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b. Abstract

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d. Methods

e. Results (Tables with titles and Figures with legends)

f. Discussion

g. Conclusion

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Each of the sections is to start on a separate page. Page should be numbered consecutively beginning from the abstract.

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• Statement of the problem with a short discussion of its importance and significance

• Review of the literature(s) related to the problem with pertinent reference

• Objectives/hypothesis/benefits should be clearly stated

Methods

• Research type, place and time

• Description of research variables

• Discussion of research population

• Selection criteria (Exclusion criteria if any)

• Approval of the research involving human subjects by ethical review committee (IRB/ERC) and description of the ethical aspects in such research

• Description of procedure, methods, apparatus, drugs or chemical as applicable

• Statistical procedure should be described and supported by reference

Result

• Present results in a logical sequence in text, table and illustration with most important finding first

• Figure should be numbered as Fig. 1 and table in Roman numerical (Tab. I)

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Letters to the editor or comments can be sent to provide commentary and analysis concerning an article published in the journal, to give information about ongoing research to draw attention to a particular subject. It may include an optional title, tables and references. These articles should not exceed 1000 words.

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2. Dr.----------
3. Dr.----------
4. Dr.----------

Editorial

Smartphone Addiction

*Saha S[1], Rizwan ASM[1]

We are blessed to enjoy numerous scientific marvels that have revolutionized the way we live. Among all other, Smartphone has become an indispensable part of our daily life. This tiny hand-held machine has changed forever our communication, social interaction and entertainment. But overindulgence in using these devices can disrupt the balance between productivity and abuse. Too much reliance on Smartphone for checking mail, social interaction, gaming etc has long term consequence on user. The unchecked use soon turns into dependency that leads to loss of control, compulsiveness and ultimately addictive behavior.

Adolescents are particularly vulnerable group to fall into the Smartphone addiction[1]. This new world problem has both physical and psychological negative impact. Researchers have shown that, Excessive use of Smartphone and internet is associated with sleep deficit, anxiety, stress, and depression[2]. Smartphone addiction

cover a variety of impulse-control problems like virtual social networking, internet pornography addiction, information overload, online compulsions. Addiction to social networking, texting, messaging, dating apps creates numerous numbers of online friends and make them more important than real-life relationships. Internet pornography impact negatively on real life relationship and mental health. Continuous web surfing, watching videos, playing games or checking news feeds cause below standard productivity at work or class performance. Online gambling, stock marketing, shopping, auction bidding often lead to financial and job-related problem. Study shows, one in three teens are hooked by their cell phone[3].

Smartphone addiction is considered to be a substance free psychological addiction that has a physiological and neuronal basis. American researcher Henry Lai has discovered that, microwaves increase the activity of brain endorphins or endogenous opioids in a way similar to morphine. Cell phones emit high electromagnetic radiation also known as radio-frequencies which interfere brain waves, the blood-brain barrier, the pineal gland, and DNA[4]. This can be held partly responsible of the pleasurable 'craving' and of the positive reinforcement observed in cell phone addicts. On the other hand, some alternative behavioral model tried to explain the health consequences from a different perspective. They have proposed that, there is an indirect relation between cell phone usage and psychological health. Adolescents use cell phones at night, which leads to insomnia which ultimately results in depression, anxiety, and depression.

Spending lot of hoursusing smartphones creates a problem when it absorbs so much time and causes to neglect face to face relationship, work, study, hobbies and other important issues of the life. Warning signs of smartphone overuse includes, problem in completing tasks at home and office, social isolation, concealing of smartphone use, having a fear of missing out, feeling anxious or panic of leaving device in home. Along with those there are several withdrawal symptoms from smartphone addiction like irritability, restless, lack of concentration, sleep disturbances and craving access for the device.

There are several steps that can be taken to control smartphone use like: recognition the trigger to reach the phone, feeling the difference between virtual and real relationships, recognition of underlying problem the support the compulsion, strengthening of support network and increase interaction with the real world. Besides these, modifications of smartphone use can control the development of addiction like setting

goals for use of phone, turning off phone before bedtime, replacing devices by healthier activities, removing social media apps, limit news feed checks and developing real friendship instead of virtual. Cognitive behavioral therapy, counselling, group supports and needful medication are the specialist treatment for the smartphone addiction.

Smartphone is an object of easy addiction. So, special attention is utmost necessary for ensuring it's proper use. Family and social bonding must be ensured to lead a healthier and peaceful productive life.

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Original Article:

E-cadherin expression in thyroid carcinoma and correlation with histologic type and nodal metastasis.

***Hassan MA[1] Jannat H[2] Kundu R[3] Mahmood HR[4] Anam SMT[5] Jeba R[6] Dewan RK[7]**

Abstract :

Background: *Thyroid cancer is the fifth most common cancer in women worldwide. The incident of thyroid cancer in both women and men has been increasing in recent years. In many cases, traditional histopathological examination has not been able to predict the aggressiveness and prognosis of thyroid carcinoma. E-cadherin molecules are involved in thyroid folliculogenesis and loss of cell-cell adhesion is a precondition for the invasive behavior of malignant tumors. If down regulation occurs in E-cadherin expression, it correlates with strong invasive potential and poor prognosis of thyroid carcinoma.* ***Objectives:*** *Evaluation of E-cadherin expression in various types of thyroid carcinoma and correlation with histologic type and nodal metastasis.* ***Method:*** *This is a descriptive cross sectional study which was carried out at the Department of Pathology, Dhaka Medical College, during the period of March, 2017 to February, 2019 with 50 thyroid carcinoma patients attending in Department of ENT, Dhaka Medical College Hospital. All collected samples were processed for routine histopathological study and selected for immunohistochemistry with E-cadherin antibody. Patients' demographic data were collected from patients' file and requisition forms. Statistical analysis was done using SPSS (version 20).* ***Results and observations:*** *In this study the mean age was 41.76 ±11.4 and male to female ratio was 1: 2.1. The predominant histologic types were papillary carcinoma (78%) and 92% of all carcinomas were well differentiated. E-cadherin expression was reduced in some follicular and papillary carcinoma and markedly reduced in anaplastic carcinoma. Nodal involvement also showed markedly reduced expression of primary thyroid carcinoma.* ***Conclusion:*** *E-cadherin expression is very important for detecting the aggressiveness of thyroid carcinoma. Down regulation in E-cadherin expression correlates with strong invasive potential and poor prognosis of thyroid carcinoma.*

