforation in 23.3% and anterior perforation in 20%. Graft uptake was significantly higher among patients who underwent myringoplasty with temporal fascia in comparison myringoplasty with sliced tragal cartilage graft (88% vs. 60%, p<0.05). This is nearly similar to the findings of Dabholkar et al[16] who found respectively 84% and 80% graft uptake in patients who underwent myringoplasty with temporal fascia and sliced tragal cartilage. This is dissimilar to the findings of Kumar et al who noted graft uptake in 86.7% cases of temporal fascia graft and 93.3% cases of sliced tragal cartilage graft [17]. Initial PTA-ABG was similar in both types of surgical groups. In case of small sized perforation, ABG improved from 24.17±2.86 dB before surgery to 15±2.58 dB in temporal fascia graft patients and from 26.17±2.56 dB to 16±2.27 dB among sliced tragal cartilage graft patients. In case of medium sized perforation, ABG improved from 32±3.15 dB before surgery to 20±3.13 dB in temporal fascia graft patients and from 34.17±3.02 dB to 22±3.29 dB among sliced tragal cartilage graft patients. The improvement was significant in both group of patients (p<0.001). But temporal fascia graft group showed slightly higher improvement than cartilage group (p<0.001). Khan and Parab also found improvement in ABG of cartilage group (31.47±3.98 dB to 7.19±2.99 dB after surgery) and temporalis fascia group (30.98±3.54 dB to 6.86±2.39 dB after surgery)[18]. But the improvement slightly higher in tragal cartilage group in their study. No statistical analysis was done in their study. Another study by Telang et al[19] found ABG improvement from 22.33±6.24 dB before surgery to 12.33±4.72 dB after surgery in temporal fascia group and from 20.77±5.75 dB to 10.50±4.46 dB after surgery in sliced cartilage group. Improvement was significant in both groups of patients. None of the procedures were found to be superior to one another. No major intraoperative and immediate postoperative complications like wound infection, sensory neural hearing loss, facial nerve palsy etc. were found in any patient of either group in the procedures. No cosmetic deformity of tragus was observed in reinforcement cartilage group. The present study endorses the finding that temporal fascia graft is superior to sliced tragal cartilage graft in the repair of tympanic membrane as it was a first-time study regarding cartilage using in tympanoplasty in our center, surgical expertise and post operative pt care may be an issue for lower graft uptake in cartilage group. The thickness of cartilage may be an issue for hearing outcome. 0.1mm thickness may give better hearing outcome in case of using sliced tragal cartilage.

Conclusion:

In conclusion, the study findings revealed that myringoplasty with temporalis fascia graft is superior to sliced tragal cartilage in chronic inactive mucosal otitis media patients. Temporalis fascia has shown its superiority in terms of graft intake and hearing improvement in subsequent follow up. However, this finding should be used with caution and further larger cohort is needed to conclude this finding.

Conflict of Interest: None.

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REVIEW ARTICLE OPEN ACCESS

Clinical Assessment of Early Morning Blood Pressure in Patients with Hypertension

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Abstract

A significant population experiencing hypertension, blood pressure (BP) demonstrates a significant rise during the awakening hours, it is linked to heightened cardiovascular complications during this time of the day. Many medications used to manage high BP fail to effectively control BP in the early morning, especially when administered once daily in the morning. Key factors to consider when choosing an efficient antihypertensive medication include the agent's pharmacokinetics, formulation, and timing of dosing. Examples of antihypertensive drugs with proven efficacy in regulating early morning BP include medications with extended pharmacologic half-lives, like telmisartan (an angiotensin II receptor blocker), amlodipine (a calcium antagonist), and bisoprolol (a beta-blocker). Administering chronotherapeutic preparations at bedtime has also been shown to be effective in managing early morning BP. There is a correlation between elevated early morning BP and cardiovascular risk, future clinical studies should emphasize evaluating the performance of antihypertensive drugs during this critical period of heightened risk. (Prev Cardiol. 2007;10:210–214) © 2007 Le Jacq

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Number of Figures; 04; Number of References; 36; Number of Correspondences: 04.

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Introduction:

Blood pressure (BP) consists of a clear daily pattern, i.e.- a significant drop during sleep (known as the nocturnal dip) and a noticeable rise around the time of waking (referred to as the morning surge) (Figure 1). The incidence of acute

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cardiovascular (CV) events, such as myocardial infarction, sudden cardiac death, and stroke, also follows a circadian rhythm, with the highest frequency observed in the morning hours (Figure 2) [1,2]. A substantial body of circumstantial evidence suggests a strong association between this heightened occurrence of CV events and the increase in BP levels during the early morning. For instance, the morning BP surge is positively linked to the extent of damage to target organs, including measures like carotid intima-media thickness[3] and left ventricular hypertrophy[4]. Furthermore, the magnitude of the morning surge independently predicts cerebrovascular and cardiac events [5,6]. Although the impact of managing early morning BP on CV risk has not yet been thoroughly investigated in clinical trials, previously presented data indicate that focusing on better control of early morning BP holds promise for the treatment of hypertensive patients. In this review, we examine the factors governing the circadian variation in BP and assess the clinical significance of BP measurements taken at various times of the day using diverse measurement techniques. These approaches encompass measurements obtained in clinical or office settings, those collected during the early morning via 24-hour ambulatory BP monitoring (ABPM), and patient self-monitoring measurements. We also delve into the prognostic value of different BP measures and provide insights into the outcomes of recent trials that have incorporated 24-hour and early morning BP assessments. Finally, we evaluate antihypertensive agents that have demonstrated notable effectiveness in controlling early morning BP based on controlled clinical trials.

