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Editorial

Emerging and Remerging Viral Diseases

21st Century world has seen a globalization of not only the resources of human-mankind but also a spread of diseases among different countries of this planet. Among the reemerging infectious diseases Dengue, Chikungunya, Nipah, Zika virus infections are a concern for increasing morbidity and mortality. HIV is another example where travel beyond borders has contributed for its increasing spread. Among the emerging diseases, SARS, MERS and Bird-flu have given the world a frightening experience few years back with their high mortality rates. Though these diseases were controlled within a short span of time but it is possible that there may emerge a disease which may spread globally and may contribute to a scenario of Pandemic for which the world will be least prepared. The Flu Pandemic of 1918 was an example where millions of people died and was caused by a new strain of Influenza A virus. A new Virus when it jumps from an animal or Bird can cause a devastating effect on the health of a community, country and like-wise the whole world as because there will be no immunity and also antiviral drugs shall be in ineffective. As such we have to improve our health sector to the extent so that we can cope up with problems as and whenever it appears.

Prof. Dr. Munir Hassan
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Original Article

Morphological Pattern of plaque in duplex study of neck vessels among acute ischemic stroke patients

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Abstract

Aims and Objectives: Cerebral ischemic stroke is the most common life threatening and disabling neurological diseases.There are many studies showing relationship between carotid artery stenosis and ischemic stroke.This study is done to assess the carotid artery morphology with the help of color Doppler sonography.

Methodology: This is a cross sectional observational study carried out in neurology department of Dhaka National Medical College Hospital (DNMCH) during the period of July 2016 to January 2018 among 30 patients admitted with acute ischemic stroke. Dopplerultrasound was performed during hospitalization to find out carotid artery stenosis. Statistics analysis was done with STATA 10.

Results: Among the 30 ischemic stroke patients 73% patient had carotid artery stenosis and most of the patient among them had smooth plaques 17(57%) with 12(40%) calcified in nature and 20(67%) have centric in distribution.

Conclusion: Carotid artery stenosis has a well-established association with ischemic stroke. Doppler studies are economic, safe, reproducible and less time consuming test to find out cerebrovascular insufficiency and recommended for primary and secondary prevention of ischemic stroke.

Keywords : Ischemic stroke, Carotid artery stenosis, Duplex study.

Introduction:

Stroke is the commonest neurological disorder, third leading cause of death, the most important cause of disability.According to world health organization estimates for the year 2020,Stroke will be the second cause of death along with ischemic heart disease.[1] The incidence of the disease is decreasing in the western population ,on the other hand the disease burden is increasing in the south Asian people.[2] In Pakistan stroke incidence is approximately 250 per 100,000 populations, which indicates that there are 350,000 new stroke patient per year in this country.[3] Disturbance of cerebral circulation leads to clinical stroke. It is either due to occlusion of cerebral blood vessel or rupture of a blood vessel. Among all stroke 85% are ischemic origin,caused by thrombotic or embolic blockage of cerebral blood vessel.[4] There are several risk factors responsible for stroke. Some arenon-modifiable like age, sex, race, family history and ethnicity, others are modifiable like hypertension, diabetes, dyslipidemia, smoking, alcoholism, ischemic heart disease, sedentary life style, carotid stenosis and TIA(Transient ischemic attack.[5] Carotid artery stenosis is one of the major risk factor for stroke. Among all ischemic stroke patients, 20-30% are due to carotid artery stenosis.[6]

We can assess the carotid artery disease by color Doppler ultrasound,digital subs traction angiography, magnetic resonance angiography computed tomographic angiography. Currently most accurate, noninvasive tools is duplex ultrasonography for the assessment of carotid artery stenosis. Several information about the degree of carotid stenosis, the velocity and character of blood flow and plaque morphology.[7] Grading of carotid artery stenosis was done according to radiological society of consensus 2008.[8] Screening of carotid artery by duplex study is recommended for high risk patient for primary as well as secondary prevention of cerebrovascular events.

Materials and methods:

In this descriptive cross-sectional observational study, total number of 30 randomly selected clinically and CT proven acute ischemic stroke patients were studied from July 2016 to January 2018 at neurology department of Dhaka National Medical College

Hospital. Patients admitted within 48 hours of the onset of stroke with CT scan of the brain showing infract was included for this study. Patients diagnosed with other diseases like infective meningitis (tuberculous or bacterial), space occupying lesions, psychosis, viral/bacterial encephalitis and multiple sclerosis were excluded. A questionnaire was designed for the purpose of this study.With proper preparation duplex study of neck vessels was done with Toshiba Aplio 400 USG machine. Morphological pattern of duplex study of neck vessels of acute ischemic stroke patients were identified. Before collecting data informed written consent was taken from patient/attendant and ethical clearance was taken from Research Review committee of DNMCH. All data were collected and compiled, and data analysis was carried out by using STATA 10 software.

Results:

This observational study was done among acute ischemic stroke patients admitted in Neurology department DNMCH, total 30 patients was enrolled with fulfilling inclusion and exclusion criteria. Among them 68% were male and 32% were female and mean age of male patients was 65.32±14.20 and female 61.67±11.46. Results on Morphological pattern of duplex study of neck vessels are given bellow.

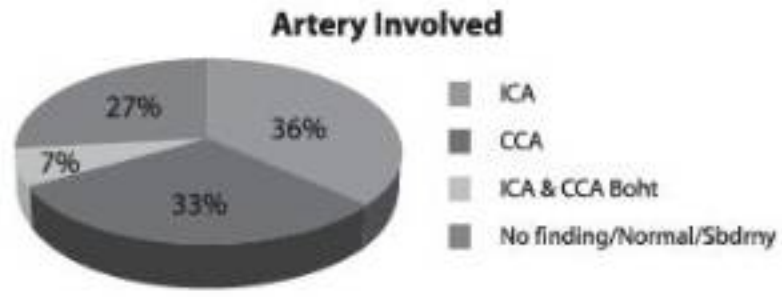

Figure-1: Graphical presentation of Artery involved in duplex study of neck vessels.

Table-1: Distribution of study population by character of plaque surface

Plaque Surface	Smooth/ regular	Irregular	Ulcerated	No finding/ Normal/ Absent
	17 (57%)	2 (7%)	0	11 (37%)

Table-1: shows plaque surface character in study population and observed smooth plaque 17(57%), Irregular plaque 2(7%), Normal 11(37%).

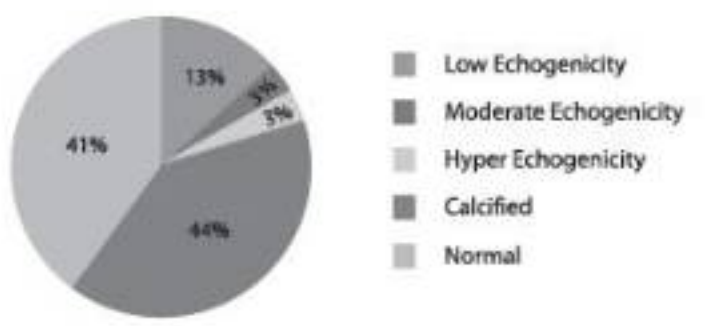

Figure-2: Graphical presentation of Plaque echogenicity in duplex study of neck vessels.

Table-2: Distribution of study population by Plaque distribution

Plaque Distribution	Concentric	Eccentric	No finding/ Normal/ Absent
	20 (67%)	9 (30%)	1 (3%)

Table-2: shows Plaque distribution in study population and observed Concentric 20(67%), Eccentric 9(30%) and Normal 1(3%).

Discussion:

We studied among 30 patients admitted in Neurology department of DNMCH with CT proven acute ischemic stroke and morphological pattern of duplex study of neck vessels among patients were observed.

Sethi et al., and Rajagopal et al., found that carotid bifurcation was the commonly involved by the atherosclerotic plaque followed by ICA and Intracranial portion of ICA.[9,10] G Shivani et al. found in their study that 35% plaques were present at bifurcation 32% plaque in ICA followed by 8% in ECA.[11] In our study we found ICA involvement 36%, common carotid artery bifurcation involved 30% which was second highest and in 7% patients both ICA & CCA involved, normal finding in 27%.

Prabhakaran S et al. found in a population based cohort that carotid plaque with irregular surface increased the risk of ischemic stroke 3-fold.[12] In our study we found regular plaque 57% and irregular plaque 7%, Prabhakaran S et al. also found most of the patient had regular plaque surface 51.8% and irregular plaque surface among 5.5%.

Plaque were also classified according to their echotexture as low echogenic, moderately echogenic, hyper echogenic and calcified. Low echogenic plaques

are soft plaques and prone to dislodge into cerebral circulation and cause transient ischemic attack, so that plaque characterization according to echogenicity is very important. In our study total 18 patient had plaques and among them 12(40%) had calcified plaque and 4(13%) had low echogenic plaque, moderate and hyper echogenic plaques were 3% in each, Sehrawat et al.,Garg S et al. found most of the plaques were low echogenic 45% and 40% accordingly.[13,14] Inour study most of the plaques were calcified may be due to most of present to us late after developing TIA or carotid artery insufficiency.

In our study we found most of the patient had concentric plaque 20(67%), than Eccentric plaque in 9(30%) study population. T. Ohara et al. found in there study most of the patient with eccentric plaque distribution and Cerebrovascular events occurred more frequently ipsilaterally to the artery with eccentric stenosis (13.5%) than to the artery with concentric stenosis (5.5%; P .013)[15]

Conclusion:

Among different risk factors of stroke carotid artery stenosis is one of the established risk factor and this can be evaluated accurately by simple noninvasive investigation modality like ultra-sonogram. In our study there were significant number of patient with carotid artery stenosis at different levels and there were various morphological patterns as well. So for primary and secondary prevention as well as proper management of cerebrovascular accident, high risk patients should be evaluated with Doppler ultrasonography of carotid vessels for the presence of carotid stenosis and plaque abnormality along with other risk factor evaluation will prevent reccurent stroke and aid in the field of treatment with neurointervention.

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Original Article

Incidence of post dural puncture headache among parturients undergoing caesarean section under spinal anaesthesia using median or paramedian approach: A comparative study

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Abstract

Background: Post dural puncture headache (PDPH) is a common complication of spinal anaesthesia. Median and paramedian approaches are used for spinal anaesthesia. Incidences of PDPH is more common among parturients due to hormonal effect leading to thining of Ligamentum Flavum.

Objectives: To compare the incidence of post dural puncture headache in parturients undergoing caesarean section under spinal anaesthesia using median and paramedian approaches.

Materials & Methods: This was a prospective, observational study, carried among 60 parturients undergo caesarean section under spinal anaesthesia at Dhaka National Medical Institute Hospital, Dhaka from May 2018 to April 2019. Patients were randomly allocated into two equal groups of thirty patients each, where Group M received spinal anaesthesia with median approach and Group P received spinal anaesthesia with paramedian approach. Incidence of PDPH, intensity of headache, complication of PDPH (nausea, vomiting, coughing) for a period of 3 days postoperatively. Haemodynamic parameters, heart rate, systolic and diastolic blood pressure were recorded for 10 minutes interval during operative procedure.

Results: Among 30 patients of Group M, mean age was 26.53 ± 5.9 years, height was 151.27 ± 3.8 cm and weight was 63.77± 9.5 kg, while in Group P mean age was 27.00 ± 6.2 years, height was 152.10 ± 4.7 cm and weight 62.97± 9.1 kg. In median approach (Group M), 2 patients (6.6%) had PDPH; whereas in paramedian approach (Group P), 3 patients (10%) had PDPH and the difference was statistically insignificant (P-value=0.64). Regarding other complications, in Group M, 3 patients (10%) developed nausea, while in Group P, 4 patients (13.33%) complained nausea. 1 patient (3.33%) in Group M had vomiting, while 2 patients (6.67%) had vomiting in Group P. But the difference was not significant statistically.