Key words: E-cadherin, Nodal metastasis, Thyroid carcinoma

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Introduction:

The thyroid gland is the largest endocrine gland of the body. The major function of the thyroid gland is to secret thyroid hormone, which maintains the level of metabolism in the tissue that is optimal for their normal function. Thyroid hormone also stimulates oxygen consumption by most of the cells in the body, help to regulate lipid and carbohydrate metabolism, and thereby influence body mass and mentation [1]. The incidence and disease pattern of thyroid varies in different geographic distribution due to dietary, environmental and genetic factors. About 5% of world population are suffering from various thyroid diseases[2] and endemic goiter is the most common disease pattern throughout the world[3], hyperplasia and benign and malignant tumor. Thyroid cancer is the fifth most common cancer in women worldwide[4]. The incident of thyroid cancer in both women and men has been increasing in recent years. Globally in 2012, the estimated number of death from thyroid cancer was 27000 in women and 13000 in men, corresponding to mortality rate approximately 6/100000 in women and 0.3/100000 in men[5]. In USA incidence have been increasing over the last few decades[6, 7]. If recent trend is maintained, thyroid cancer might become the fourth most common cancer by 2030 in USA[8]. Thyroid cancers comprise a heterogeneous group of malig-

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nant tumors. Differentiated thyroid cancers are usually associated with a good prognosis. Undifferentiated cancer is a highly malignant tumor that usually leads to patient's death. Poorly differentiated thyroid cancers occupy, both morphologically and clinically, an intermediate place between the well differentiated and undifferentiated cancers. In many cases, traditional histopathological examination has not been able to predict which differentiated cancers have the potential to behave aggressively. Adhesive interactions between cells are dynamic and regulated during tissue development and homeostasis. Cadherins are major cell-cell adhesion molecules involved in the development and maintenance of solid tissue. Cadherins are transmembrane glycoproteins localized in the plasma membrane of cells in most of the solid tissue. Most of them mediate Ca2+ dependent cell-cell adhesion molecule that contributes to morphogenesis by hemophilic interaction[9]. More than 30 human members of cadherin family are identified. The classic epithelial type cadherin is generally referred to as E-cadherin[10]. E-cadherin molecules are involved in thyroid folliculogenesis. Studies in normal thyroid tissue demonstrated a basolateral expression of E-cadherin. Loss of cell-cell adhesion is a precondition for the invasive behavior of malignant tumors. Adherens junctions or desmosome mediated cell-cell adhesion is maintained by members of the cadherin family of transmembrane proteins and their connections to a group of cytoplasmic proteins named catenins[10]. If down regulation occurs in E-cadherin expression, it correlates with strong invasive potential and poor prognosis of thyroid carcinoma[11]. Some studies have been done regarding E-cadherin expression in thyroid carcinoma in various countries but no studies done regarding these parameters in our country. In this present study, evaluation of E-cadherin expression in thyroid carcinoma was done in relation to their histopathologic type, extent of local invasion and lymph node involvement.

Materials and Method:

This is a prospective observational study carried out at the department of pathology, Dhaka Medical College from March 2017 to February 2019. Ethical issues were address accordingly. Fifty cases were taken and routine histology test were done and each histological specimen were examined to determine histological type & grade of the tumor according to the World Health Organization and to select one representative paraffin block for immunohistochemical analysis. Immunohistochemical findingswas assessed semi-quantitatively by the evaluation of 1,000 cells in each lesion. The staining was regarded as positive in the case of membrane expression of E-CAD. The results were expressed in an ordinal scale from 0 to 4. 0 = no membrane staining or staining present in 5% of cells, 1 = membrane staining present in 6–30% of cells, 2 = membrane staining present in 31–60% of cells, 3 = membrane staining present in 61–90% of cells, and 4 = membrane staining present in more than 90% of cells. Grades 0 and 1 were classified as markedly reduced. Grade 2 - as reduced, and Grades 3 and 4 - as preserved[12].

Observations and result

A total of 50 cases of thyroid carcinoma sample were enrolled in this study. After detail gross examinations of the specimens, hematoxylin and eosin stained sections were examined under microscope for histological examination and E-cadherin immunostaining were done.

Mean age of the patients were 41.76±11.4 with age range from 18 to 66 years, 16 cases were male (32%) and 34 cases were female (64%) and the male female ratio was 1: 2.1. There are female predominance upto 50 years of age group (36 cases, 72.0%) and after 50 years of age the male and female ratio is equal (14cases, 28.0%). Among

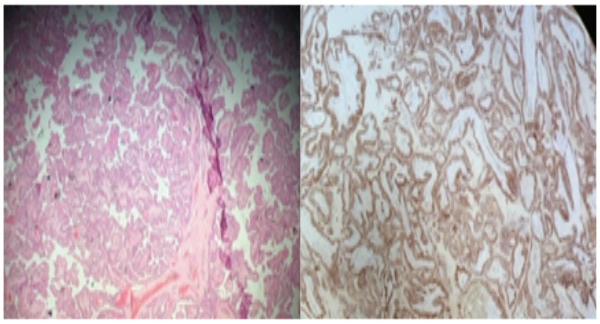

Figure 1: Photomicrography showing Papillary carcinoma of thyroid and showing preserved E-cadherin immunostain.

the 50 cases, the highest number were diagnosed as papillary carcinoma (36 cases, 72 %) followed by follicular carcinoma (7cases, 14%). Follicular variant of papillary carcinoma was observed in 3cases (6%). The number of medullary carcinoma and anaplastic carcinoma were equal (2 cases, 4%) each.