Physiologic and Pathologic Circadian Variations in BP:

The morning surge in blood pressure (BP) is influenced by various contributory factors. These factors possess alterations in autonomic and renin-angiotensin-aldosterone system activity, as discussed in previous studies[7]. Additionally, dietary sodium intake was also identified as a relevant factor[8]. In the early morning hours, several physiological changes occur that may potentially enhance cardiovascular (CV) risk. These changes include increased heart rate, increased vascular tone, elevated blood viscosity, and enhanced platelet aggregability[9]. Utilizing ambulatory blood pressure monitoring (ABPM) has proven instrumental in not only identifying individuals with excessive morning surges[10] but also in enabling the assessment of the efficacy of antihypertensive agents that are effective in particular groups of hypertensive populations.

The typical nighttime reduction in blood pressure (BP), usually ranging between 10% and 20%, is primarily influenced by shifts in autonomic activity [11]. Furthermore, the renin-angiotensin-aldosterone system, a crucial BP regulator, might also play a role, particularly in individuals sensitive to salt. The nocturnal BP pattern can be influenced by the intake of sodium and potassium in such cases [11]. Ambulatory blood pressure monitoring (ABPM) has enabled the identification of patients who exhibit deviations from the standard nocturnal BP pattern. These categories encompass Extreme Dippers: Individuals who manifest a significant ≥ 20% decline in nocturnal BP compared to daytime BP. Nondippers: These individuals experience a nocturnal BP decrease of less than 10% compared to their daytime BP. Inverted Dippers/Risers: This group includes patients in whom BP either remains stable or actually increases during the nighttime [Figure 1] [12]. These deviations in the nocturnal BP pattern have been linked to an elevated risk of cardiovascular disease and mortality[12,13]. Individuals classified as nondippers and risers typically do not exhibit a surge in BP upon awakening, but instead, they often experience sustained early morning hypertension (HTN). Conversely, extreme dippers frequently display an excessive morning surge[14]. It is crucial to acknowledge that physiologic and pathologic variations in BP are dynamic rather than static. Relying solely on a few BP measurements taken in a clinical setting provides isolated data points of a continuously evolving variable. Valuable clinical insights into BP behavior and its overall "burden" can be gleaned from monitoring systems that allow for the evaluation of nocturnal, early morning, and 24-hour BP patterns.

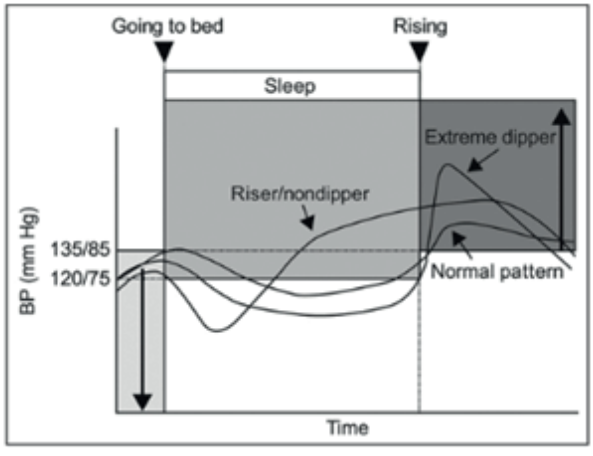

Figure 1: Normal circadian blood pressure (BP) rhythm is modified in some patients. The normal circadian BP rhythm features a nocturnal decrease in BP between 10% and 20% followed by a BP surge on awakening. Patients who exhibit this magnitude of nocturnal decrease in BP are known as dippers. Pathologic deviations from this normal pattern include extreme dipping (≥20% decline in nocturnal BP compared with daytime), nondipping (nocturnal BP decrease <10% of daytime BP), and inverted dipping/rising (no nocturnal decrease/nocturnal increase)[12]. Patients who exhibit excess dipping typically show an excessive morning BP surge[14]. Adapted with permission from Giles[7].

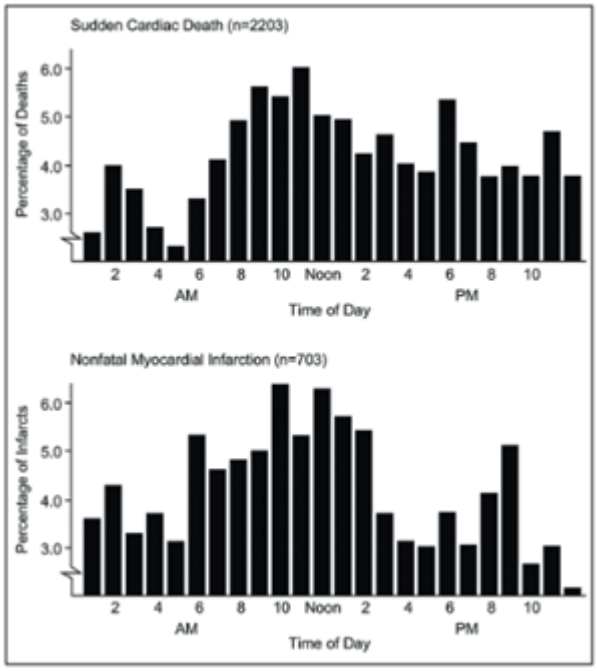

Figure 2: Occurrence of cardiovascular events peaks during the morning hours. Sudden cardiac death and nonfatal myocardial infarction both occur in a marked circadian rhythm, with a trough between midnight and 4 a.m. and a peak between 6 a.m. and noon. Reproduced with permission from Muller et al.[1]