Conclusion: There is no statistically significant difference regarding the incidence of PDPH between median and paramedian approach among parturients undergoing caesarean section.

Keywords: Post dural puncture headache, caesarean section, spinal anaesthesia, median approach, paramedian approach.

Introduction

Spinal anaesthesia or subarachnoid block (SAB), the first major regional technique evolved at the end of 19th century,[1] remains one of the most popular forms of anaesthesia, particularly for surgery involving the lower abdomen, lower extremities and the perineum.[2] Most of the caesarean sections are done by spinal anaesthesia because of its advantages like dense block, simplicity, ease of performance, requirement of minimum apparatus, avoidance of airway manipulation, reduces the metabolic stress response to surgery, reduction in blood loss, has minimal effect on blood biochemistry, ensures optimum level of arterial blood gases, patient remains conscious during surgery, requires minimal postoperative care and analgesia, decrease in the incidence of venous thromboembolism.[3,4] Although major complications are rare but possess risk of hypotension, bradycardia, cardiac arrest, intraoperative discomfort, post dural puncture headache and neurologic toxicity.[5,6]

Since introduction of spinal anaesthesia, post dural puncture headache (PDPH) has remained as a major complication. Post dural puncture headache presents as a dull throbbing pain with a frontal-occipital distribution, headache develops within 5 days after dural puncture, mostly within 48-72 hours and

disappears spontaneously within 1 week, or up to 48 h after an epidural blood patch. The headache may be accompanied by neck stiffness, tinnitus, hypoacusia, photophobia, and nausea, and typically the headache is aggravated by sitting or standing, and is reduced by lying down.[7,8] The actual mechanism producing the headache is unclear. There are two possible explanations. First, the decrease in CSF pressure may cause traction on the pain-sensitive intracranial structures in the upright position, leading to the characteristic headache. Secondly, the loss of CSF may produce a compensatory vasodilatation.[9,10] Causes reported to influence the incidence of PDPH are age, sex, pregnancy, previous history of headache (migraine, tension or cluster headache), previous history of PDPH, needle tip shape, needle size, bevel orientation, number of lumbar puncture attempts, median versus paramedian approach, type of local anesthetic solution and clinical experience of the person operating the procedure.[11-17] The parturients are at particular risk of PDPH because of their sex, pregnancy, and the widespread application of spinal anaesthesia. [18,19]

Spinal anaesthesia can be achieved either median or paramedian approach. For most patients, the median approach is faster, easy to administer and less painful.[20] The paramedian approach is a useful technique that allows for successful identification of the subarachnoid or epidural space, especially in difficult cases, in obese patients, in pregnant patients and in geriatric patients. The median approach involves passage of the needle through supraspinous, interspinous ligaments and ligamentum flavum, while the paramedian approach avoids supraspinous and interspinous ligaments and hits ligamentum flavum directly after passing through paraspinal muscles.[21, 22] Researchers around the world conducted several studies to compare the median and paramedian approach regarding the incidence of PDPH but yet now no consensus is achieved.[23-27] So current study was done to compare the incidence of post dural puncture headache among parturients undergoing caesarean section under spinal anaesthesia using median and paramedian approach.

Material & Methods

Place and duration of the study

This was a Prospective Observational study, conducted in Dhaka National Medical Institute Hospital, Dhaka from May 2018 to April 2019

Procedure

This study was carried out with patients who undergo caesarean section under SAB in Dhaka National Medical Institute Hospital, Dhaka according to inclusion and exclusion criteria. During pre-anesthetic assessment, every patient underwent thorogh physical examination with ASA classifications. Total anaesthetic procedure was explained and informed consent was taken from the participants of the study.

Age eligibility for study: 18-45 years old (child bearing age)

Genders eligibility for study: Female

Screening method: The preliminary screening panel for each patient was included the complete history, physical examination and the necessary laboratory tests.

Inclusion criteria:

1. ASA class I & II
2. Patients agree to participate in the study signing an informed written consent

Exclusion criteria:

1. Patient with psychiatric disorder
2. Patient with cluster headache, tension headache, H/O migraine or any chronic headache
3. Previous H/O of PDPH
4. Patient with chronic pain e.g. chronic low back pain
5. More than one dural puncture
6. Patient with preeclampsia, eclampsia
7. Patient with neurological disorder
8. Abnormalities of vertebral column
9. ASA class III and IV
10. Coagulopathy

Sixty (60) patients, scheduled for Caesarean section under spinal anaesthesia were included in this study. They were divided into two groups (Group M- received spinal anaesthesia with median approach and Group P received spinal anaesthesia with paramedian approach) of thirty patients each.

Intravenous access was established with 18 G cannula. Premedication was done with intravenous (IV) Ranitidine 1mg/ kg body wt and Ondansetron 0.1 mg/ kg body wt was given just before anaesthesia followed by preloading with 15-20ml/kg. Lactated ringers solution. Standard monitoring (ECG, non-invasive blood pressure, and pulse oxymeter) was done. Under full aseptic precaution, spinal anaesthesia was carried out in sitting position at lumbar 3-4 inter space using 25 G Quinke's spinal needle. The bevel of the spinal needle

was kept lateral, so that the dural fibers were splitted rather than cut due to longitudinal arrangement of the dural fiber. The spinal anaesthesia was given in the following technique, [28]:

i) Median approach: The patient is placed in the sitting position. A stool/bench was provided as a footrest and a pillow placed on the lap. The patient is maintained in a vertical plane while the patient's neck was flexed and the patient's lower back pushed out. The needle was inserted below the lower edge of the spinous process of the selected upper vertebrae. After successful puncture 10 mg of 0.5% Inj. Bupivacaine heavy was used to achieve spinal anaesthesia.

ii) Paramedian approach: A skin wheal is raised 1 cm lateral and 1 cm caudal to the L4 spinous process. A longer needle is used to infiltrate deeper tissues in a cephalomedial plane. The spinal needle was inserted 10 to 15 degrees off the sagittal plane in a cephalomedial plane. Once the cerebrospinal fluid (CSF) was obtained after ligamentum flavum punctured, 10 mg of Inj. Bupivacaine heavy was injected to achieve spinal anaesthesia.

iii) In both Group: The level of analgesia and time to achieve were noted. After the block was administered, supine position was given and a wedge was placed to tilt the patient towards left side. In both the approaches, maximum of three attempts at L3-L4 space done. If not successful, the L4-L5 space was selected.

After the surgical procedure was done, the patient was shifted to postoperative care unit. The patients were observed for PDPH in post-operative period. Severity of the headache was measured by Visual Analogue Scale (VAS). The severity was defined as mild, moderate, and severe according to VAS (0–10), where 0 = no headache, 1–3 = mild headache, 4–7 = moderate headache, >7 = severe headache. Post dural puncture head was defined as headache developed within 6-72 hours from the day of spinal anaesthesia, increased with sitting or standing position and relieved or reduced in intensity by lying down.29 PDPH was managed by advising the patient to lie down, drink plenty of fluids and coffee and with analgesics (Paracetamol or Tramadol). Data were collected regarding age, height, weight, type of approach, pulse, blood pressure (just before spinal anaesthesia, immediately after spinal anaesthesia, 3 minutes after spinal anaesthesia, 5 minutes after spinal anaesthesia, 10 minutes after spinal anaesthesia and 20 minutes after spinal anaesthesia), PDPH, intensity of headache, complication of PDPH (nausea, vomiting, coughing), ambulation of the patient, posture of the patient.

Statistical analysis

Data was compiled, presented and appropriate statistical test was done in this study for drawing an appropriate conclusion. Quantitative variables, i.e., age, height, weight, pulse, blood pressure and VAS score were calculated as mean ± SD. Qualitative variables such as PDPH, intensity of headache, complication of PDPH (nausea, vomiting, coughing) were presented as percentage. Students' unpaired t-test was applied for comparison of quantitative variables in both groups. Chi-square test was applied for comparison of qualitative variables in both groups. $P<0.05$ was considered statistically significant.

Observation and Results

Comparison of mean age, height and weight are presented in Table-1, and there were no significant difference between two groups.

Table-I: Demographic characteristics

Variable	Group-M	Group-P	P-value
Age (years)	26.53 ± 5.9	27.00 ± 6.2	0.77
Height (cm)	151.27 ± 3.8	152.10 ± 4.7	0.46
Weight (kg)	63.77 ± 9.5	62.97 ± 9.1	0.74

Data expressed as mean (SD) and analysed students unpaired't' test, $P<0.05$- Significant

Table-II: Incidence of PDPH

Incidence of PDPH	Group-M (n=30)	Group-P (n=30)	P-value
Mild headache	1 (3.3%)	1 (3.33%)	-
Moderate headache	1 (3.3%)	1 (3.33%)	-
Severe headache	0 (0.00%)	1 (3.33%)	-
Total	2 (6.6%)	3 (10%)	0.64

Data analyzed using Chi square test, $P<0.05$- Significant

In Group M, 2 (6.6%) patients developed mild to moderate postdural puncture headache of which no incidence of severe headache. On the other hand, 3 (10%) patients of Group P developed postdural puncture headache. There was no significant difference between two groups.

Table-III: Incidence of adverse effects

Incidence of adverse effects	Group-M (n=30)	Group-P (n=30)	P-value
Nausea	3 (10%)	4 (13.33%)	0.69
Vomiting	1 (3.33%)	2 (6.67%)	0.55
Coughing	0 (0.00%)	0 (0.00%)	-

Data analyzed using Chi square test, $P<0.05$- Significant

In Group M, 3 (10%) patients developed nausea and 1

(3.33%) patient developed vomiting. On the other hand, 4 (13.33%) patients of Group P developed nausea while 2 (6.67%) patients vomiting, and regarding these adverse effects, two groups were statistically insignificant (P value 0.69 and 0.55). There was no incidence of coughing in studied groups.

There was no significant change in pulse and bloood pressure (systolic and diastolic) in any patient of both groups.

Discussion

Post dural puncture headache (PDPH) is a common complication of spinal anaesthesia. Because of female gender, young age, pregnancy and widespread use of spinal anaesthesia, parturients undergoing caesarean section are more prone to develop PDPH. PDPH has a negative impact on quality of life, patient satisfaction, the postpartum experience with the mother's inability to bond with and care for her baby and it delay discharge of the patient. Therefore, it is necessary to prevent or decrease its incidence and severity. Current study was conducted to compare the incidence of PDPH with spinal anaesthesia using median & paramedian approach in patients undergoing caesarean section.

In this study, incidence of PDPH was 6.6% in median group, while 10% in paramedian group and difference was not statistically significant. This finding was similar to studies conducted on parturients women undergoing caesarean section.[27-30] Our findings are different from study conducted by Haider et al as authors concluded that paramedian approach reduces the incidence of PDPH.[23] The reason could be due to the identical tearing of the longitudinal dural fibers. Alternatively, despite having a different angle, due to the cylindrical shape of the dura, the orientation of the needle insertion might be the same.[24]

Although results were insignificant, incidence of PDPH is more frequent with paramedian approach and corresponds with study conducted in one developing country.[27] But the incidence is higher than other studies conducted on obstetric patients[26,29] On the other hand, in median group, 6.6% patients developed PDPH which is similar to two recent studies.[29,26]

Conclusions

It can be concluded that there is no statistically significant difference between median and paramedian approach for SAB regarding the incidence of post dural puncture headache among parturients. It should be mentioned that median apporach is more easier than paramedian apporach & commonly used technique. But paramedian apporach can be used in difficult cases like obese patients.

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Original Article

Correlation between serum ferritin, serum iron and blood glucose level in patients of type 2 diabetes mellitus

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Abstract

Background: Diabetes Mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Ferritin is a ubiquitous intracellular protein complex that reflects the iron stores of the body. Many cross-sectional studies indicate that increased body iron stores have been associated with the development of glucose intolerance, type 2 diabetes,metabolic syndrome. This study was carried out to find out the relationship between serum ferritin, serum iron and type 2 diabetes and to see the influence of body iron storesand blood glucose.