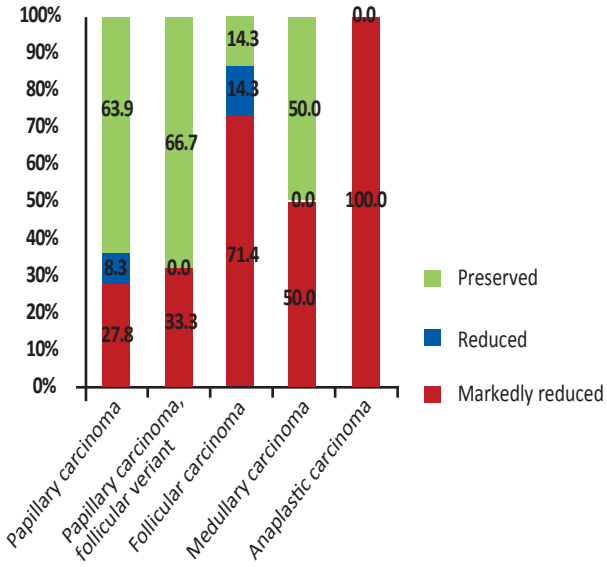

Figure 2: Bar diagram showing Correlation of E-cadherin expression with different histologic type of thyroid carcinoma (%) [p value = 0.269]

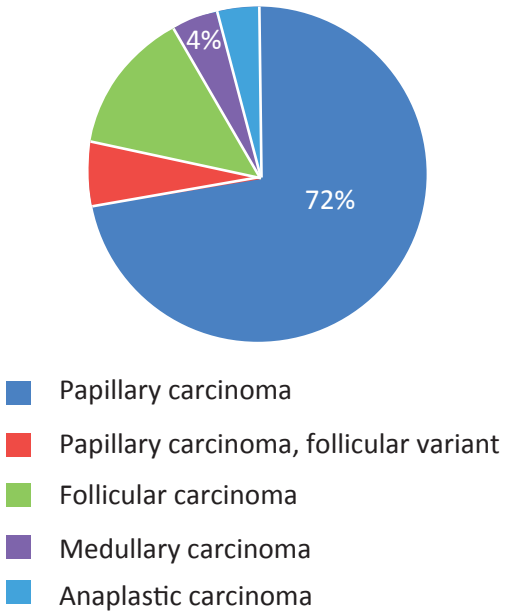

Figure 3: Pie Chart Showing Frequency of histologic type of different thyroid carcinoma.

Among the 50 cases, 46 (92%) were well differentiated and rest 4 (8%) cases were poorly differentiated. Among the well differentiated cases, 26 (56.5%) cases showed preserved, 16 (34.8%) cases showed markedly reduced and 4 (8.7%) cases showed reduced E-cadherin immunostaining. 3(75%) cases of poorly differentiated cases showed markedly reduced and 1 (25%) case showed preserved E-cadherin immunostaining.

Out of 50 cases 7 cases have regional lymph nodes involvement (pN1). All of the cases 100% (5 papillary, 2 follicular) showed markedly reduced E-cadherin immunostaining. Remaining 43 cases (31 papillary, 5 follicular, 2 medullary, 2 anaplastic and 3 follicular variant of papillary carcinoma) showing preserved expression in 27 cases (23 papillary, 2 follicular variant of papillary carcinoma, 1 follicular carcinoma, and 1 medullary carcinoma), reduced expression in 4 cases (3 papillary, 1 follicular carcinoma) and markedly reduced in 12 cases (5 papillary, 1 follicular variant of papillary carcinoma, 3 follicular carcinoma, 1 medullary carcinoma and 2 anaplastic carcinoma).

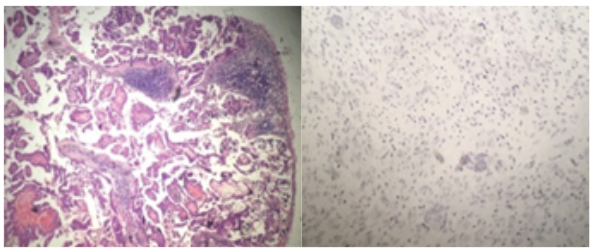

Figure 4: Photomicrograph showing metastatic papillary carcinoma in a lymph node and markedly reduced E-cadherin expression in primary tumor.

Table I: Correlation Of E-cadherin Expression With Different Histologic Parameters Of Thyroid Carcinoma (n=50)

Histopathological parameters		No. of cases	E- Cadherin comment			p-value
			Markedly reduced	Reduced	Preserved	
Histologic type	Papillary carcinoma	36	27.8% (10)	8.3% (3)	63.9% (23)	0.269
	Papillary carcinoma, follicular variant	3	33.3% (1)	0.0% (0)	66.7% (2)	
	Follicular carcinoma	7	71.4% (5)	14.3% (1)	14.3% (1)	
	Medullary carcinoma	2	50.0% (1)	0.0% (0)	50.0% (1)	
	Anaplastic carcinoma	2	100.0% (2)	0.0% (0)	0.0% (0)	
Lymphnode involvement	Involved	7	100.0% (7)	0.0% (0)	0.0% (0)	0.001
	Not involved	43	27.9% (12)	9.3% (4)	62.8% (27)	

Discussion

Carcinomas of thyroid are accounting for about 1.5% of all cancers. A female predominance has been noted among patients who develop thyroid carcinoma in the early and middle adult years. The incidence in women are about 6%. In contrast, cases presenting in childhood and late adult life are distributed equally among males and females. Most thyroid carcinomas are derived from the thyroid follicular epithelium and of these, the vast majority are well differentiated lesions [3].

E-cadherins a transmembrane glycoprotein has a small cytoplasmic component and the remaining portion of the protein is extracellular. The extracellular domain connects the cytoskeleton through a complex of proteins mainly catenins. E-cadherin-catenin complex has the potential to inhibit mitogenic signaling through growth factor receptors and maintain the molecular determinants of epithelial polarity[13]. E-cadherin is a potent invasive suppressor. If down regulation occurs in E-cadherin expression, it correlates with strong invasive potential and poor prognosis of thyroid carcinoma[14]. In this study, total 50 cases were included. The age ranged from 18 to 66 years and the mean age was 41.76±11.4. Most of the study subject were between 41 to 50 years of age group (14 cases, 28 %) followed by 31 to 40 and 51 to 60 years of age group (12 cases, 24 % each). There was another group 21 to 30 years of age (9cases, 18%). The fifth group was above 61 years of age (2cases, 4%). There was no case below 18 years or above 66 years. The least number of sample was below 20 years of age (1 case, 2 %). E-cadherin expression was reduced with increasing the age and expression was preserved at younger age group.