Measurement of BP:

Blood pressure (BP) assessment can occur within clinical settings, where medical professionals, including physicians or nurses, utilize various methods such as Ambulatory Blood Pressure Monitoring (ABPM), or in the comfort of one's home through self-monitoring or home-based monitoring [15]. Despite the well-established clinical relevance of BP measurements conducted in a clinical environment, there are inherent limitations associated with this approach. These limitations encompass potential equipment calibration issues, deviations from recommended measurement protocols by healthcare practitioners, and the well-known phenomenon known as the "white coat effect." Notably, clinic-based BP measurements do not provide a comprehensive view of BP values 12 to 24 hours after medication dosing and are unable to capture BP fluctuations during sleep or the post-awakening surge. In the clinical context, an upper limit of normalcy for BP measurements is typically defined as 140/90 mm Hg for most patients[15,16]. However, individuals with hypertension (HTN) alongside diabetes mellitus or kidney disease are often assigned a lower BP target of <130/80 mm Hg[16]. In the context of ambulatory blood pressure (ABP) measurements, consensus guidelines established through a comprehensive review of existing literature have defined the reference values. These ABP assessments involve calculating averages during the daytime (while individuals are awake), nighttime (during the sleep cycle), and across a complete 24-hour cycle. According to consensus criteria endorsed by an expert group affiliated with the American Heart Association, hypertension is diagnosed when ABPM readings equal or surpass the threshold of ≥135/85 mm Hg during daytime hours and ≥120/70 mm Hg during nighttime hours, or ≥ 130/80 mm Hg when considering the entire 24-hour period [15].

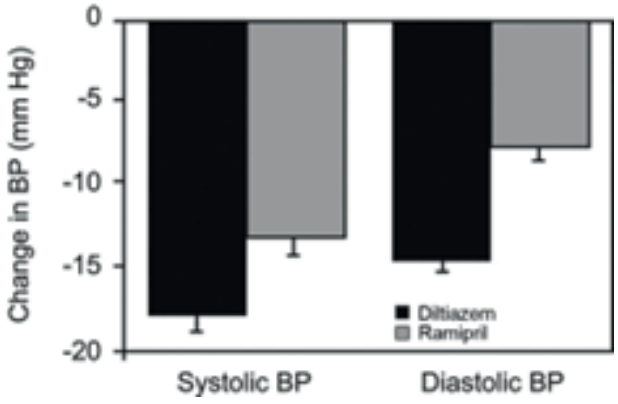

Figure 3: Bedtime administration of extended-release diltiazem (240–540 mg) is significantly more effective than bedtime administration of ramipril (5–20 mg) in reducing systolic and diastolic blood pressure (BP) in the first 4 hours after awakening (P≤.002). Adapted with permission from White et al.[27]

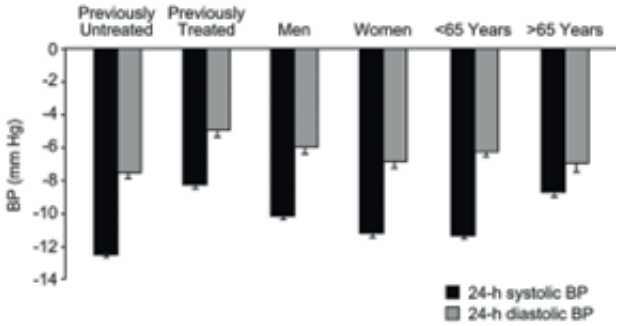

Figure 4: Reductions in 24-hour systolic and diastolic blood pressure (BP) after treatment with telmisartan alone or in combination with hydrochlorothiazide from the MICCAT-2 trial. In a 6- to 10-week community-based trial, a cohort of treated (n=675) and untreated (n=940) hypertensive patients were switched to/started with telmisartan-based antihypertensive therapy (telmisartan, 40–80 mg ± hydrochlorothiazide, 12.5 mg). Patient BP was monitored in the physician's office and using ambulatory BP monitoring. Telmisartan-based therapy was associated with significant reductions in systolic and diastolic BP in previously treated and previously untreated patients, in men and women, and in patients younger than 65 years and those aged 65 years or older (P<.0001 for all values). Adapted with permission from White et al.[33]

It's noteworthy that ABPM measurements typically yield lower values compared to BP measurements taken in clinical settings, resulting in a corresponding reduction in the threshold for defining normal daytime BP (<135/85 mm Hg versus <140/90 mm Hg). Furthermore, BP readings are generally lower when measured by patients at home compared to in-office measurements[15]. A recent examination of home-based, office-based, and ABPM readings proposed that individuals with home BP measurements below <125/76 mm Hg could be categorized as normotensive, those with home BP values ≥135/85 mm Hg should be classified as hypertensive, while individuals with intermediate home BP readings should undergo further evaluation, preferably utilizing ABPM[17]. Self-monitoring of BP presents several advantages over traditional clinic-based BP measurement, particularly when employing modern, validated electronic devices [15]. A recent meta-analysis of 18 rigorously conducted randomized controlled trials revealed that self-monitoring of BP was linked to significantly improved BP control compared to the customary office-based measurement approach[18]. Self-monitoring at home also provides patients with a heightened sense of control and engagement in their health. While it may not facilitate the assessment of the nighttime BP pattern, diligent self-monitoring can serve as a valuable tool in identifying early morning hypertension.