Methods: This study includes 81 patients suffering from type 2 diabetes and compared with controls at BIRDEM General Hospital. Serumferritin ,serum iron andFasting Blood Sugar (FBS)were measured.

Results: Serum ferritin was significantly higher ($p<0.0001$) in the patients suffering from type 2 diabetes. The levels of serum ferritin were positively correlated with values of FBS.

Conclusions: There is a positive association between elevated iron stores measured by serum ferritin levels, serum iron and type 2 diabetes mellitus.Theassociation of age category of study groups with serum ferritin were also seen.

Keywords: Type 2 diabetes mellitus, serum ferritin, serum iron and FBS.

Introduction

Diabetes Mellitus (DM) is a group of common metabolic disorders that share the phenotype of hyperglycemia. Depending on the etiology of diabetes mellitus, factors contributing hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production.[1] It has been suggested that in the diabetic patients a positive correlation between increased serum ferritin and glycaemic level.[2]

Increased ferritin may induce diabetes through a variety of mechanisms including oxidative damage to pancreatic beta cells, impairment of hepatic insulin extraction by the liver and interference with insulin's ability to suppress hepatic glucose production.[3]

It's also observed that ferritin levels correlated with individual components of the metabolic syndrome particularly serum triglycerides and plasma glucose as well as markers of insulin resistance.[4]

Thus present study is designed to evaluate the correlation between serum ferritin and glycaemic control in patients of type 2 diabetes mellitus which will help to understand the significance of ferritin for the better management of type 2 diabetes mellitus.

Methods

The study was designed as a case control study. The study was conducted over a period of January 2018 to January 2019. In the present study 81 cases of known type 2 diabetes mellitus, they were primarily diagnosed by clinical examination and further evaluated by biochemical investigationsand 82 apparently healthy subjects as a control group were studied.

All cases were selected from the patients attending Out Patient Departments of BIRDEM General Hospital and the control subjects were selected randomly. Consent was taken from all the participants.

To find out the influence of body iron stores on biochemical parameters diabetics underwent the following investigations: Serum Ferritin, serum iron and blood glucoseamong the age groups ranging from20 to 50 years old type 2 diabetic patients.

Data collection

A detailed proforma was filled up for each patientwhich included age, sex, past history of coronary artery disease, cerebrovascular accident, history of hypertension.

The age of onset and duration of diabetes was recorded. Also recorded was treatment history of patient whether on oral hypoglycemic agents, insulin or diet control alone.

Serum ferritin was done by Enzyme-Immunoassay (EIA) for the quantitative determination. For this ferritin estimation in human serum store at 20° C to 8o° C. (Ref white, .D., Kramer, D., Johndon, G., Dick. F and Hamilton, H. Am. J. Clin. Path. 72-346;1986). Normal reference range for serum ferritin isfor male 16.4 -323.0 ng/ml and for female 6.9 – 282.55 ng/ml.Serum iron was done by reagent kit which containguanidinium hydrochloride and hydroxylamine (cat. No 1-419-0150).Refference of normal rangeserum iron is for men 59 - 158µg/dl and female 37-145µg/dl.

Serum fasting glucose were estimated by glucose oxidase(GOD) enzymatic method(Ref Kaplan L.A. Glucose Kaplan A et al. ClinChem The C.V Mosby Co. St Lois Torento. Princeton 1984; 1032-1036.).Blood sample was collected from patients after an overnight (8-12hr) fasting.

Statistical analysis was done using SPSS software.

In data analysis, comparison of all parameters between control and study group was carried out by applying unpaired t-test and correlation with serum ferritin, serum iron and FBG.In the present study the Mean ± SD of age in study group was 44.68 ± 6.68 years as compared to 34.71 ± 7.86 in control group.

Result

Table-1: Comparison of biochemical parameters between case and control groups

Case Control	N	Mean	Std. Deviation	Std. Error Mean	t	p
Age(yr)						
Case	81	44.68	6.68	.742	8.72	.000
Control	82	34.71	7.86	.868		
Serum ferritin						
(ng/ml)	81	300.07	244.68	27.19	1.98	.050
Case	82	221.49	261.85	28.92		
Control						
Serum iron						
(µgm/ml)						
Case	81	223.26	225.19	25.02	4.08	.000
Control	82	116.47	73.97	8.17		
FBS						
(mmol/l)						
Case	81	9.26	5.98	.66	6.71	.000
Control	82	4.73	1.27	.14		

Note: *p<0.05 – significant; **p<0.001 - highly significant; #p≥0.05 - not significant

Table-2: correlation of serum ferritin with other biochemical parameters in study groups

Name of parameter	Mean value	Two tailed P value	Pearson coefficient (r)
Serum ferritin	300.07	P<0.00001	0.600
Case	221.49		
Control			
Serum iron	223.26	P<0.0001	0.526
Case	116.47		
Control			
FBS	9.26	P<0.0001	0.701
Case	4.73		
Control			

Serum ferritin (r=0.600, p<0.0001), serum iron (r=0.526, p<0.0001), FBS (r=0.701, p<0.0001).

Above table shows the positive correlation between Ferritin, serum iron and FBS respectively.

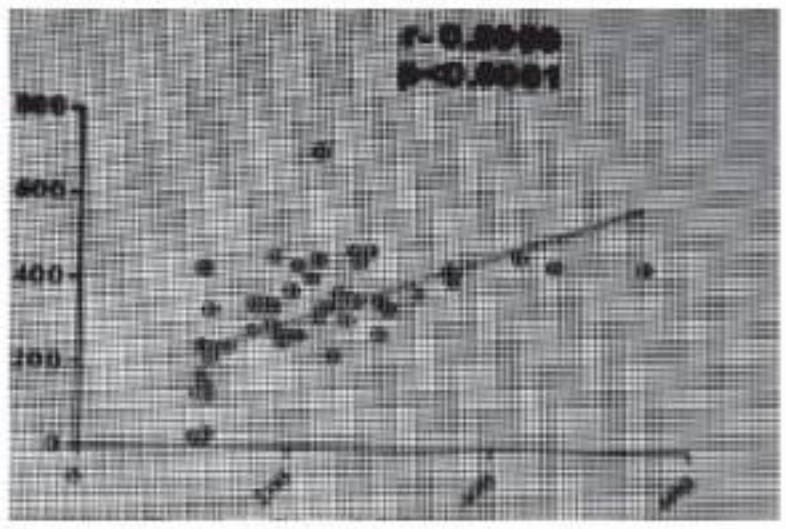

Fig: Shows correlation of serum ferritin blood sugarlevel with fasting

Discussion

It's obvious evident from the study that increased body iron stores reflected by Serum Ferritin levels had a statistically significant directly proportional correlation with FBS.

There is an increasing concern about the relationship between iron stores and type 2 diabetes with the evidence that elevated serum ferritin levels were independently predicted incident of type 2 diabetes in studies among apparently healthy men and women.[4]

Ferritin is an iron-phosphorus-protein complex that is a biomarker for evaluating body iron contents.Tissue and organ damage occurs when iron concentrations are elevated.[5] Increased accumulation of iron affects insulin synthesis and its secretion from the pancreas and interferes with the insulin-extracting capacity of the liver. Iron deposition in muscle decreases glucose uptake because of muscle damage.

Conversely, insulin stimulates cellular iron uptake through increased transferring receptor externalization. Thus, insulin and iron can mutually potentiate their effects leading after a vicious cycle to insulin resistance and diabetes.[6] Our findings are in agreement to by Rui Jiang among type 2 DM cases who reported the mean concentration of Ferritin were significantly higher in study group as compared to control subjects.[7]

It's evident from the study that ferritin levels were positively correlated with FBS. Similar study conducted by Sumeet Smotra et al.[8] and Jeevan K. Shetty et al.[9] found increased levels of Serum Ferritin and also reported that diabetics with increased level of Serum Ferritin had significantly poor glycaemic control reflected as compared to diabetes cases under good glycaemic control and healthy controls.

Positive correlation between FBS with serum ferritin and serum iron indicate hyperglycemia causing increased glycation of hemoglobin and increased release of free iron from glycated proteins like hemoglobin. This makes a vicious cycle of hyperglycemia, glycation of hemoglobin and increase in levels of free iron and ferritin. This increased presence of iron pool will enhance oxidant generation leading damage to biomolecules.[9]

In the present study, ferritin levels were significantly higher in patients of type 2 DM (300.o7 ± 244.68 vs. 221.49± 261.85ng/ml, p<0.0001) as compared to controls (Table 1) which were consistent with the reports published by F. Sharifi and colleagues. They concluded that the ferritin (101 ± 73 mg/ml vs. 43.5 ± 42 mg/ml, p<0.001) were significantly higher in patients of type 2 diabetes as compared to control subjects.[7]

Our findings are in agreement to by Rui Jiang among type 2 DM cases who reported the mean concentration of Ferritin were significantly higher in study group as compared to control subjects.[7]

Conclusion

Our findings suggest that iron overload reflected by increased serum ferritin and serum iron levels has the potential role in the development of type 2 diabetes. Therefore, in agreementwith previous studies we suggest that serum ferritin and serum iron should be included in standard screening protocol to identify patients who are at risk of developing type 2 DM and also to assess the glyacemic control in patients who have already developed the disease.

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Original Article

Pretreatment with intravenous Magnesium Sulphate reduces incidence of Succinylcholine induced Postoperative Myalgia among patients undergoing elective surgery under General Anaesthesia-A Prospective study

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Abstract:

Background: Succinylcholine is the most commonly used depolarizing muscle relaxant for endotracheal intubation. The most common side effect of succinylcholine is postoperative myalgia which is distressing to the patient.

Aim of study: This study was designed to evaluate effectiveness of intravenous magnesium sulfate in reducing the incidence of succinylcholine induced postoperative myalgia.

Materials and Methods: 80 (Eighty) adult patients of ASA grade I and II of both sexes for elective surgery under general anesthesia were randomly allocated into two equal groups, magnesium sulfate group and normal saline as placebo group. The patients of magnesium sulfate group were pretreated with magnesium sulfate 40 mg/kg body weight in 10 mL volume, while patients of normal saline (placebo) group were given isotonic saline 0.9% in the same volume (10 mL) intravenously slowly over 10 minutes. Premedication was done by injecting 1.5 mg/kg of fentanyl in iv route. Thereafter, anaesthesia was induced in all patients, by 2 mg/kg of propofol intravenously. Following the loss of eyelid reflex, 1.5 mg/kg of succinylcholine was injected intravenously as a muscle relaxant and then the patients were intubated. The incidence and severity of myalgia were assessed by a blinded observer 24 hours after surgery.

Results: Postoperative myalgia recorded immediately in the postoperative ward and upto 48 hours of postoperative period. Postoperative myalgia were recorded in magnesium sulfate group with 15 (37.5%) patients and 27 (67.5%) patients in normal saline (placebo) group respectively which was statistically significant.

Conclusion: Pretreatment with intravenous Magnesium sulfate 40 mg/kg reduces the incidence of succinylcholine-induced postoperative myalgia using Propofol as induction agent.

Key words: Magnesium Sulfate, Succinylcholine, Propofol, Postoperative Myalgia.