All the cases below 18 years showed preserved E-cadherin staining. The study group in between 21 to 30 years showed 66.7% preserved staining, age group 31 to 40 showed 58.3% preserved staining, age group 41 to 50 and 51 to 60 showed 50% preserved staining. All the cases above 60 years of age showed no preservation of E-cadherin immunostaining and both of them showed markedly reduced staining. So, this result showed an important relation between E-cadherin expression and different age group. Naito[9] had done similar type of study. But they did not get any correlation between age and E-cadherin expression. Brabant [15] also done E-cadherin expression on thyroid carcinoma and their observation was similar to this study. In this current study, 16 cases were male (32%) and 34 cases were female (64%) and male female ratio was 1: 2.1. No correlation was found

between E-cadherin expression and sex group. Study by Kapran[10] found mean age of the patients were 37.3±11.2 years with male female ratio 1: 4.9. Similar study by Slowinska-Klencka[12] showed mean age of the patient were 50.02 ± 17.45 with a marked female predominance where male female ratio was 1: 7.1. None of them found any correlation between sex group and E- cadherin expression.

All the 50 cases of thyroid carcinoma 72% were papillary carcinoma, 14% follicular carcinoma, 6% follicular variant of papillary carcinoma, 4% medullary carcinoma and remaining 4% were anaplastic carcinoma. Among them 92% were well differentiated and remaining 8% were poorly differentiated.

Out of 36 cases of papillary carcinoma, 23(63.9%) showed preserved immunostaining, 10(27.8%) cases showed markedly reduced and 3(8.3%) cases showed reduced E-cadherin immunostaining. Out of 7cases of follicular carcinoma 5(71.4%) cases of follicular carcinoma showed markedly reduced, 1(14.3%) case showed reduced and 1(14.3%) case showed preserved E-cadherin immunostaining. Out of 46 cases of well differentiated carcinoma, 36 are papillary carcinoma, 7cases are follicular carcinoma and 3 cases are follicular variant of papillary carcinoma. Among the well differentiated cases, 26 (56.5%) cases showed preserved, 16 (34.8%) cases showed markedly reduced and 4 (8.7%) cases showed reduced E-cadherin immunostaining. 4 cases are poorly differentiated. 2cases are medullary carcinoma and 2 cases are anaplastic carcinoma. 3(75%) cases of poorly differentiated cases showed markedly reduced and 1(25%) case showed preserved E-cadherin immunostaining.

Similar study was done in the department of pathology, Samsung Medical Centre, Seoul, Korea by Choi[16]. In their study among 150 cases papillary carcinoma were 53.6%, follicular carcinoma 24%, poorly differentiated carcinoma 9.6%, undifferentiated carcinoma 8% and Hurthle cell carcinoma 4.8%. Here E-cadherin staining expression is similar with our study. Another study by Rocha[17] showed that out of 17% cases of poorly differentiated thyroid carcinoma 15 cases showed reduced E-cadherin expression.

In immunohistochemical studies, tumors with preserve epithelial morphology (Differentiated type) express high amount of cadherin, whereas undifferentiated type have reduced amount of these molecules. There is significant correlation between reduced expression of E-cadherin and loss of tumor differentiation. The impaired expression of E-cadherin is frequently observed in tumors with aggressive histopathologic character that is invasiveness, lymph node involvement and distant metastasis[18].

Out of 50 cases 7 cases have regional lymph nodes involvement (pN1). All of the cases 100% (5 papillary, 2 follicular) showed markedly reduced E-cadherin immunostaining. Remaining 43 cases (31papillary, 5follicular, 2medullary, 2 anaplastic and 3 follicular variant of papillary carcinoma) showing preserved expression in 27 cases (23 papillary, 2 follicular variant of papillary carcinoma, 1follicular carcinoma, and 1 medullary carcinoma), reduced expression in 4cases (3papillary, 1 follicular carcinoma) and markedly reduced in 12 cases (5 papillary, 1 follicular variant of papillary carcinoma, 3 follicular carcinoma, 1 medullary carcinoma and 2 anaplastic carcinoma.

Conclusion:

The incidence of thyroid tumor is increasing about 5% per year and it is fifth most common tumor of women. Well differentiated tumors have good prognosis but undifferentiated tumors are highly malignant and leads to patient death. Routine histopathologic procedures can categorize the tumor in different types but cannot estimate the prognosis in poorly differentiated thyroid carcinoma. So, E-cadherin expression estimation is very important for such cases. In our country no study has been done regarding incidence, histological types and associated biomarkers expression in thyroid carcinoma.The aim of the study

was to evaluateE-cadherin expression in thyroid carcinoma in relation to their histopathological type and lymph node involvement. This cross-sectional study was carried out at the Department of Pathology, Dhaka Medical College, from January 2017 to December 2018. Histopathological examinations of thyroid carcinoma of 50 patients were done followed by evaluation of IHC expression of E-cadherin. In this study mean age were 41.6 ± 11.4 ranges from 18 to 66 years with female predominance where male female ratio was 1:2.1. Papillary carcinoma was the most common type of cancer in this study (72%) followed by follicular carcinoma (14%), Follicular variant of papillary carcinoma (6%), Medullary carcinoma (4%), Anaplastic carcinoma (4%). Papillary carcinoma was common in early age group and anaplastic carcinoma was in late age. 14% cases showed lymph node involvement but no distant metastasis seen. Significant correlation was found between E-cadherin expression histologic type and lymph node involvement.