Prognostic Value of Different BP Measurements:

Monitoring blood pressure at home has been found in various studies to be more accurate in predicting cardiovascular events, cardiovascular-related deaths, and damage to target organs when compared to clinic-based blood pressure measurements [19–21]. However, many of these studies were conducted on general populations, making it challenging to establish normal self-monitoring values based solely on their findings.

In a particular study involving 393 untreated elderly patients, with an average age of 70, suffering from isolated systolic hypertension and enrolled in the Systolic Hypertension in Europe (Syst-Eur) trial, it was discovered that ambulatory systolic blood pressure emerged as a significant predictor of cardiovascular risk, while systolic blood pressure measured in a clinical setting did not exhibit the same predictive power [22]. Intriguingly, nighttime systolic blood pressure proved to be an even more accurate predictor of risk than daytime measurements. Similar results were reported by Clement and colleagues in a 5-year prospective cohort study, which involved 1963 middle-aged patients receiving antihypertensive treatment (with a mean baseline age of 56–57 years) [23]. In this prospective cohort study, baseline ambulatory blood pressure monitoring values remained significant independent predictors of cardiovascular events, even after accounting for major cardiovascular risk factors and clinic-based blood pressure readings [23].

Furthermore, through multivariate analyses that considered serum cholesterol levels, smoking habits, and the presence of diabetes, Björklund and associates demonstrated that ambulatory daytime systolic blood pressure and the presence of isolated ambulatory hypertension (defined as having a normal office-measured blood pressure but elevated ambulatory blood pressure, also known as masked or hidden hypertension) were both independent predictors of cardiovascular disease, while clinic-based systolic blood pressure measurements did not provide the same level of prediction [24].

Lastly, when comparing the efficacy of ambulatory blood pressure monitoring and clinic-based measurements in managing hypertensive patients, it was observed that, although both clinic and ambulatory readings were associated with similar levels of antihypertensive control and inhibition of left ventricular enlargement, patients monitored using ambulatory blood pressure monitoring required less intensive drug treatment [25].

Efficacy of Antihypertensive Agents in Controlling 24-Hour and Early Morning BP:

Achieving effective control of early morning and 24-hour mean ambulatory blood pressure [ABP] has become a highly sought-after feature of antihypertensive treatments. The extent to which antihypertensive agents can regulate blood pressure during the night and early morning hours depends on various factors, including pharmacokinetics, formulation, and timing of administration.

For instance, graded-release diltiazem is a chronotherapeutic formulation designed to counteract the circadian rhythm of blood pressure. When administered in the evening, it proves more effective than morning administration in lowering blood pressure between 6 AM and noon [26]. Furthermore, in a double-blind, titration-to-effect trial, White and colleagues demonstrated that bedtime administration of graded-release diltiazem was notably more effective at reducing early morning blood pressure than bedtime administration of ramipril (Figure 3) [27]. Similarly, administering a controlled-onset extended-release verapamil formulation at bedtime proved superior in lowering early morning blood pressure compared to the morning administration of enalapril or losartan [28].

Utilizing agents with longer half-lives has also shown promise in enhancing early morning blood pressure control. For example, a single 10-mg dose of the beta-blocker bisoprolol, taken in the morning, effectively lowered blood pressure throughout the entire 24-hour period. After four weeks of treatment in a group of 25 patients with essential hypertension, bisoprolol reduced the mean morning blood pressure from 145/97 mm Hg to 133/88 mm Hg [29]. Similarly, the calcium channel blocker amlodipine reduced morning systolic blood pressure and mitigated the magnitude of the morning systolic blood

pressure surge. In a study involving 38 hypertensive patients who received amlodipine (2.5–10 mg) immediately after breakfast for 8 to 16 weeks, the mean morning systolic blood pressure decreased from 156 mm Hg to 142 mm Hg, and the morning surge diminished by 6.1 mm Hg [30].

Recent insights into the activation of the renin-angiotensin-aldosterone system during sleep and in the early morning have prompted the investigation of angiotensin II blockade as a strategy for controlling early morning hypertension. Telmisartan, an angiotensin receptor blocker with an extended half-life, has proven effective in reducing early morning blood pressure [10,31]. In two large-scale trials comparing telmisartan with valsartan, telmisartan at doses of 40–80 mg outperformed valsartan at doses of 80–160 mg in reducing blood pressure during the last 6 hours of the inter dosing interval, aligning with the early morning period [31,32].

Moreover, the effectiveness of this therapeutic approach to ABP was evaluated in a significant, prospective, open-label trial conducted in a primary care setting [the Micardis Community Ambulatory Monitoring Trial (MICCAT-2)]. In this trial, telmisartan [with or without hydrochlorothiazide] significantly reduced 24-hour, daytime, nighttime, and early morning [post awakening] mean blood pressure in both previously treated and untreated hypertensive patients [10,33]. Specifically, post awakening blood pressure decreased by an average of 17.2/10.1 mm Hg in patients with an excessive morning blood pressure surge, surpassing the effect observed in the overall population (reduction of 11.5/7.0 mm Hg) [10].