Introduction

Succinylcholine is a depolarizing skeletal muscle relaxant that remains the accepted standard for facilitating endotracheal intubation in many countries.[1] This medication may cause some adverse effects in patients such as increased levels of creatinine kinase (CK) and potassium in blood,[2] apnea, malignant hyperthermia, increased intraocular pressure and increased intracranial pressure,[3,4] emesis with aspiration,[3] fasciculation during induction and postoperative myalgia.[3,5]

Although postoperative myalgia is minor adverse effect of succinylcholine, this may be very unpleasant experience for the patient till 24–48 h after surgery.[5,6] To decrease the rate of fasciculation and postoperative myalgia various methods have been tested. For example, use of Vitamin C,[7] ketamine and propofol,[8,9] calcium gluconate,[10] lidocaine,[11] magnesium sulfate,[9] diclofenac,[12] benzodiazepines,[13] thiopentone,[14] dexmedetomidine,[15] remifentanil,[16] isoflurane,[17] and non-depolarizing neuromuscular blocking agents.[18]

Propofol has also been identified to be a better agent than thiopentone sodium to control succinylcholine -induced myalgia. 19 This study was designed for induction of anesthesia with propofol, after pretreatment with magnesium sulfate to assess the

effect on incidence and severity of succinylcholine-induced postoperative myalgia. Magnesium affects the neuromuscular junction and competes with calcium at prejunctional site. These both ions antagonize each other—high magnesium concentrations inhibit release of acetylcholine, while high calcium concentration increases the release of acetylcholine from the presynaptic nerve terminals.[20] This may explain the control of succinylcholine-induced fasciculation and myalgia by magnesium.

Materials and Methods

This is a randomized controlled double blind study conducted from May to July 2018 in a private clinic named Health Care Pvt. Ltd., Ranking Street, Wari, Dhaka. All 80 adult patients were randomly allocated into two equal groups, magnesium sulfate group was designated as group I and normal saline (placebo group) as group II. The inclusion criteria were American Society of Anesthesiologists (ASA) physical status I and II, need for general anesthesia with endotracheal intubation, not being addicted to any drugs, being 20–50 years of age. The exclusion criteria were hepatic or renal impairment, cardiac ischemia, pulmonary, neuromuscular or metabolic diseases and pregnancy. All participants provided written consent to participate in the study.

Preoperative evaluation included medical history, physical and upper airway examination. A complete blood test, renal function tests, liver function tests and electrocardiogram were conducted on all patients. Routine monitoring like pulse oxymetry ,NIBP ,ECG was conducted after patients arriving in operating room with a monitor. A 20 G cannula was inserted to the dorsum of left hand of the patient and Ringer's Lactate solution was started at a rate of 100ml/hour. The patients of magnesium sulfate group were pretreated with magnesium sulfate 40 mg/kg body weight in 10 ml volume, while patients of normal saline (placebo) group were given isotonic saline 0.9% in the same volume (10ml) intravenously slowly over 10 minutes. Premedication was done by injecting 1.5 mg/kg of fentanyl in iv route. Thereafter, anaesthesia was induced in all patients, by 2 mg/kg of propofol intravenously. Following the loss of eyelid reflex, 1.5 mg/kg of succinylcholine was injected intravenously as a muscle relaxant and then the patients were intubated. The maintenance of anesthesia was continued using a mixture of oxygen, nitrous oxide, halothane and vecuroneum as muscle relaxant. At the end of the surgery, muscle relaxation was reversed using neostigmine and atropine. After the desired spontaneous ventilation, the patients were extubated. The patients were transferred to the recovery room and later in the ward.

The incidence and severity of succinylcholine induced postoperative myalgia in the patients were determined 24 hours after surgery by an anesthesiologist who was unaware of the grouping.. Postoperative myalgia (POM) is defined as "a pain with no surgical interference" and is graded based on Kararmaz et al's2 four-point scale as follows:

0= no muscle pain.
1= muscle stiffness limited to one area of the body.
2= muscle pain or stiffness noticed spontaneously by a patient who requires analgesics.
3= incapacitating generalized, severe muscle stiffness or pain.

Statistical Analysis

Date was summarized as mean ± SD. Unpaired t-test was applied for quantitative data and Chi-square test for qualitative data. P value < 0.05 was taken as significant.

Results

There was no significant difference in terms of age, body weight, sex and ASA status between the groups (Table I). In group I fifteen (37.5%) out of the 40 patients had postoperative myalgia (POM), whereas 27 (67.5%) out of the 40 patients had POM in group II ($P<0.05$). Grade 1 POM was lower number of patients in group I when compared with group II (11 versus 18; $P<0.05$). Grade 2 POM was also lower number of patients in group I when compared with group II (4versus 9; $P<0.05$) and there was no grade 3 POM in any of the two groups (Table II). The baseline values of systolic and diastolic blood pressure and heart rate in both groups were similar and there was no any adverse effect.

Table-I: Comparison of demographic data between the groups

Parameter	Group I (Magnesium sulfate group) n=40	Group II (Saline group) n=40	P-value
Age in year (mean±SD)	34.58±9.47	35.28±9.26	p>0.05
Weight in kg (mean±SD)	55.27±7.42	54.43±7.32	p>0.05
Sex (M/F)	24/16	23/17	p>0.05
ASA status I/II	38/2	37/3	p>0.05

Table II: Incidence and severity of postoperative myalgia

Postoperative myalgia (POM)	Group I (Magnesium sulfate group) n=40	Group II (Saline group) n=40	P-value
Incidence of myalgia number (%)	15 (37.5%)	27 (67.5%)	p<0.05
Grading of myalgia number (%)			
0	25 (62.5%)	13 (32.5%)	p<0.05
1	11 (27.5%)	18 (45%)	p<0.05
2	4 (10%)	9 (22.5%)	p<0.05
3	0	0	-

Discussion

Succinylcholine is a depolarizing muscle relaxant drug with unique status in clinical practice because it quickly and acceptably relaxes muscles followed by spontaneous recovery. Despite its limitations and side effects, succinylcholine is still a drug of choice for endotracheal intubation in operating rooms. Postoperative myalgia is an adverse effect of succinylcholine that may be a very unpleasant experience for patients.

Pretreatment with various drugs have been tried to reduce these side effects. Magnesium sulfate was tried to decrease the postoperative myalgia in the present study. The findings of present study shows, in group I (magnesium sulfate group) fifteen (37.5%) out of the 40 patients had postoperative myalgia (POM), whereas 27 (67.5%) out of the 40 patients had POM in group II (saline group) (P<0.05). Grade 1 POM was lower number of patients in group I when compared with group II (11 versus 18; P<0.05). Grade 2 POM was also lower number of patients in group I when compared with group II (4 versus 9; P<0.05) and there was no grade III POM in any of the two groups.

Raman A et al.[21] used 40mg/kg magnesium sulfate as pretreatment before induction with propofol and observed the incidence of myalgia to be 40% in magnesium sulfate group as compared to 86.6% in the control group (p<0.05). Present study shows myalgia in magnesium group is 37.5% which is comparable to Raman A et al's study who found 40% myalgia in magnesium group.

Kumar Met al.[9] reported 30% postoperative myalgia in control group compared to none in magnesium sulfate group.Ursekar Ret al[22] reported no significant difference in postoperative myalgia between control group and the group receiving magnesium sulphate. The present study is supported by the study of McClymont C[19] who found significantly lower incidence of suxamethonium myalgia (19%) compared with thiopentone group (63%) (P<0.05) using magnesium sulfate as pretreatment. Stacey MR[23] et al noticed no significant difference in the effect of magnesium sulfate on succinylcholine-induced myalgia. Incidences were similar in both the groups.The difference may be due to the fact that in the above study, thiopentone sodium was used as an induction agent, whereas in present study, propofol was used. The lower incidence of myalgia maybe due to synergistic effect of propofol and magnesium sulfate.

Conclusion

Pretreatment with intravenous Magnesium sulfate 40 mg/kg reduces the incidence of succinylcholine-induced postoperative myalgia using Propofol as induction agent.

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Original Article

Evaluation of complications of laparoscopic cholecystectomy in a single centre experience

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Abstract:

Background: Laparoscopic cholecystectomy first introduced by Muhe in 1985 followed by Muret in1987, it is becoming more popular and now it is gold standard for symtomatic gallstone disease.

Objective: To determine the complication of Laparoscopic cholecystectomy in our series.

Materials and Methods: A total 150 patients with gallstone disease whose wall thickness of gallbladder were 3mm were selected for Laparoscopic cholecystectomy, Acute cholecystitis, choledocholithiasis, obstructive jaundice, Gallbladder mass or dilated CBD, were excluded. Details histroy, physical examination, and relevant investigation were done (including LFT, HbsAg, Anti HCV) and patients were checked for anesthesia fitness, then laparoscopic cholecystectomy were done, operative finding and outcome observed.

Results: Among 150 patients there were 126patients were female and 24 patients were Male, age ranges from 16 to 65 yrs. Laparoscopic cholecystectomy were done successfully in 140 patients (92%) and conversion done in teen patients(6.6%). Major complications were seen in five (3.3%) patients, including common bile duct (CBD) injury in two patients, duodenal injury in one patient, bleeding from gall bladder bed in two patients. There was no mortality in the study.

Conclusion: Laparoscopic cholecystectomy is a safe and effective treatment for gallstone disease.

Key Words: Gall stone, Lapparoscopic cholecystectomy, morbidity, mortility.

Introduction

Gall stone disease is a major health problem world wide, particularly in the adult population.[1] Laparoscopic cholecystectomy has becoming the gold standard treatment for benign gall bladder disease.[2] Laparoscopic cholecystectomy is defined as removal of gallbladder through a keyhole size incision being the traditional procedure using two 10mm ports and two 5mm ports, but it can be done with 3 ports. Which is associated with less post operative pain and better anesthetic results.[3] With increasing expertise and technological development laparoscopic procedure become safer.[4]

Material and Methods

This prospective observational study was carried out in the surgery department in Dhaka national medical college hospital (DNMC) from November2016 to october2018 over period of two years. In this study total 150 patients with gall stone disease where wall thickness of gall bladder were 3mm were selected for laparoscopic cholecystectomy. Acute cholecystitis, choledocholithiasis, obstructive jaundice, gall bladder mass or dilated CBD were excluded. Detailed history, physical examination and all relevant investigations were done also viral marker and patients were checked for anesthesia fitness, then laparoscopic cholecystectomy were done, operative finding and outcome observed for two year.

Age of the patients

Age	Number of patients	Percentage
<20	10	6.66
21-40	70	46.6
41-60	50	33.3
>60	20	13.3

Sex of the patients

Age	Number of patients	Percentage
Male	24	16
Female	126	84

Major complication

Complication	Management
CBD injury 2 (two) cases.	Repair of CBD with placement of T tube.
Bleeding from Gall bladder bed 2(two) cases.	Conversion to open procedure and haemostasis done, then kept a drain in hepatorenal pouch.
Duodenal injury 1 (one) case.	Conversion to open procedure and then repair and kept two drain.

Minor complication

Complication	Management
Gall bladder perforation 15 (fifteen) cases.	Irrigation, suction and stone removed
Haemorrhage at Calot's triangle 10 (ten) cases.	Haemostasis, secured with clip.
Port site infection 5 (five) cases.	Appropriate antibiotics after C/S.

Results

Out of 150 patients, 126 (84%) were female and 24 (16%) were male, giving rise to a female to male ratio 5:1. The age range from 16 to 65 yrs, mean age being 40-45 yrs. Majority were in 4th (46.6%) and 5th (33.3%) decade of life. Two (1.3%) had diabetes mellitus, Ten (6.6%) had hypertension, 3 (2%) had ischemic heart disease and 135 (90%) had no co-morbidity for anesthesia or surgery. Majority of the patients (70%) had multiple stones, and 30% had single stones. Laparoscopic cholecystectomy were done satisfactory in 140 (92%) patients and conversion done in 10 (6.6) patients. Major complications were 5 patients, like bile duct injury were 2 cases (1.3%), duodenal injury was one patient, bleeding from gallbladder bed 2 (1.3%) patients, and others are due to dense adhesions and other minor injury also occurs like gallbladder perforation, port site infections.