Recommendation

Immunohistochemical expression of E-cadherin in all type of thyroid carcinoma may be included as part of routine pathological evaluations. Follow up study should be included for proper evaluation of patients

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Original Article:

Interpupillary Distance of Bangladeshi Medical Students – A Photo-Anthropometric Study

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Abstract :

Background: *Interpupillary distance (IPD) is the distance between the center of the pupils. It helps to identify race, age & gender of an individual. It is an essential guide to reconstructive surgery like ocular prosthetics, blepharoplasty, ptosis correction. It is also useful for evaluation of various dysmorphic syndromes and also useful factor in selecting artificial teeth.* ***Objectives:*** *Many studies were carried out in various populations to determine normal values of interpupillary distance. However, there is no published article on this topic in Bangladesh. So, this study was aimed to measure the interpupillary distance among the medical students of Bangladesh and to find out the variations in interpupillary distance between male and female medical students.* ***Methods:*** *This cross-sectional analytical study was carried out in the department of anatomy, Sir Salimullah Medical College, Dhaka from July 2017 to June 2018. Digital photographs of face in frontal view both in opened and closed eyes of the study subjects were taken from 200 consented medical students (100 male and 100 female) aged between 20 to 25 years. The actual "nose height" of the study subjects was measured from nasion to subscale by slide caliper. Then the "nose height" of individual photograph was transformed into physically measured value by using transform option of Adobe Photoshop version: CC 2014 and ultimately photograph of eye was converted into actual size. Then the interpupillary distance was measured from photograph by MB ruler software and the data were analyzed with the help of SPSS software package.* ***Results:*** *The mean ± SD of interpupillary distance was 60.81±5.79 mm (range 33.44 - 79.52 mm) in male and 57.07±5.34 mm (range 45.75 - 71.96 mm) in female. Interpupillary distance is significantly higher in male than female (P < 0.01).* ***Conclusion:*** *Interpupillary distance shows sexual dimorphism.*

Keywords: Interpupillary distance, Medical students, Photo-anthropometry.

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Introduction

The human eye is an important key determinant of face in the perception of facial attractiveness, youthfulness and health[1]. Anthropometry is concerned with measurement of physical sizes and shapes of human body[2]. Interpupillary distance is an important tool used by genetic counselor and in reconstructive surgery. The diagnosis of many dysmorphic syndromes is based on advanced cytogenetic and molecular techniques[3].

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Physical growth is a fundamental vital process and the common property of life. The normal distance between the pupils varies during embryogenesis and after birth in accordance with the general craniofacial development. Hypertelorism is an excessive distance between eyes and it is an integral part of various syndromes e.g. Cat eye syndrome. Dysmorphic characters are usually reported by clinicians in descriptive terms such as 'wide set eyes', 'broad nose' or 'largemouth'[3]. Interpupillary distance is the best method to quantify it[4]. Using both morphological features and measurements, the face can either be reconstructed (identifying the dead), superimposed or compared to a facial photograph (mistaken identities or missing personal or for the reconstruction surgeries after accidents). Congenital posttraumatic deformities can be better treated with the knowledge of normal values for this region to produce the best esthetic and functional result.3 It

is also used for the estimation of combined width of the maxillary six anterior teeth and serve as a useful factor in selecting artificial teeth[5].

Materials And Methods

This cross-sectional analytical study was carried out in the Department of Anatomy, Sir Salimullah Medical College, Dhaka from July 2017 to June 2018. The study was carried out on 200 medical students (100 male and 100 female) with age ranged from 20 to 25 years (The ossification of all bones of the face is completed by the age of twenty years. So, fully ossified face achieves its adult form and fixed measurements after this age. So, study subjects included in the study were between 20-25 years of age)[6].

At first the nature of the work was explained to the study subject (student). A written informed consent was taken from each study subject. Information was collected from each study subject with the help of a questionnaire. Age of the study subject was recorded from birth certificate or from national identity card. Subject who had no history of congenital and acquired orbital anomaly like squint, oculoplastic surgery or orbital trauma, medical conditions like ptosis, facial palsy, hyperthyroidism were included in the study[7].

Digital photographs of face – frontal view both in opened and closed eyes of the study subjects were taken in the Anatomy departments of Sir Salimullah Medical College, Dhaka, Mugda Medical College, Dhaka and Green Life Medical College, Dhaka.

The study subject was allowed to seat comfortably on a chair looking straight forward. The camera was set up on a tripod. Frontal facial photograph was taken with a digital camera at a 7.2 megapixel resolution under same lighting condition using flash mode from a fixed distance of 4 feet using zoom function. The subject's head was at the same level with the camera. The frontal facial photograph was taken at a particular time between 9 AM to 2 PM to avoid diurnal variation. Before taking frontal facial photograph of each study subject the "nose height" was measured from nasion (its manifestation on the visible surface of the face is a distinctly depressed area directly between the eyes, just superior to the bridge of the nose) to subscale (the point at which the nasal septum merges in the mid sagittal plane with the upper lip) by slide caliper and marked on the skin by black ball point. Then photograph was taken with the landmark "nasion" to "subscale" and the "nose height" of individual photograph was transformed into physically measured value by using transform option of Adobe Photoshop version: CC 2014 and ultimately photograph of eye was converted into actual size[8]. Then the variables were measured from the photograph of eye using MB ruler software[9] and the data were analyzed with the help of SPSS software package. (IBM SPSS statistics for windows, version 22.0; IBM corp; Armon K, New york.)

Procedure of measuring interpupillary distance (IPD):

Interpupillary distance (IPD) is the distance between the center of the pupils[10].

To get the interpupillary distance, center of one eye to the center of another eye was identified in a frontal digital photograph of face. Then the distance between the points was measured by using 'MB Ruler' software and was recorded on data sheet.

Ethical clearance:

To avoid any medicolegal questions for collection of digital photographs of face from the study subjects, a written clearance from the Institutional Ethics committee of Sir Salimullah Medical College, Dhaka was taken.

Result

Result of the study are shown in Table I and Figure 2. In male, the mean ± SD of interpupillary distance was 60.81±5.79 mm (range 33.44 - 79.52 mm)and in female, the mean ± SD of interpupillary distance was 57.07±5.34 (range 45.75 - 71.96 mm).The mean was significantly higher (p=0.000) in the male than in the female (Table I).