The Prospective Randomized Investigation of the Safety and Efficacy of Micardis vs. Ramipril Using ABPM (PRISMA) studies also examined the effectiveness of telmisartan 80 mg/day compared to ramipril 10 mg/day in controlling the morning blood pressure surge in patients with mild to moderate hypertension. Pooled data from PRISMA I and II demonstrated that telmisartan reduced the overall mean morning systolic blood pressure surge, whereas patients taking ramipril experienced an increase in the morning blood pressure surge [36]. Notably, the reduction in morning systolic blood pressure surge was most pronounced in patients with the highest baseline morning systolic blood pressure surge [36]. Telmisartan also significantly reduced the magnitude of the systolic morning blood pressure surge in diapers compared to ramipril, although no significant difference was observed in nondippers [36].

Conclusions:

In individuals with good health, blood pressure exhibits a highly consistent circadian rhythm. Analyzing and understanding this pattern has been significantly enhanced by ambulatory blood pressure monitoring (ABPM), a technique proven to be more effective than clinic-based blood pressure measurements in predicting adverse events. ABPM has also enabled healthcare professionals to identify several pathological variations in this pattern, many of which are linked to an elevated risk of adverse events. These variations encompass phenomena like nocturnal nondipping and excessive morning blood pressure surges.

The early morning surge in blood pressure is of particular concern because it aligns with the peak occurrence time of cardiovascular events. Consequently, physicians and pharmaceutical researchers have directed their attention toward developing antihypertensive agents specifically tailored to address this critical morning period. Notable among these are chronotherapeutic formulations of diltiazem and verapamil, as well as medications with extended half-lives, typically spanning 20 to 30 hours. Examples include the angiotensin II receptor blocker telmisartan and the beta-blocker bisoprolol, both of which exhibit significant efficacy during the early morning hypertensive phase.

Given the well-established association between early morning blood pressure and cardiovascular risk, it is imperative that future clinical trials place a deliberate focus on evaluating the effectiveness of antihypertensive drugs during this crucial time window.

Conflict of Interest: None.

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REVIEW ARTICLE OPEN ACCESS

Role of Sertaconazole in the Treatment of Dermatophytosis

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Abstract:

Dermatophytosis is a major health burden worldwide and is now increasing day by day. Dermatophytosis is also becoming increasingly unresponsive to topical conventional antifungals now a day. Newer topical antifungals may be more effective in these patients. Sertaconazole is a new, broad spectrum, fungicidal and fungistatic imidazole with added antipruritic and anti-inflammatory activity that may be effective and beneficial in improving the quality of life for the patient with dermatophytoses. It is indicated in the European Union(EU) for the treatment of superficial skin mycoses such as dermatophytosis (including tinea corporis, tinea cruris, tinea manus, tinea barbae and tinea pedis), cutaneous candidiasis, pityriasis versicolor and seborrhoeic dermatitis of the scalp, and in the US for tinea pedis only. Sertaconazole has broad-spectrum antifungal activity against dermatophytes of the Trichophyton, Epidermophyton and Microsporum genera, and yeasts of the genera Candida and Cryptococcus; additionally, it is effective against opportunistic filamentous fungi and Gram-positive bacteria. Moreover, the antifungal activity of sertaconazole is maintained in clinical isolates of dermatophytes that show reduced susceptibility to other azoles. While the drug has good dermal penetration, this is not associated with systemic absorption. In clinical trials in patients with superficial mycoses, 2% sertaconazole cream applied twice daily was effective in the eradication of a range of dermatophytoses, and a significantly greater proportion of patients were cured compared with those receiving 2% miconazole cream twice-daily treatment. Both as a topical cream and suppository preparation, sertaconazole was generally well tolerated. Sertaconazole is a well-established antifungal agent, which is now available in a variety of formulations, and remains a useful treatment option particularly in patients with fungal infections resistant to other azoles.

Key words: *Sartaconazole, antifungal, dermatophytosis.*

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Introduction:

Dermatophytoses are the superficial fungal infections of skin, hair, and nail, caused by keratinophilic fungi called dermatophytes. 'Dermatophytes' which include three genera, namely, Epidermophyton, Microsporum, and Trichophyton[1,2]. Dermatophytoses is commonly called as tinea. The two varieties of tinea most commonly encountered are tinea corporis (affecting trunk and limbs) and tinea cruris (affecting the inguinal region)[3,4]. Tinea corporis presents as radially advancing, flat, scaly, pruritic macules with a raised border and a characteristic central clearing which earns the sobriquet 'ringworm' for these lesions. Tinea cruris begins in the inguinal folds and presents usually as bilateral, scaly, dull red, pruritic plaques whose leading edge advances in a sharply demarcated, raised, scaly border[5]. Many topical antifungals of different groups are available for the treatment of dermatophytoses such as azole derivatives, allylamines, benzylamines, morpholine, etc[1,6.] Topical antifungal drugs are usually sufficient and effective in localized infections. The traditional azoles, such as clotrimazole, miconazole, and ketoconazole, which belongs to the imidazole class of antifungals, are fungistatic and most commonly used[7-9]. Sertaconazole, one of the newer azoles, is structurally unique due to a benzothiophene ring. It is the only azole with a fungicidal action due to its ability to cause direct fungal cell membrane damage[4]. Sertaconazole shows good in vitro fungistatic activity against a broad range of dermatophytes and yeasts of the genera Candida and opportunistic fungi[10]. Like other azoles, sertaconazole inhibits the synthesis of ergosterol, an essential component of fungal cell walls resulting in disruption of mycelial growth and replication. However, at higher concentrations, sertaconazole binds directly to non-sterol lipids in the fungal cell wall, which leads to increased permeability and subsequent lysis of the mycelium. Thus, depending on concentration, sertaconazole may exhibit both fungistatic and fungicidal activities[8]. Sertaconazole has additional anti-inflammatory and antipruritic actions[11]. It has shown efficacy even against dermatophyte isolates resistant to other azoles[12]. Its faster and superior cure rates as compared to other azoles are well documented[13,14] . The geometric minimum inhibitory concentration (MIC) of sertaconazole ranged from 0.06 to 1 microg/mL against a variety of dermatophyte isolates (n = 456), which included 114 isolates with reduced susceptibility to fluconazole (MICs > or = 16