Discussion

Laparoscopic cholecystectomy has gained favour among surgeons and popularity among the patients as it offers minimal surgical trauma, reduced hospital stay and early resumption of normal activity.[5] This study aims at assessing the complication of laparoscopic cholecystectomy. Sometimes complication in laparoscopic cholecystectomy are seen during the creation of the pneumoperitonium i.e while introducing the veress needle and insertion of trocars, which can directly damage the internal structure.[5, 6] These complications were not seen in our study, we introduced trochar and cannula through the umbilicus after neke over the umbilicus by BP handle with blade 11, we used artery forcep for clear the umbilical tissue. In our study female to male ratio 5:1 which is in accordance to Francesco (2003) showing increase incidence of calcular disease in female[7, 8]. In our study the incidence of conversion from laparoscopic cholecystectomy to open cholecystectomy was 6.6% while peter[9] reported an incidence of 14% mostly due to difficult dissection secondary to inflammation or dense adhesion. In our study CBD injury was 1.3% while the incidence of CBD injury reported by Mahatharadol[10] 0.59%, Ahmed[11] 1%, which are similar to our study. In our study there was one duodenal injury (.6%) which was recognized per operative and repaired by open surgery. Singh[12] reported duodenal injury in .17% of patients. In our study gallbladder perforation with bile leakage occurs in 15 (10%) cases, then irrigation and suction done. In four cases (2.6%) spillage of gall stone occurs, which were removed from abdominal cavity by 10mm wide bore cylindrical metallic tube through the epigastric port after removal of epigastric cannula successfully. In study of 1100 LCS, Arain's reported gall bladder perforation and bile leakage in 9.8% and spillage of the stone 3.9%.

Conclusion

Laparoscopic cholecystectomy is a safe and effective procedure in our set up to the accepted standard as compared to national and international studies. Proper training of the young surgeons is necessary and equipments are essential for good surgical outcome.

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Original Article

Evaluation of different presentation and outcome of Ectopic Pregnancy

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Abstract:

Background: An ectopic pregnancy occurs outside the uterus and is a relatively common condition among women of childbearing age. Most ectopic pregnancies occur in the Fallopian tube (so-called tubal pregnancies), but implantation can also occur in the cervix, ovaries, and abdomen.

Objective: To evaluate different presentation and outcome of ectopic pregnancy.

Material and Methods: This study was undertaken among the patients admitted in the Department of Obstetrics and Gyrtaecology, Dhaka National Medical College Hospital, Dhaka during the period from October 2017 to March 2018. Clinical evaluation of cases of ectopic pregnancy in terms of sociodemographic factors, presentations, risk factors, examination findings, per operative findings and management offered to the patients.

Results: Most of the patients were 20-30 years age group and mean age was 28.08±4.24 years. Commonest presentation was lower abdominal pain (94%), amenorrhoea (100%), P/V bleeding (38%) and syncopal attack (48%). Previous history of abortion/MR (50%), history of pelvic infection (30%) and history of D&C (16%) constitute the main bulk of risk factors. Most of the patients managed by laparotomy followed by salpingectomy which is still the standard treatment in many cases.

Conclusion: Study has found that previous abortions are major etiological factor for ectopic pregnancy than previous pelvic infection. Most of the patients were managed by laparotomy. The general public should be made aware the sign and symptoms of ectopic pregnancy. Proper and modern diagnostic tools and training programme for these should be made available in all tertiary level hospital.

Keywords: Ectopic Pregnancy, Fallopian tube.

Introduction

Ectopic pregnancy is a condition where the fertilized ovum gets implanted and develops in a site other than normal uterine cavity. It presents a major health problem for women of childbearing age. Given the potential mortality & reduced subsequent fertility associated with this condition, the trend toward increased ectopic pregnancy is of serious concern.[1] Over the last few decades, the incidence of ectopic pregnancy has increased almost to the extent of an epidemic disease. Ectopic pregnancy is one of the commonest acute abdominal emergencies.[2,3,4]

The most common sites of Ectopic pregnancies are Fallopian tube (95 to 98% of cases) including ampullary (55%) isthmic (25%), fimbrial (17%), Interstitial (2%). However they can occur in other locations such as uterine cornue (22.5%) ovary, cervix, and abdominal cavity.[5] It is more common on the right side. Ectopic pregnancy may be concurrent with an intra-uterine pregnancy (Heterotrophic), but these circumstances are rare.[6] It may occur any time from menarche to menopause. One study has conducted that 75% Ectopic pregnancy occurs in the age group 20-30 years.[4]

Multiple factors contribute to the relative risk of ectopic pregnancy. The rising incidence is strongly associated with an increased incidence of PID. The incidence of tubal damage increases after successive episodes of PID (i.e. 13% after 1 episode, 35% after 2 episodes, 75% after 3 episodes). History of prior ectopic pregnancy (7- to 13-fold increase), History of tubal surgery and conception after tubal ligation, Use of fertility drugs or assisted reproductive technology (4-fold increase), use of an intrauterine device (3-4%), smoking and STD relative risk of Ectopic pregnancy increases with the age of mother, 35-44 years (3-4 fold increase).[7]

Diagnosis of Ectopic pregnancy mostly depends on proper history taking and accurate physical examination. The classic signs and symptoms of ectopic pregnancy include short period of amenorrhoea (85%) followed by abdominal pain (100%) & per vaginal bleeding or intermittent bleeding (50%). Fifty percent have a palpable adnexal mass and 75% presented with cervical movement tenderness. Approximately 20% of patients with Ectopic pregnancy are haemodynamically compromised at initial presentation, which is highly suggestive of rupture.[7]

Management of Ectopic pregnancy depends on proper history taking, physical examination, relevant investigations, improvement of general condition of the patient and then specific treatment. Specific treatment of Ectopic pregnancy are of following types: (i) Expectant management, (ii) Medical management (use of Inj. Methotrexate, 20% potassium chloride, prostaglandins, RU486, Hyperosmolar glucose, vasopressin & actinomycin), (iii) Laparoscopy (if the patient is haemodynamically stable– 35% of Ectopic pregnancy are currently managed Laparoscopycally), and (iv) Laparotomy followed by Salpingostomy or Salpingectomy & Salpingo-oophorectomy. The advent of methotrexate treatment for ectopic pregnancy has reduced the need for surgery. This intervention may be laparoscopic or through a larger incision known as a laparotomy.[7]

Materials And Methods

It was a descriptive type of cross sectional observational study was undertaken among the patients admitted in the Department of Obstetrics and Gyrtaecology, Dhaka Medical College Hospital during the period from October 2012 to March 2018. Total 50 samples were included in this study. Data were collected using a structured questionnaire (research instrument) containing all the variables of interest. The questionnaire was finalized following pre-testing, after taking informed consent from eligible patient. Patient's details were taken from history, record of admission and physical examination was performed and complications were evaluated. Data were analyzed using statistical package for social science (SPSS) for windows version 20.

Results

Table-I: Age distribution of patients (n=50)

Age in years	Number	Percentage	Mean±SD
20-25	12	24	28.08±4.24
26-30	26	52	
31-35	9	18	
36-40	3	6	
Total	**50**	**100**	

Table-II: Presenting symptoms of ectopic pregnancy (n=50)

Symptoms	Number of Cases	Percentage
Abdominal pain	47	94
H/O of amenorrhoea	50	100
Syncopal attack	24	48
Loss of appetite	10	20
P/V bleeding	19	38
P/V discharge	13	26
Fever	3	6

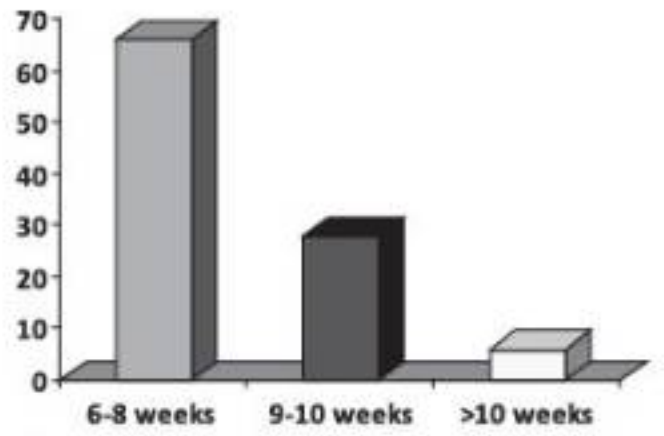

Fig. -1: Duration of pregnancy (n=50)

Table-III : Predisposing factors (n=50)

Risk factors	Number of Cases	Percentage
Previous abortion/MR	25	50
Pelvic infection	15	30
Previous C/S	6	12
Previous D&C	8	16
Previous IUCD insertion	3	6
Previous ectopic pregnancy	1	2
Previous tubal ligation	1	2
Previous appendicectomy	1	2
Endometriosis	2	2

Table-IV: Sites of ectopic pregnancy (n=50)

Site	Number of Cases	Percentage
Tubal		
Isthmus	6	6
Ampulla	44	88
Ectopic sac		
Tube	33	66
Ovary	17	34

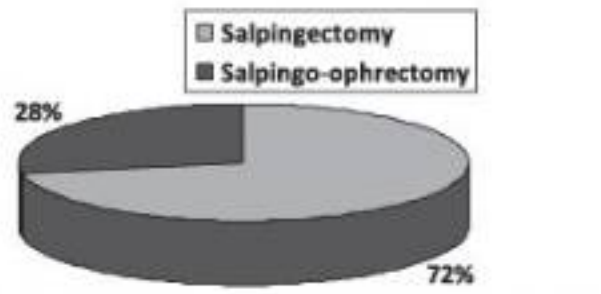

Fig. 2: Types of operation performed (n=50)

Table-V : Management

Management	Number of Cases	Percentage
Laparatomy	42	84
Medical management	7	14
Expected treatment	1	2

Table-VI: Post operative hospital stay (n=50)

Hospital stay	Number of Cases	Percentage
Less than7 days	44	88
More than 8 days	6	12
Total	**50**	**100**

Discussion:

Ectopic pregnancy is an implantation of a fertilized egg outside the uterine cavity. It is an important cause of maternal morbidity[8] and mortality. The incidence of ectopic pregnancy varies greatly throughout the world8 and incidence is increasing world wide.[9]

Ectopic pregnancy may occur at any age during the reproductive period. In this study maximum patients (52%) belonged to the age group 26-30 years. The range varied between 20-40 years. Almost similar observation has been made by Archibong et al.10 and Khan et al.[11] where showed 79.99% patients in 15-34 years of age group. Another study Tom et al. found 81.9% were among the age group of 21-30 years.

The presenting symptoms of ectopic pregnancy were analyzed. It was found that almost all patients had history of amenorrhoea, 94% had lower abdominal pain, 38% had P/V bleeding and 48% gave history of syncopal attack. This finding consisted with Pradhan et al.[12] they found 94.4% had abdominal pain and 72% had ammonorrhoea. Storeide13 had found that 100% had lower abdominal pain, 81% presented with amenorrhoea and 88% with abnormal vaginal bleeding.

This study showed the patients who presented with amenorrhoea, majorities (66%) had short period (6-8 weeks) of amenorrhoea. In a study by Khan et al.[11] showed that 35% had no history of amenorrhoea and 65% had history of amenorrhoea and among them 61.67% had 6-8 weeks amenorrhoea. So other study including this study has showed that commonest duration of amenorrhoea is 6-8 weeks. Another study by Airede et al.[14] found Abdominal tenderness (93%), ammenorrhoea (84%) and vaginal bleeding (62%) were the commonest presentation.

Among the risk factors that was identified in this series history of previous abortion/MR (50%), pelvic infection (30%), history of ovulation inducing drugs (29.09%) and history of D&C (16%) constituted the main bulk of risk factors for ectopic pregnancy and H/O taking IUCD (3.63%) came to the next. But no patient had IUCD in situ when presented with ectopic pregnancy. Gharoro et al. studied showed 63% had history of previous abortion and 41% had pelvic infection.[15]

Sinnathuria et al.[16] believed that infection following induced abortion is major cause of PID in Asia and the risk of ectopic pregnancy is 10 times higher in areas with a high incidence of illegal abortion[15] and 6 times higher following clinical salpingitis.[17] Several case control studies have reported a strong association between ectopic pregnancy and chlamydial trachomatis infections[18] and gonococcal infection.[19] Unfortunately our patients were not screened for these organisms. Bouyer et al.[20] in a large case control, population based study in France have shown that 1.1% cases had history of previous ectopic pregnancy. So previous history of ectopic pregnancy also a risk factor for recurrent ectopic pregnancy.