Discussion

Results of photographic variable of interpupillary distance were compared with the photographic variable of other studies from different countries like India, Nigeria, Pakistan and Iran.

The study showed some similarities as well as

Table I: Descriptive statistics of the measured Interpuillary distance

Sex	Interpupillary distance (in mm) Mean ±SD)
Mele (n=100)	60.81±5.79 (33.44-79.52)
Female (n=100)	57.07±5.34 (45.75-71.96)
P value	0.000**

Figure in parenthesis indicate range

Comparison between sex was done by unpaired Student's t' test

** = Significant at P < 0.01 (2 tailed)

n= sample size

SD = Standard Deviation

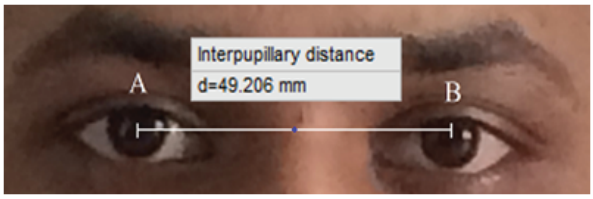

Figure 1: Digital photograph of face in frontal view showing the measurement of interpupillary distance. A- center of one eye, B- center of another eye and AB- interpupillary distance.

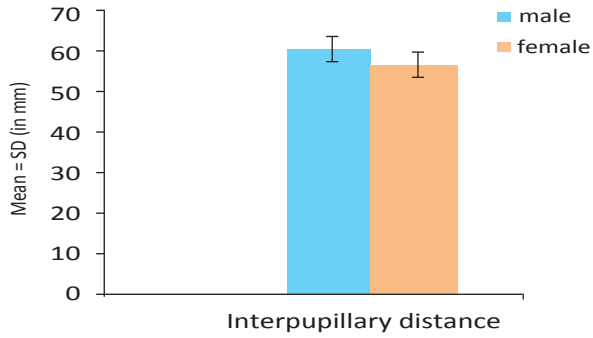

Figure 2: Bar diagram showing interpupillary distance (in mm) in male and female.

dissimilarities with otherstudies when the mean value of interpupillary distance was compared. Similarities were found with the people of India[4] and Nigeria.[11] Dissimilarities was found with the people of Pakistan[12] and Iran.[13] Similarities in findings might be due to almost similar race (mixed) present all over the Indo Bangla sub-continent. Dissimilarities in the findings with other studies might be due to mixture of different races, different climates, dietary habits and different geographical topography.[14] Use of different techniques for measurements might also be another cause of difference.

Many anthropologists believe that the Bengalis, the people of Bangladesh and different state of India make a vastly mixed race. The people of Iran and Pakistan belongs to Caucasoid race. The people of Nigeria came from Negroid race. Their nutritional habit was also different (more protein than carbohydrate).[15] So, the values of interpupillary distance was more than the study subjects.

Conclusion

The present study was an attempt to construct photo-anthropometric data on different measurements of eye in medical students of Dhaka city. Interpupillary distance of two hundred study subjects aged between 20-25 years were measured from digital photograph of face - frontal view both in opened and closed eyes to serve the purpose. This attempt may provide the direction to construct baseline photographic data of interpupillary distance in medical students of Dhaka city.

Result of the present study stated that interpupillary distance was found to be significantly higher in the male than in the female and also showed significant sexual dimorphism.

Data of the present study were compared with those of other countries.

This may contribute to the understanding of the relative status of the present study population in the context of the photographic variations of other study population around the world.

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Original Article:

Evaluation of the Efficacy of Oral Fluconazole 150 mg in the Treatment of Tinea corporis and Tinea cruris

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Abstract :

Background: *ISuperficial fungal infections are one of the most prevalent skin diseases worldwide. According to clinical reports, dermatophytosis has been the most prevalent form of superficial infections. Results of topical dermatomycosis treatment are often unsatisfactory, particularly in patients with extended or multiple infection sites.* ***Objectives:*** *This study aimed to evaluate the efficacy of oral fluconazole 150mg weekly in the treatment of tinea corporis and cruris.* ***Material and methods:*** *This cross-sectional study conducted in the department of Pharmacology in collaboration with department of Dermatology & Venereology at Mymensing Medical College, Mymensing from January 2016-December 2016. Total 108 clinically diagnosed patients with tineasis were selected nonrandomly and they were treated with oral fluconazole 150 mg once weekly for six weeks. Thereafter they were clinically evaluated at the end of 1st week, 2nd week and 6th week.* ***Results:*** *89(82.41%) patients were found to be clinically healed at the end of the treatment period.* ***Conclusion:*** *Our current study reveals that, fluconazole was quite effective in the treatment of tinea corporis and cruris. Fluconazole can be an excellent choice to treat dermatophytosis considering its low cost and weekly schedule.*

Keywords: Fluconazole, Tinea corporis, Tinea cruris

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Introduction

Dermatophytes are fungi capable of causing skin changes of the type known as ringworm or dermatophytosis. The ringworm species are all molds belonging to three asexual genera: Microsporum, Trichophyton and Epidermophyton1. It is most commonly caused by Trichophyton species, which digest keratin in the cells of the stratum corneum. T. rubrumis the most common infectious agent in the world and is the source of 47% of tinea corporis cases[2]. Despite numerous advances in health and medical sciences, superficial fungal infections have retained their position as one of the most important skin diseases[3, 4]. Dermatophytes can cause different manifestations in humans and the majors ones are Tinea corporis and Tinea cruris.

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These can be seen in the skin of the trunk, groin and genital area[5,6]. They have the tendency of making skin keratin to use them as nitrogen source. Cutaneous fungal infections have been reported worldwide as being one of the most common human infectious diseases in clinical practice.