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microg/mL). Additionally, sertaconazole showed antibacterial activity with a geometric MIC of 0.88 microg/mL against 21 isolates of Gram-positive bacteria. When applied topically in experimental models of inflammation, sertaconazole showed some evidence of anti-inflammatory action[10]. In addition to this antifungal efficacy, it has a good safety profile, sustained cutaneous retention, and low systemic absorption, all of which make it ideal for topical applications[15,16] .

Discussion:

Jerajani et al conducted a study with 83 patients with tinea corporis and tinea cruris infections in a multicentre, randomized, open label parallel study to compare efficacy and safety of sertaconazole, terbinafine and luliconazole in patients with dermatophytoses. The initial 'Treatment Phase' involved three groups receiving either sertaconazole 2% cream applied topically twice daily for four weeks, terbinafine 1% cream once daily for two weeks, luliconazole 1% cream once daily for two weeks. Of the 83 patients, 62 completed the study, sertaconazole (n = 20), terbinafine (n = 22) and luliconazole (n = 20). The primary efficacy variables including change in pruritus, erythema, vesicle, desquamation and mycological cure were significantly improved in all the three groups, as compared to baseline, in the Treatment and Follow-up phase. Greater proportion of patients in sertaconazole group (85%) showed resolution of pruritus as compared to terbinafine (54.6%); and luliconazole (70%), (P < 0.05 sertaconazole vs terbinafine). There was a greater reduction in mean total composite score (pruritus, erythema, vesicle and desquamation) in sertaconazole group (97.1%) as compared to terbinafine (91.2%) and luliconazole (92.9%). All groups showed equal negative mycological assessment without any relapses. All three study drugs were well tolerated. Only one patient in sertaconazole group withdrew from the study due to suspected allergic contact dermatitis. They concluded that sertaconazole was better than terbinafine and luliconazole in relieving signs and symptoms during study and follow up period. At the end of 'Treatment Phase' and 'Follow-up' Phase, all patients showed negative mycological assessment in all three treatment groups suggesting no recurrence of the disease[4]. Das et al conducted a study to evaluate and compare the efficacy and safety of amorolfine 0.25% cream and sertaconazole 2% cream in limited tinea cruris/corporis. A single-center, randomized (1:1), double-blind, active-controlled trial was performed. Sixty-six untreated adults with acutely symptomatic tinea cruris/corporis were included in the study. All patients had limited cutaneous involvement and were KOH mount positive. Group A received amorolfine 0.25% cream, and group B received sertaconazole 2% cream twice daily application to the lesions for 4 weeks. After the baseline visit, four follow-up visits were carried out. The outcome measures for effectiveness were clinical and mycological cure. Both sertaconazole and amorolfine significantly reduced symptoms (P < 0.001) in both groups. However, improvement in symptoms (pruritus, burning sensation, erythema, scaling and crusting) was significantly greater in the sertaconazole group at every follow-up visit. Sertaconazole cream was also more effective than amorolfine cream in reducing the number of lesions (P = 0.002 at 12 weeks) and improving the Dermatology Life Quality Index (P < 0.001) at all the follow-up visits. Adverse events were similar in the two groups (P = 0.117). Fungal cultures became negative in 92.3% of the sertaconazole group as compared to 80% in the amorolfine group (P = 0.010)[9].

Thaker et al conducted a study to compare the efficacy, safety and cost effectiveness of topical 2% sertaconazole cream and 1% butenafine in tinea infections of skin. Patients were randomly allocated to two treatment groups. They were advised to apply the drug topically twice a day for one month on the lesions. They were followed up at an interval of 10 days. Clinical score and Global Evaluation Response were assessed at baseline and during each follow up. A total 125 patients were recruited, out of them 111 completed the whole study. Median Sign and Symptom Score of tinea on the baseline was 9 [5,9] that was reduced to 0 [0,4] by 2% sertaconazole while it was 9 [6,9] in the butenafine group on the baseline that was reduced to 0 [0,6] at the end of the treatment. 90% and 98% of the patients got complete clearance of the lesions with sertaconazole and butenafine respectively. Treatment with butenafine was more cost effective as compared to sertaconazole[10]. Choudhary et al conducted a randomized control trial with treatment with terbinafine cream and sertaconazole cream respectively. A majority of their patients in both the group showed Trichophyton rubrum followed by Trichophyton mentagrophytes growth on culture. Comparison showed that at the end of 3 weeks both terbinafine and sertaconazole groups had 100% complete cure. When the two groups were compared for complete cure, at the end of 1st and 2nd week, statistically non-significant results were observed (P = 0.461 and P = 0.679 respectively). However, at the end of 2nd week, complete cure rate for terbinafine was 80% as compared to 73.35% for sertaconazole with no statistical significance. In both Group A and Group B, clinically significant local side effects like erythema, swelling, stinging sensation, or increased itching were not noticed. The newer fungistatic drug sertaconazole nitrate 2% cream was as effective as terbinafine hydrochloride 1% cream which is one of the fungicidal drugs. Both the drugs showed good tolerability with no adverse effects[16]. Chatterjee et al conducted a randomized study with 88 patients on sertaconazole and 91 on terbinafine. At 2 weeks, the clinical cure rates were comparable at 77.27% for sertaconazole and 73.63% for terbinafine (P = 0.606). Fourteen patients in either group improved and on further treatment showed complete healing by another 2 weeks. The final cure rate at 4 weeks was also comparable at 93.18% and 89.01% respectively (P = 0.914). At 2 weeks, 6 (6.82%) sertaconazole and 10 (10.99%) terbinafine recipients were considered as “clinical failure.” Tolerability of both preparations was excellent. The