This study showed that 72% operation was unilateral salpingectomy and 28% was salpingo-ophorectomy. Airede et al.[14] reported unilateral sulpingectomy was the most frequent procedure that was performed. Pradhan et al.[12] studied showed 75% were salpingectomy, 22% salpingo-ophorectomy and 3% salpingostomy.

Archibong et al.[10] has noted that in 90% cases salpingectomy was performed. Most of patients presented with ruptured or grossly damaged tube when conservative treatment where not possible. Another study Khan et al.[11] have shown unilateral salpingectomy in 71% cases, unilateral salpingoophorectomy in 2% cases, unilateral salpingectomy with other sided tubectomy in 24.66% cases, salpingostomy done in 4 cases, removal of abdominal pregnancy in 4 cases and resection of rudimentary horn in 3 cases.

This study shows majority (88%) of cases, ampulla were affected and 66% cases ectopic sac was in fallopian tube. Lozeau et al.[21] Reported pregnancies in the fallopian tube account for 97 percent of ectopic pregnancies: 55 percent in the ampulla; 25 percent in the isthmus; 17 percent in the fimbria; and 3 percent in the abdominal cavity, ovary, and cervix. Another study Pradhan et al.[12] found 80% in ampulla, 11.1% in isthmus, 5.6% in fimbria and 2.8% in ovary.

After opening the abdomen tubal ectopic pregnancy were detected in right side than the left 64% and 36%

respectively. Most of our patients 68% had ruptured tubal pregnancy which reflects lack of health facilities in the community level and delay in the diagnosis and delay to take our patients to tertiary level hospital in the moribund state. In 32% cases tubes were found distended and unruptured.. Almost similar observation has been made by Bouyer et al.[22] in 10 year population based study of 1800 cases have shown that most (70%) of the tubal pregnancy occur in ampullary part, this study also shows that current IUCD use protects against interstitial pregnancies, which are the most difficult to manage.

This study shows majority of patients were managed by laparatomy (84%) followed by blood transfusion, 58% needed resuscitation, 14% needed medical management, 12% laparsocopic and 2 needed expected management. Medical treatment with systemic methotrexate is considered an acceptable management option for women presenting with haemodynamically stable patients with unruptured, small ectopic sac and low serum HCG values. A randomised trial of clinically stable women with unruptured tubal ectopic pregnancies compared the efficacy of a multiple dose systemic methotrexate regimen to laparoscopic salpingostomy.[23] A study that pooled results from four randomised trials that compared single dose systemic methotrexate to laparoscopic salpingotomy found medical treatment to be significantly less successful than surgery.[24]

Conclusion

This study showed that history of short period of amenorrhoea, abdominal pain, P/V bleeding, syncopal attack were common clinical presentations. The main risk factors were history of previous abortion/MR, history of D&C, ovulation inducing drugs. Most of the patients were managed by laparatomy followed by salpingectomy. The frequency can be reduced by awareness of reproductive health care, liberal contraceptive utilization and acceptable adequate family planning method. Early diagnosis and timely referral may be helpful in treating the patients prior to tubal rupture with decreased morbidity and mortality. We believe that there is a window of opportunity to ascertain the exact causes and suggest appropriate interventions to reduce this upward trend of ectopic pregnancy.

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Original Article

Comparison of efficacy of clindamycin (1%) - benzoyl peroxide (5%) combination gel with adapalene (0.1%) - benzoyl peroxide (2.5%) combination gel in treatment of mild to moderate facial acne vulgaris: A randomized prospective study

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Abstract:

Background: Fixed-combination topical products are available for the treatment of facial acne vulgaris. The benefits of combined regimens include reduced risk of antibiotic resistance and improved treatment outcomes. Fixed-combination products are reported to be effective, well tolerated and more convenient for patients than multiple individual agents. Clindamycin- BPO combinations and adapalene-BPO combinations are recommended as standard treatment strategies in treating of mild to moderate facial acne vulgaris. Various clinical studies have assessed the efficacy of those topical combination therapy for facial acne vulgaris & demonstrated significantly greater and faster results.

Objective: The aim of this study was to compare the efficacy of clindamycin (1%) - benzoyl peroxide (5%) combination gel with adapalene (0.1%) - benzoyl peroxide (2.5%) combination gel in treatment of mild to moderate facial acne vulgaris.

Methods: A prospective, randomized and comparative study was conducted on diagnosed cases of facial acne vulgaris aged 12 to 35 years, attending at outpatient department of Dermatology & Venereology, Dhaka National Medical College & Hospital, Dhaka from July 2017 to December 2017. A total of 60 patients of acne were selected as per inclusion & exclusion criteria and randomly divided into two groups, 30 patients in group A and 30 patients in group B. Clindamycin (1%)- benzoyl peroxide (5%) combination gel was given for 12 weeks in the group A, while adapalene (0.1%)-benzoyl peroxide (2.5%) combination gel was given to the group B patients for same duration. All the drugs were provided in the gel form. The efficacy of the drugs were evaluated at week 2, 4, 8 and 12 weeks follow up by spot counting of acne lesions on the face. The number of inflammatory lesions (pustules, papules) and non inflammatory lesions (open and closed comedones) were noted during each visit in a separate chart for each patient. All parameters were compared between two groups. Quantitative data was expressed as mean±SD. Values of the different parameters were compared to see the difference between two groups by using unpaired t-test. $p<0.05$ was considered as significant and $p>0.05$ was taken as non significant. 95% confidence limit was taken as the level of significance.

Results: A/BPO combination gel were more effective in reducing total acne lesions including comedones, papules & pastules than C/BPO combination gel.

Conclusion: Adapalene (0.1%) - benzoyl peroxide (2.5%) combination gel is more effective than clindamycin (1%) - benzoyl peroxide (5%) combination gel in the treatment of mild to moderate facial acne vulgaris.

Keywords: Efficacy, Clindamycin, Benzoyl peroxide, Adapalene, Facial acne vulgaris.

Introduction:

Acne vulgaris is a chronic inflammatory dermatosis of the pilosebaceous unit characterized by open or closed comedones and inflammatory papules, pustules, nodules, or cysts.[1] Four major factors associated with the pathogenesis of acne are increased sebum production, follicular hyperkeratinization, Propionibacterium acnes proliferation, and inflammation. No single topical acne therapy is effective in treating all of these pathogenic factors.[2]

Topical combination therapy can target multiple pathogenic mechanisms and therefore is currently recommended as the standard of care in the treatment of mild-to-moderate acne, particularly in patients with an inflammatory component. The benefits of combined regimens include complementary mechanisms of action, reduced risk of antibiotic resistance, and improved treatment outcomes. An increasing number of antibiotic-retinoid and antibiotic-benzoyl peroxide combinations are now available.[3]

The Global Alliance to Improve Outcomes in Acne recommends the combination of a retinoid with an antimicrobial, preferably the non antibiotic benzoyl peroxide (BPO), as first-line therapy for mild-to-moderate acne. Topical antibiotics also have a role in acne management, but they should be used in combination with BPO to limit the development of P. acnes resistance.[3]

Adapalene is a receptor-selective naphthoic acid derivative with anti-inflammatory, comedolytic, and anticomedogenic properties.[4] The efficacy of adapalene in the treatment of acne vulgaris have been studied in numerous clinical trials.[5-6] Recent clinical studies investigating the efficacy of adapalene when used in combination with several antibiotics (oral lymecycline, oral doxycycline and topical clindamycin) for the treatment of inflammatory acne showed that the adapalene-antibiotic combinations were consistently more effective than antibiotic monotherapy.[7]

BPO is a safe and effective antimicrobial agent for the treatment of acne. It is a powerful antimicrobial agent destroying both surface and ductal bacterial organisms and yeasts. Its lipophilic properties permit penetration of the pilosebaceous duct and its efficacy it largely against superficial inflammatory lesions. It also has effects on non inflammatory lesions by reducing follicular hyperkeratosis to some degree. Benzoly peroxide formulations offer a useful approach in acne patients owing to their highly effective bactericidal effect. They are not associated with antimicrobial resistance and are active against fully sensitive and resistant stratins of Propionibacterium acnes.[7]

Clindamycin improves acne by reducing the levels of P. acnes and decreasing inflammation.[8] Combination therapy with clindamycin and benzoyl peroxide is a well accepted treatment regimen for mild to moderate acne as documented in clinical trials and meta-analysis reports. The advantages of this combination therapy are keratolytic action of benzoyl peroxide is possibly synergistic with the antibacterial activity of clindamycin and benzoyl peroxide may reduce chances of antimicrobial resistance to topical antibacterials like erythromycin and clindamycin.[8-9]

Various clinical studies have assessed the efficacy of combination therapy for acne. These studies demonstrate significantly greater and faster results with the combination therapy than with the single agents alone. Combinations of topical antibiotics plus topical benzoyl peroxide, topical retinoids plus topical or oral antibiotics, and topical retinoids plus topical benzoyl peroxide have all been investigated.[3] The present study is the first one study to compare the efficacy of clindamycin-benzoyl peroxide combination gel with adapalene- benzoyl peroxide combination gel in treatment of mild to moderate facial acne vulgaris in Bangladesh.

Materials & Methods

A prospective, randomized and comparative study was conducted on diagnosed cases of mild to moderate facial acne vulgaris attending at outpatient department of Dermatology & Venereology, Dhaka National Medical College & Hospital, Dhaka from July 2017 to December 2017. It was an observational and open-label clinical trial in which both male and female patients in the age group of 12 to 35 years enrolled as per inclusion & exclusion criteria. Complete history, general physical examination and dermatological examinations were done after enrollment. The ethical clearance was obtained from the research advisory committee and Institutional Ethics committee. The study was started after obtaining written informed consent from each patient.

A total of 60 patients of acne were selected as per inclusion & exclusion criteria and randomly divided into two groups, 30 patients in group A and 30 patients in group B. Clindamycin (1%)- benzoyl peroxide (5%) combination gel was given for 12 weeks in the group A, while adapalene (0.1%)-benzoyl peroxide (2.5%) combination gel was given to the group B patients for same duration. All the drugs were provided in the gel form. The efficacy of the drugs were evaluated at week 2, 4, 8 and 12 weeks follow up by spot counting of acne lesions on the face. The number of inflammatory lesions (pustules, papules) and non inflammatory lesions (open and closed comedones) were noted during each visit in a separate chart for each patient.10 All parameters were compared between two groups. Quantitative data was expressed as mean±SD. Values of the different parameters was compared to see the difference between two groups by using student's t-test. $p<0.05$

was considered as significant and p>0.05 was taken as non significant. 95% confidence limit was taken as the level of significance.

Fig. : I Before treatment (Group A) After treatment (Group A)

Fig. : II Before treatment (Group B) After treatment (Group B

Results

Table-I : Number of Comedones in different follow up

Comedones	Groups		P-value
	Group A (C/BPO) (Mean ±SD)	Group A (A/BPO) (Mean ±SD)	
Baseline	13.20±1.78	12.83±1.96	0.453ns
1st follow up	10.06±2.33	11.03±2.60	0.136ns
2nd follow up	9.56±2.48	7.33±1.88	0.0001***
3rd follow up	7.23±1.83	5.40±1.45	0.0001***
Final follow up	4.83±1.26	2.73±1.55	0.0001***

ns=Non significant (P>0.05) ,***=P<0.001, **=P<0.01, *=P<0.05. Data were expressed as Mean±SD. Unpaired t test was done to measure the level of significance.