In spite of therapeutic advances in the last decades, the prevalence of cutaneous mycoses is still increasing[7, 8]. They are usually spread through contact with infected humans (anthropophilic), animals (zoophilic) and soil (geophilic)[9], 10. Tinea corporis refers to tinea infection anywhere on the body except the scalp, beard, feet, or hands. This lesion presents as an annular plaque with a slightly raised and often scaly, advancing border and is commonly known as ringworm. Each lesion may have one or several concentric rings with red papules or plaques in the center. As the lesion progresses, the center may clear, leaving post-inflammatory hypopigmentation or hyperpigmentation[10]. Patients typically present with an annular patch or plaque with an advanc-

ing, raised, scaling border and central clearing. As the ring expands, the central portion of the lesion often clears. This pattern leads to the formation of irregular circles that gives tinea corporis its common name, ringworm[11]. The clinical signs of dermatophytosis depend on the affected region of the body; however, pruritis is the most observed symptom in human[12, 13].

Humidity in high rates, over-population and poor hygienic conditions are common risk factors for dermatophytosis[14, 15]. In recent years, the number of fungi recognized as human pathogens has risen, partly in debilitated and immunocompromised patients[16].

Most patients with tinea corporis are diagnosed clinically. To avoid a misdiagnosis, identification of dermatophytes infections requires both a fungal culture on Sabouraud's agar media, and a mycological examination, consisting of a 10% to 15% KOH preparation, from skin scrapings.

Although topical antifungals may be sufficient for treatment of tinea corporis & cruris, but systemic medications are used for patients with severe infection, for infections that do not respond to topical therapy, when the infected areas are large, macerated with a secondary infection, or in immunocompromised individuals[11]. Despite numerous advances in health and medical sciences, superficial fungal infections have retained their position as one of the most important skin diseases[3,4].

A survey conducted by World Health Organization on the prevalence of dermatophytic infection has shown that 20% of people presenting for clinical advice are suffering from cutaneous fungal infections worldwide[17].

Common systemic antifungal agents used are oral griseofulvin, terbinafine, fluconazole and itraconazole. Azole and Allylamine agents appear to have greater efficacy and fewer side effects than oral Griseofulvin[18, 19]. An alternative is fluconazole which is given orally once a week for up to six consecutive weeks. Fluconazole, a synthetic triazole derivative, is an azole antifungal agent [20].

The aim of this study to evaluate the efficacy of oral fluconazole 150 mg in the treatment of Tinea corporis and Tinea cruris.

Materials and Methods

A cross-sectional study was conducted in the department of Pharmacology in collaboration with department of Dermatology & Venereology at Mymensing Medical College, Mymensing from January 2016-December 2016. Patients was selected non-randomly withtin cases of Tinea corporis & Tinea cruris attending Dermatology OPD. Study Design: Cross sectional type of analytical observational study. Inclusion criteria: Patient with Tineacorporis and Tineacruris of both sexes, newly diagnosed case, lesion more than 3 in number & present in different parts of the body. Patient more than 18 years of age but less than 65 years. Exclusion criteria: Patient with comorbid condition: Diabetes mellitus, hypothyroidism, asthmatic patient and malignancy, psychologically ill patient. Hypersensitivity and intolerance to treatment. Pregnant and lactating mother. Sampling technique: Non random sampling was employed for collecting data to analyze the pattern of taking fluconazole for Tinea corporis and Tinea cruris. Study drugs: The patients were instructed to take fluconazole 150 mg once daily for six weeks. The patient was advised to use the medication as per the study schedule. Assessment of efficacy and safety: During the first visit, the patient was screened which also served as the baseline visit if he/she was not receiving any interacting drug. On the second visit at day 14, Clinical assessment was repeated. The end-of-trial visit was 6 weeks thereafter, on day 42 from inclusion of the subject. The clinical parameters for evaluation were signs and symptoms, which included itching, erythema and scaling. These parameters were assessed on a pre-determined four-point scale as: absent, mild, moderate and severe. The signs and symptoms were rated as clinical score 0 to 3: 0, absent; 1, mild; 2, moderate; or 3, severe,

for the above three target symptoms. At the global clinical evaluations, we rated the clinical findings as: Healed (absence of signs and symptoms), Markedly improved (>50% clinical improvement). Considerable residual lesions (< 50% clinical improvement. No change Worse. Statistical analysis: Efficacy data were evaluated for subjects who reported for the follow-up visit at the end of six weeks. Data entry was done in Microsoft Excel Sheet and analysis was carried out in SPSS version 21 and Z test was done.

Result

Table I showing that among 108cases, on 1st week follow up most cases came with residual lesion 56(51.85%), healed were 9(8.33%), on 2nd week follow up most cases came with markedly improved were 51(47.22%), healed were 27(25%), on 6th week follow up, healed were 89 (82.41%) cases, markedly improved were 12(11.11%) cases, Residual lesion were 03(2.78%) cases, No change was noted in 01(0.92%) cases, 03(2.78%) cases were worsen.

Table II showing clinical score and their comparison in different follow up. At base line mean±SD was 2.36±0.67. There was significant decrease in the clinical score beginning from baseline to the end of 6th weeks. P<0.05 beginning from 1st week to the end of 6th weeks, which is statistically significant.

Table I: Follow up and outcome of patients treated with Fluconazole (n=108)

Outcome	1st week	2nd week	6th week
Healed (absence of sign & symptom)	09 (8.33%)	27 (25%)	89 (82.41%)
Markedly improve (>50% clinical improvement)	29(26.85%)	51(47.22%)	12 (11.11%)
Residual lesion (<50% clinical improvement)	56 (51.85%)	21 (19.45%)	03 (2.78%)
No change	14 (12.97%)	07 (6.48%)	01 (0.92%)
Worsen	00	02 (1.85%)	03 (2.78%)
Total	**108 (100%)**	**108 (100%)**	**108 (100%)**