results suggest that once-daily topical sertaconazole is effective in localized tinea infections[17]. Carrillo-Muñoz et al conducted a clinical trial including patients with vulvovaginal candidiasis, a single dose of sertaconazole produced a higher cure rate compared with other topical azoles such as econazole and clotrimazole, in shorter periods. Sertaconazole had shown an anti-inflammatory effect that is very useful for the relief of unpleasant symptoms[18]. Romaguera et al was conducted a randomized double-blind clinical trial in 78 atopical volunteers of both sexes. Sertaconazole in 2% dermatological cream form was compared with 5 other commercially available antimycotics (econazole, ketoconazole, bifonazole, clotrimazole and miconazole), using the excipient of the cream without sertaconazole and 2% sertaconazole in vaseline as controls. At the end of the trial, only miconazole showed a positive allergy (vesiculation) in two of the 78 individuals studied. The other substances did not demonstrate any sensitizing capacity, including sertaconazole and its excipient. This trial showed that sertaconazole in 2% dermatological cream form does not possess a sensitizing capacity for causing contact dermatitis which confirmed its excellent safety in topical use[19]. Alomar et al carried out a double-blind, controlled multicentre trial with 631 patients suffering from superficial cutaneous mycosis (sertaconazole n = 317, miconazole n = 314). The rate of clinical cures for both treatments at the end of the follow-up was 95.6% for sertaconazole and 88.1% for miconazole, with the difference being statistically significant. In the comparative analysis, it was observed that the patients treated with sertaconazole were cured earlier and in a higher proportion than those treated with miconazole, with the difference being significant. The negative result of the microscope examination and culture test confirmed the superiority of sertaconazole over miconazole, already after 14 days of treatment. At the end of the follow-up, 98.6% of the patients in the sertaconazole group obtained a negative culture test result, as opposed to 91.7% in the miconazole group, with the difference being highly significant[20]. Shivamurthy et al conducted astudy to compare the efficacy of topical antifungal agents, Sertaconazole and Clotrimazole in Tinea corporis patients. A total of 60(n=60) patients were included in the study. They were divided into two groups of 30 patients each. First group included patients treated with topical Sertaconazole as test drug whereas the second group constituted patients treated with topical Clotrimazole as standard drug. The patients were advised to apply the drug on affected area twice daily for three weeks. The parameters like erythema, scaling, itching, margins and size of the lesion and KOH mount were taken for the assessment of efficacy. The total score included all grades in erythema, itching, scaling, margins and size of lesion and KOH mount. There was significant reduction in erythema ($p<0.02$) and highly significant reduction in scaling ($p<0.001$), itching ($p<0.001$) and margins of lesion ($p<0.001$) among Sertaconazole group. The mean difference and the standard deviation of total scores for Clotrimazole were 7.20 and 1.69 and for Sertaconazole group 8.80 and 1.52 respectively. The p-value on application of students unpaired t- test was $p<0.001$ (Highly significant). From the present study, it can be concluded that topical Sertaconazole shows better improvement in the clinical parameters than topical Clotrimazole within a span of three weeks in the treatment of T corporis[21]. Borelli et al carried out a randomized, controlled study to compare the efficacy of a solution containing 2% sertaconazole with the well-established 2% sertaconazole cream formulation in patients with tinea corporis, tinea pedis interdigitalis. Patients received either sertaconazole solution or cream twice daily for 28 days. The full analysis set comprised 160 patients in the solution group and 153 patients in the cream group. The primary efficacy parameter was a combination of culture test result and total clinical score. Efficacy was defined by eradication of the pathogen and reduction of the total clinical score between pretreatment and the final visit. Efficacy was documented in 90.6% of patients using the solution and 88.9% of those using the cream (full analysis set). No adverse events occurred. They concluded that solution and cream formulations of 2% sertaconazole applied for 28 days were associated with comparable efficacy and safety in the treatment of fungal skin infections[22]. Weinberg et al conducted a small (n=32) clinical trial designed to determine whether sertaconazole nitrate 2% cream, used once daily, is as effective as the traditional regimen. Results demonstrated that sertaconazole is as effective when used once daily for four weeks. Patients showed rapid improvement in pruritus as early as week 2, and at six weeks' follow up, all patients were free of erythema while 93.8 percent were free of pruritus; no relapses had occurred. These encouraging findings suggest that sertaconazole nitrate may be useful in a once-daily regimen[23]. Savin et al conducted a study to determine the safety and efficacy of topical sertaconazole nitrate cream 2% in the treatment of tinea pedis, 2 randomized, multicenter, double-blinded, parallel group, vehicle-controlled studies. A total of 588 subjects were enrolled, and 383 subjects were randomized to treatment with sertaconazole or vehicle applied twice daily for 4 weeks. Improvements in symptoms were noted at week 1 in the active treatment group. At week 4, mycologic cure was seen in 70.3% of sertaconazole-treated subjects and 36.7% of vehicle-treated subjects ($P<.0001$). At week 6, 46.7% of sertaconazole-treated subjects had successful treatment outcomes compared with 14.9% of vehicle-treated subjects ($P<.0001$). No serious adverse events were reported, and rates of cutaneous adverse events were comparable between treatment groups. They concluded that sertaconazole nitrate cream 2% was well-tolerated, offered rapid relief of symptoms, and achieved high rates of mycologic cure. The stability of the mycologic cure rates through weeks 5 and 6 (2 weeks after cessation of therapy) indicate that sertaconazole protects against reinfection[24].