Table: I shows number of Comedones in different follow up. The mean number of Comedones was 13.20±1.78 in C/BPO group & 12.83±1.96 in A/BPO group at base line. In 1st follow up mean number of Comedones were 10.06±2.33 & 11.03±2.60 in C/BPO group & A/BPO group respectively. There were no significant mean difference between two groups (P>0.05). In C/BPO group , mean number of Comedones were 9.56±2.48, 7.23±1.83 & 4.83±1.26 in 2nd, 3rd & final follow up respectively. In A/BPO group, the mean number of Comedones were 7.33±1.88, 5.40±1.45 & 2.73±1.55 in 2nd, 3rd & final follow up respectively. Significant mean difference were found (P< 0.001) between two groups, indicating A/BPO combination gel were more effective than C/BPO combination gel in treating comedones.

Table-II : Number of Papules in different follow up

Papules	Groups		P-value
	Group A (C/BPO) (Mean ±SD)	Group A (A/BPO) (Mean ±SD)	
Baseline	16.53±3.12	17.56±3.85	0.259ns
1st follow up	14.40±4.09	15.73±3.25	0.168ns
2nd follow up	13.53±5.11	11.63±4.39	0.128ns
3rd follow up	11.46±3.01	9.23±4.67	0.032*
Final follow up	9.16±4.29	6.26±2.13	0.001***

ns=Non significant (P>0.05),***=P<0.001, **=P<0.01, *=P<0.05. Data were expressed as Mean±SD. Unpaired t test was done to measure the level of significance.

Table-: II shows number of Papules in different follow up. At base line mean number of Papules were 16.53±3.12 in C/BPO group & 17.56±3.85 in A/BPO group . In 1st follow up, mean number of Papules were 14.40±4.09 & 15.73±3.25 in C/BPO group & A/BPO group respectively. In 2nd follow up, mean number of Papules were 13.53±5.11 & 11.63±4.39 in C/BPO & A/BPO group respectively. There were no significant mean difference between two groups (P>0.05). In C/BPO group, mean number of Papules were 11.46±3.01 & 9.16±4.29 in 3rd & final follow up respectively. In A/BPO group, the mean number of Papules were 9.23±4.67 & 6.26±2.13 in 3rd & final follow up respectively. Significant mean difference was found between two groups, indicating A/BPO combination gel were more effective than C/BPO combination gel in treating Papules.

Table-III : Number of Pastules in different follow up

Pastules	Groups		P-value
	Group A (C/BPO) (Mean ±SD)	Group A (A/BPO) (Mean ±SD)	
Baseline	4.26±1.91	4.16±2.37	0.858ns
1st follow up	2.83±1.53	2.56±1.40	0.485ns
2nd follow up	1.83±0.91	1.73±0.73	0.643ns
3rd follow up	1.66±0.92	1.06±0.54	0.003*
Final follow up	1.56±0.72	0.70±0.55	0.0001***

ns=Non significant (P>0.05) ,***=P<0.001, **=P<0.01, *=P<0.05. Data were expressed as Mean±SD. Unpaired t test was done to measure the level of significance.

Table-III : shows number of Pustules in different follow up. At base line mean number of Pustules were 4.26±1.91 in C/BPO group & 4.16±2.37 in A/BPO group. In 1st follow up, mean number of Pustules were 2.83±1.53 & 2.56±1.40 in C/BPO & A/BPO group respectively. In 2nd follow up, mean number of Pustules were 1.83±0.91 & 1.73±0.73 in C/BPO group A & A/BPO group respectively. There were no significant mean difference between two groups (P>0.05). In C/BPO group, the mean number of Pustules were 1.66±0.92 & 1.56±0.72 in 3rd & final follow up respectively. In A/BPO group, the mean number of Pustules were 1.06±0.54 & 0.70±0.55 in 3rd & final follow up respectively. Significant mean difference was found between two groups, indicating A/BPO combination gel were more effective than C/BPO combination gel in treating Pastules.

Table-IV : Mean of total acne score in different follow up

Pastules	Groups		P-value
	Group A (C/BPO) (Mean ±SD)	Group A (A/BPO) (Mean ±SD)	
Baseline	33.96±2.94	34.53±3.61	0.508ns
1st follow up	27.26±4.82	29.33±5.30	0.120ns
2nd follow up	24.93±6.37	20.66±3.03	0.002**
3rd follow up	20.33±3.45	15.66±3.98	0.0001***
Final follow up	15.56±3.77	9.63±2.15	0.0001***

ns=Non significant (P>0.05) ,***=P<0.001, **=P<0.01, *=P<0.05. Data were expressed as Mean±SD. Unpaired t test was done to measure the level of significance.

Table-IV : shows the mean of total acne scores were 33.96±2.94 in C/BPO group & 34.53±3.61 in A/BPO group at base line. In 1st follow up, mean of total acne scores were 27.26±4.82 & 29.33±5.30 in C/BPO group & A/BPO group respectively. There were no significant mean difference between two groups (P>0.05). In 2nd follow up, mean of total acne scores were 24.93±6.37 & 20.66±3.03 in C/BPO group & A/BPO group respectively. In C/BPO group, the mean of total acne scores were 20.33±3.45 & 15.56±3.77 in 3rd & final follow up respectively. In A/BPO group, the mean of total acne scores were 15.66±3.98 & 9.63±2.15 in 3rd & final follow up respectively. Significant mean difference were found (P< 0.001) between two groups, indicating A/BPO combination gel were more effective in reducing total acne lesions than C/BPO combination gel.

Discussion

Pathogenesis of acne vulgaris is complex and and multifactorial which includes abnormal sebum production, follicular hyperkeratinization, bacterial proliferation and inflammation. So the treatment goals are directed to reduce activity of the sebaceous glands, normalize follicular proliferation, reduce bacterial colonization and control inflammation. There are different treatment options available for treatment of acne valgaris & all approaches have advantage and disadvantages.[11] But A/BPO and C/BPO combination gel are well tolerated & effective in reducing both inflammatory and non inflammatory acne vulgaris.[12-13]

The present study was conducted to compare the efficacy and safety of clindamycin-benzoyl peroxide combination gel with adapalene- benzoyl peroxide combination gel in treatment of mild to moderate facial acne vulgaris. The patients only with mild to moderate acne vulgaris were included in the present study who were randomly divided into two groups, 30 patients in group A and 30 patients in group B. Clindamycin (1%)-benzoyl peroxide (5%) combination gel was given for 12 weeks in the group A, while adapalene (0.1%)-benzoyl peroxide (2.5%) combination gel was given to the group B patients for same duration. The efficacy of the drugs were evaluated at week 2, 4, 8 and 12 weeks follow up by spot counting of acne lesions on the face. The number of inflammatory lesions (pustules, papules) and non inflammatory lesions (open and closed comedones) were noted during each visit in a separate chart for each patient.

The present study revealed A/BPO combination gel were more effective in reducing total acne lesions including comedones, papules & pastules than C/BPO combination gel. Zouboulis et al.[14] performed a similar study and demonstrated that clindamycin/benzoyl peroxide combination (C/BPO) and adapalene/benzoyl peroxide (A/BPO) have comparable efficacy in the topical treatment of acne. Both treatments effectively reduced inflammatory, non inflammatory & total lesion counts over the 12 week treatment period. Based on data reported in the literature, Adapalene-BPO appears to induce similar magnitude of effect in reducing lesion counts relative to other available fixed-dose combinations, such as clindamycin-BPO.[15] In another study conducted by Langner et al.[16] concluded that benzoyl peroxide-clindamycin combination was found to have a significantly earlier onset of action, and was significantly more effective against inflammatory and total lesions. Gollnick H.P.M et al.[17] revealed that Adapalene-BPO have significantly greater & synergistic efficacy and faster onset of action with an acceptable safety profile in treatment of acne vulgaris. Our study comply with the results reported by Leyden et al.[18] who

evaluated the fixed-dose combination gel containing adapalene 0.1% and benzoyl peroxide 2.5%. They reported that this combination gel effectively inhibited both antibiotic-susceptible and antibiotic-resistant Propionibacterium acnes and reduced skin colonization by antibiotic-sensitive and antibiotic-resistant Propionibacterium acnes. This high effectiveness of the drug is due to potential synergistic effect of adapalene - BPO combination gel. A synergistic anti-inflammatory effect may result from BPO eliminating P. acnes and adapalene down regulating the cell surface receptor[19] (toll-like receptor 2) that P. acnes uses to induce inflammatory cytokine production. As a result, these two active ingredients could then synergistically decrease the impact of P. acnes in acne. In addition, the penetration of BPO is likely to be enhanced when combined with a adapalene, which alters the follicular microclimate.[2] Thiboutot et al.[3] & Diane M et al.[20] reported that the fixed-dose combination of adapalene and BPO provided significantly greater efficacy for the treatment of acne vulgaris as early as week 1 relative to monotherapies. But the results of our study disagree with the results of study conducted by Lawrence et al.[21] Several multicenter, double-blind, randomized and controlled studies demonstrated a favorable efficacy & safety profile of the combination gel of adapalene-BPO.[3]

Conclusion

From above discussion it may be concluded that adapalene (0.1%)-benzoyl peroxide (2.5%) combination gel is more effective than clindamycin (1%) - benzoyl peroxide (5%) combination gel in the treatment of mild to moderate facial acne vulgaris.

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Case Report

LEOPARD Syndrome with APS-2

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Abstract:

LEOPARD syndrome is a phenotypic expression of mutations in several genes: PTPN11, RAF1 and BRAF. This rare autosomal dominant disorder is characterized by high variability of clinical manifestations. Here we report a case of LEOPARD syndrome with APS type -2. A 28 years old lady known diabetic and hypothyroidism presented with us recurrent abdominal pain and vomiting along with uncontrolled blood sugar. She is a third issue of consanguineous marriage. On query her mother gave H/O primary amenorrhea and hearing loss. On examination there is ocular hypertelorism, widely spaced nipple, loss of scalp hair, eye brow and tooth. There are multiple skin lentigines(dark skin spot), lack of secondary sexual characteristics with tanner stage-1. After evaluation she was found hypergonadotrophic hypogonadism, acute on chronic pancreatitis and dyslipidemia. Her conservative management was given for pancreatitis. Hormone replacement therapy was started and advised to continue levothyroxine and insulin. Also advised for regular follow-up on endocrine OPD of BIRDEM general hospital.

Key Words: LEOPARD syndrome, Hypertelorism, skin lentigines, APS

Introduction

LEOPARD syndrome is a phenotypic expression of PTPN11, RAF1 and BRAF gene mutations. It is an autosomal dominant disorder having high variability of clinical manifestations. These genes are responsible for Ras/MARK signaling pathway, which are important for cell cycle regulation, differentiation, growth, and aging. Mutations result in anomalies of skin, skeletal, and cardiovascular systems. The LEOPARD syndrome means lentigines, electrocardiographic conducting abnormalities, ocular hypertelorism, pulmonary stenosis, abnormal genitalia, retarded growth and deafness. Mutations affect tyrosine proteases, which are included in the signal pathway between the cell membrane and the nucleus. Usually only lentigines are common. Clinical diagnosis is based on lentigines and 2 other symptoms; in cases without lentigines – 3 symptoms and at least one affected first-line relative.[1]

Case details

Miss X 28 years Known type-1 diabetic, primary hypothyroidism and chronic pancreatitis hailing from Munshigonj, Dhaka with H/O consanguineous marriage between parents was admitted in BIRDEM general hospital on 13th May 2018 with the complains of vomiting and recurrent abdominal pain with uncontrolled blood sugar. She is primarily amenorrheoic with lack of secondary sexual characteristics. On query her mother noticed of gradual loss of hear, hair, teeth (from upper jaw) and developed characteristics skin changes from the age of fourteen. O/E her BMI is 18.2 kg/m2, MPH 148.5 cm, there is ocular hypertelorism, widely spaced nipple, multiple skin lentigines, vitiligo and tanner stage is B1 P1. Other systemic examination reveals no abnormality except NPDR on fundoscopy.

Her hormonal analysis reveals primary hypothyroidism (TSH: 8.46mIU/ml, FT4: 13.97 Pmol/L and positive anti TPO antibody) primary hypogonadism (Increased FSH: 33.49 mIU/ml, LH: 17.17 mIU/ml and decreased oestradiol: 21.80pg/ml). She was suffered from type-1 DM which was evident by C-peptide negativity (0.23 ng/ml) but antibody could not be done. ANA is negative, normal B12 assay with increased serum lipase (405 U/L). Her USG shows grade-II fatty change in liver,

small infantile uterus and ovaries could not visualized. Karyotype is 46XX (female) and echocardiography shows normal finding. Other routine examination shows normal findings except presence of normocytic normochromic anemia and high triglyceride (614mg/dl).

We advised her to follow the diet chart and to maintain regular exercise. We also gave diabetic education and counseled properly about her fertility issue. We prescribed Levothyroxine 25 mcg once daily, split mix human insulin, pancreatic enzyme and started hormone replacement therapy. We requested her to come on follow-up on BIRDEM endocrine OPD after one month with sugar profile, TSH, Lipase and CBC. Ophthalmological follow-up was scheduled every three months. Audiologist advised her to use hearing aid.

Discussion

The LEOPARD syndrome is an exceptional autosomal dominant disease.[1] The first case was described in 1936 but the LEOPARD term was first used in 1969.[2] Up to date, about 300 cases have been reported.[3] Many synonyms exist: cardiomyopathic progressive lentiginosis, multiple lentigines syndrome, cardio-cutaneous syndrome or Moynahan syndrome.[1] The LEOPARD syndrome is currently also referred to as Noonan syndrome with multiple lentigines or NSML (OMIM 151100).[3]

The penetrance is very high and the expression highly variable. In about 90% of the cases, it is linked to a germline PTPN11 missense mutation with loss of function.[1,4] The major clinical features are diffuse lentiginosis, ECG abnormalities, ocular hypertelorism, hypertrophic cardiomyopathy, pulmonary stenosis, genital anomalies, retardation of growth and deafness. Additional characteristics are a facial dysmorphism, skeletal abnormalities, and neurological troubles, hypotonia at birth, learning disabilities (present in this case) with mental retardation, oculomotor defects and EEG abnormalities.[1,5] Rare cases of cancer, including melanoma, had been reported. Nevertheless, as total case number is so low, no particular cancer susceptibility is currently established.[3] The diagnosis of a LEOPARD syndrome requires diffuse lentiginosis and two other syndrome traits. If diffuse lentigines are absent, the presence of a first degree affected relative and three other distinct features are necessary. However the diagnosis is not always obvious, especially as some signs are lacking or only appear at an advanced age. Furthermore, it shares lots of characteristics with other genetic syndromes like the Noonan syndrome, also mediated by a PTPN11 mutation but of the gain function type.[1] In atypical cases of LEOPARD syndrome, a missense PTPN11 mutation confirms the diagnosis.[4] In case of negativity, a RAF1 mutation should be searched for that is present in 1/3 of the patients without a PTPN11 mutation.[1] In less than 5%, a BRAF mutation can be associated.[6] Molecular analysis provides additional interesting clinical information helping in the long-term management and follow-up of these patients. Indeed, the prevalence of cardiac conduction disorders, ventricular or left auricular hypertrophy and familial history of sudden death is significantly higher in PTPN11 mutation negative patients. The mortality and morbidity predominantly depend on the extent of the cardiac abnormalities. A complete checkup, including rigorous clinical examination, growth parameters monitoring in children, hearing test (1/year until adulthood) and cardiological (1/year mainly when lentigines appear if none cardiac lesion was previously detected), neurological and urogenital evaluations, is highly recommended. In contrast, the management of other abnormalities does not differ from those in general population.[1]

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Case Report

Eight-and-a Half Syndrome: A Rare Presentation of Gaze Palsy in Ischemic Stroke.

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Abstract:

Eight- and-a- Half –syndrome is a rare clinical manifestation of stroke, where involvement of ocular motor movement manifested by horizontal gaze palsy to one direction, internuclearophthalmoplegia in the other and ipsilateral lower motor neuron seventh cranial nerve palsy.We report a case of eight-a- half syndrome.A 55 years old female known to have Type 2 Diabetes Mellitus, ischemic heart disease presented with double vision, dizziness, deviation of the mouth to the right for 2 days. Her vision was normal, no symptoms of raised intracranial pressure, no limb weakness, slurring of speech. At presentation, patient had poorly controlled diabetes. There were left eye limitation in abduction with contralateral right abducting eye nystagmus, left eye limited abduction consistent with right one and half syndrome. There was also left lower motor neuron facial nerve (7th) palsy. Eight –and-a –half syndrome is a combination of ipsilateral one-and-half syndrome and lower motor neuron facial(7th) nerve palsy. Brainstem conjugate gaze palsy is an important clinical finding, help in diagnosis even a small pontine lesion.

Keywords: Internuclearophthalmoplegia, one and a half syndrome, eight and a half syndrome.

Introduction

Horizontal gaze palsy in one eye and internuclearophthalmolplegia in the other eye, combination of both was first described by Freeman et al, in 1943.[1] Later, C Miller fisher introduced the term as one and a half syndrome.[2] The syndrome was more commonly found in stroke, but rarely in demyelinating and neoplastic lesion.This syndrome is produced by involving the medial longitudinal fasciculus (MLF) and paramedian pontine reticular formation. In 1998 Eggenberger came out with the term eight-and-a half syndrome, a combination one and a half syndrome and ipsilateral lower motor neuron type facial nerve palsy.[3] Although it is a rare syndrome, help the neurologist or any clinician to localize the lesion. Herein, we report a patient with Eight and a Half syndrome.

Case Report

A 55years old female presented with double vision, dizziness, deviation of the mouth to the right for 2 days. It was sudden in onset and non progressive. She was known case of diabetes and ischemic heart disease for 2 years and had regular follow up and medication. Patient gave no history of trauma, she was afebrile, no history of visual disturbance and ocular surgery.

On general examination, she was well and alert, conscious, oriented about time, place, person with Glasgow Coma Scale 15/15, blood pressure 120/80, random blood glucose 19.1 mmol/l and afebrile. Neurological examination revealed left horizontal paresis (figure-1) and limitation of left eye adduction with abducting nystagmus of the right eye (left internuclearophthalmoplegia) (figure-2).There was also left lower motor neuron type seventh cranial nerve palsy characterized by deviation of the angle of the mouth to the right and loss of left nasolabial fold. (figure-5) Bell's reflexes was prominent. Vertical gaze was intact. (figure-3 and 4) Horizontal and vertical vestibulo-ocular reflexes were intact. There were no cerebellar signs, motor and sensory function of upper and lower limbs were normal.Other cranial nerves were intact. Ocular examinations were unremarkable. Computed tomography of brain showed right frontoparietal lobe as well as both thalamic infarct. Magnetic resonance imaging of brain revealed hyperintensity in the right pontine tegmentum just anterior to the fourth ventricle on diffusion-weighted imaging sequence suggestive of an acute ischemic stroke. Patient was treated with antiplatelet.

Figure-1 : Left horizontal gaze paresis (Patient can't move the eyeball to the left)

Figure-2 : Internuclearophthalmoplegia on the right gaze shown by limitation of adduction on left eye and adducting nystagmus on the right eye.

Figure-3 : Intact down gaze

Figure-4 : Intact upgaze

Figure-5 : Left lower motor neuron seventh cranial nerve palsy

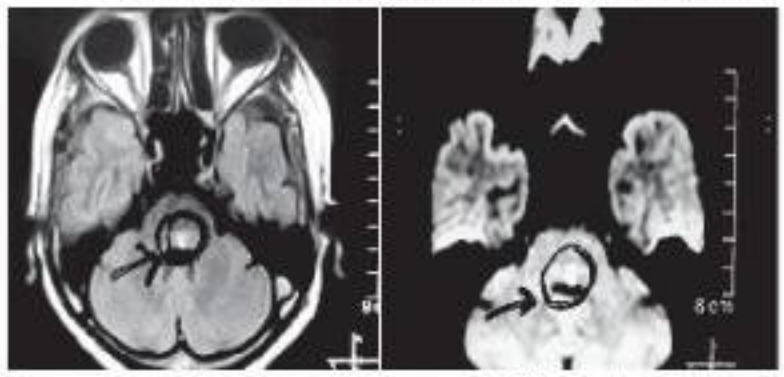

Figure-6 : Hyperintensity on FLAIR and restricted diffusion area on Diffusion-weighted imaging sequence, in the left pontine tegmentum just anterior to the forth ventricle.

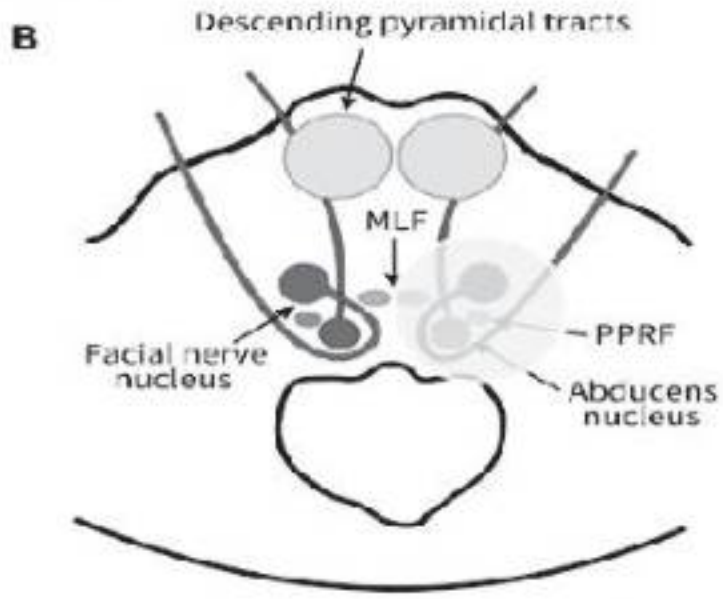

Figure-7 : Axial section through the caudal pons, showing the genu of the facial nerve (red) looping around the abducent nucleus(blue) in the pontine tegmentum and location of the lesion (yellow) with relevant structures affected. MLF: Medial longitudinal fasciculus, PPRF: Paramedian pontine reticular formation.

Discussion

Eight –and –a half eye syndrome is aclinical syndrome of internuclearophthalmoplegia, horizontal gaze paresis and ipsilateral lower motor neuron seventh cranial nerve palsy, a combination of one and half eye syndrome with lower motor neuron seventh cranial nerve palsy.[3] These clinical feature were due to lesion affecting the medial longitudinal fasciculus, paramedian pontine reticular formation or abducens nucleus and adjacent facial nucleus/fascicle at the level of dorsal tegmentum of caudal pons.[5] Those mentioned structures remain very closely in dorsal aspect of the pons and makes it vulnerable to a vascular event and demyelination.[2] Blood supply of the dorsal pontine tegmentum derived from paramedian pontine arteries, branches of basial artery. In previous case report demonstrated that

unremarkable high-quality MRI in patient with eight –and-a half syndrome highlighted the importance of clinical recognition of the syndrome.[3] On the other hand MRA is recommended as it is not only valuable to demonstrate the vascular pathology but also assisting in therapeutic management. In a case of ischemic stroke, treatment with anti-platelet and rehabilitation has been shown to improve the neurological deficit over a period of 3-6 months.Other etiology that contributes to lesion in the lower pontine tegmentum includes multiple sclerosis, vasculitis and brainstem tuberculoma.[4]

Conclusion

Diagnosis of eight-and-a-half syndrome mainly by clinical signs. It is a rare presentation and we should be capable to recognize the sign. The imaging modalities like MRI brain can help in localization of the lesion and occasionally give some clues for the etiology of that lesion. The diagnosis of the syndrome made precise anatomical localization and ensure proper treatment being given to the patient.

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