Borelli conducted a study a study to evaluate the safety and efficacy of sertaconazole nitrate cream 2%, specifically in participants with tinea pedis interdigitalis (ie, fungal skin disease of the toe web) of dermatophyte origin. A total of 92 participants were included in their analysis. The primary end points were eradication of the pathogen (confirmed by fungal culture results) and reduction in total clinical score (TCS) of at least 2 points. After 4 weeks of treatment, 88.8% (79/89) of evaluable participants achieved success on the primary end points. Most participants also demonstrated substantial improvement in signs and symptoms after 4 weeks of treatment: 63.7% (58/91) were free of erythema, 33.0% (30/91) were free of desquamation, and 91.2% (83/91) were free of itch. The rate of reported AEs was low (8.7% [8/92]), and none were considered serious. These findings indicate that sertaconazole nitrate cream 2% is highly safe and effective in the treatment of tinea pedis interdigitalis[25].

Nasarre et al was studied in a randomized parallel double-blind clinical trial on 21 patients suffering from Pityriasis versicolor (confirmed by KOH microscopic examination and exploration with Wood's light). The patients were divided into two treatment groups: one with 11 patients receiving sertaconazole 1% cream and the other with 10 patients receiving sertaconazole 2% cream. The cream was applied twice a day during 4 weeks. The data were assessed clinically and microscopically (optical and fluorescence). All the patients were cured (100% cure), showing excellent efficacy. A check-up performed after the end of the treatment showed no relapses of infection. The drug safety was optimum, since no local or general undesirable effects were recorded, nor were there any changes in the analytical parameters studied in the 21 patients[26].

In a study done by Sharma et al. on the efficacy and tolerability of sertaconazole nitrate 2% cream vs miconazole 1% cream in patients with cutaneous dermatophytosis, sertaconazole nitrate 2% cream was used twice daily for 2 weeks and they observed that 62.3% patients had a complete clinical cure. Sertaconazole was well tolerated without clinically significant side effects13. Esso et al. in their study of sertaconazole in the treatment of paediatric patients with cutaneous dermatophyte infections used 2% sertaconazole once daily for a period of 2 weeks and observed that clinical cure was achieved in 75% and 100% patients after 2 and 4 weeks, respectively. No local adverse effects were observed in their study[27].

Conclusion:

On the basis of the review of literature, it can be concluded that sartaconazole is highly effective and well tolerated by patients in the treatment of dermatomycoses.

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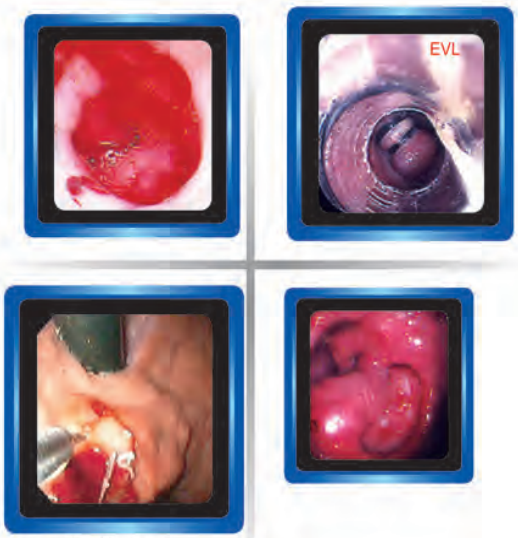

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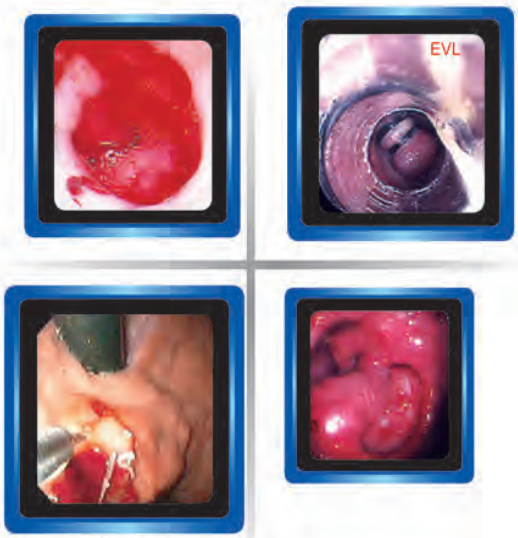

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