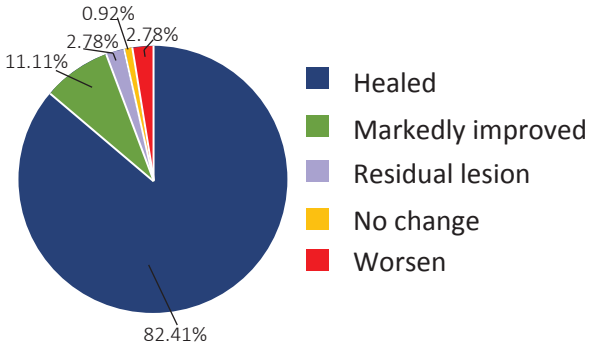

Figure 1: Bar diagram showing outcome of disease

Table II: clinical score and their comparison

Clinical score				
	At baseline	1st week	2nd week	6th week
mean±SD	2.36±0.67	1.69±0.80	1.11±0.88	0.28±0.69
p value		<0.05	<0.05	<0.05

Discussion

In recent years, prevalence of fungal infections has increased and this is believed to proceed from growth in at-risk population[21]. Studies have reported that epidemiology and distribution of superficial fungal infections especially dermatophytes have changed over the past decades[14]. Males are infected more than females. Infection can occur from direct or indirect contact with skin and scalp lesions of infected persons or animals[11]. Age, sex and race are important epidemiologic factors as dermatophyte infections are [5] times more prevalent in males than females[22]. The higher incidence in young males could be due to greater physical activity and increased sweating[23]. Dermatophytes are fungi that infect epidermis of the skin, hair and nail due to colonization in the keratinized layer. Dermatophytes of the anthropophilic species usually produce mild but chronic lesions. The dermatophytes are restricted to the keratinized tissues although inflammation involves the dermis and malpighian stratum of epidermis. The most common dermatophytes that cause tinea corporis are T. rubrum, T. mentagrophytes, M. canis, T. tonsurans.[1]

Topical treatment in Tinea infections is limited

because of the lengthy duration of treatment, poor patient compliance and high relapse rates at specific body sites [24].

Topical formulations may eradicate smaller areas of infection, but oral therapy may be required where larger areas are involved or where infection is chronic or recurrent [25]. Oral therapy is often chosen because of its shorter duration and potential for greater patient compliance[26].

A study done in India by suchil and others and conducted that employing fluconazole for Tinea, clinical cure rate was (88%) which was similar to this study.[27]

In 1997, A study done by Faergemann J and others conducted fluconazole 150 mg once a week for 4-6 weeks in the treatment of tinea corporis and tinea cruris. In the fluconazole group, 74% (80 out of 114) were clinically cured; which was similar to this study.[28]

A study done in Farukkhabad, India done by Kumar A et al., and showed that the clinical response rate of fluconazole was 37 out of 50 (74%) which was also similar to this study.[11]

In this study after 6 weeks of treatment with fluconazole 150 mg once a week, 89 out of 108 (82.41%) clinically cured and clinical scored was statistically significant ($p<0.05$).

Conclusion

Tinea corporis and tinea cruris is a common encountered problem in clinical practice. It is more common in male than female. It mainly involve lower extremities and trunk. It is more common young people. For treatment of tinea corporis and cruris, oral fluconazole 150 mg is quite effective and clinical score $p<0.05$, which is statistically significant.

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Original Article:

An observational study on the effect of Azithromycin in treatment of Acne Vulgaris

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Abstract :

Background: *Acne vulgaris or simply acne is a common dermatological problem. Acne most commonly seen in adolescence age caused by increased androgens in both sexes. It is caused by propionibacterium acne. In spite of many ranges of antibiotics available, Azithromycin is one of the antibiotics that has been recently prescribe for treatment of acne which is as effective as doxycycline and minocycline. This study is undertaken to see the efficacy of Azithromycin in the treatment of acne vulgaris.* ***Objective:*** *The main objective of this report was to assess the efficacy of 500 mg of azithromycin administered thrice weekly for 12 weeks in the treatment of acne vulgaris.* ***Methods:*** *This study was performed on 100 patients (50 male and 50 female) in Jahurul Islam Medical College and Hospital, Bajitpur, Kishoregonj, using special grading system GAGS. The exclusion criteria for the study were pregnancy, a history of macrolide sensitization and retinoid therapy.* ***Result:*** *Grade I patient showed effect 80%, Grade II 90% recovery Grade III is also effective as a 90% recovery but Grade 4 were not much effective only 65% recovered.* ***Conclusion:*** *This study showed that, azithromycin has greatest advantage over other systemic antibacterial in acne because it is long-acting drug and can be used in single dose three times weekly.*

Keywords: Acne vulgaris, Azithromycin, GAGS, Propionibacterium acnes.

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Introduction

Acne vulgaris is a common inflammatory disorder of the Pilo-sebaceous follicles. It is a multi-factorial disease and its pathophysiology centers on the interplay of follicular hyper-keratinization, colonization with Propionibacterium acnes (PA), increased sebum production, and inflammation.

This disease has a high prevalence, occurring mainly in adolescence. Although the peak of prevalence is around the 17th year of life, acne lesions can appear earlier and are not uncommonly observed in the age group ranging from 12 to 14 years, in which the conditions is under reported[1]. Antibiotic therapy has long been found useful in the management of moderate-to-severe acne vulgaris. Mechanisms of action include suppressing growth of PA, reducing the production of inflammatory mediators, and acting in immune modulation.

Commonly prescribe antibiotics include tetracyclines, doxycycline, minocycline, limecycline and erythromycin. Azithromycin is one of the antibiotics that has been recently prescribe for treatment of acne which is at least as effective as doxycycline and minocycline[2,3].

Azithromycin is a nitrogen-containing macrolide antibacterial agent and a methy1 derivative of erythromycin with actions and uses similar to those of erythromycin[4,5]. Its extensive distribution in the tissues allows pulse-dose regimen recommendation for increased compliance[6].

Material and Method

The primary focus of this open-label non-comparative therapeutic study was to assess the efficacy of 500 mg of azithromycin thrice weekly (once on every other day) for 8 weeks in the treatment of Acne vulgaris in patients. This study enrolled 100 patients from the outpatient Derma-

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tology Department in Jahurul Islam Medical college and hospital during the period from December 2018 to December 2019. Patients were examined by dermatologists and an assessment was made, including a full count of acne lesions, we used special grading system of GAGS. The lesions were counted at the beginning of the treatment and at weeks. The difference between the number of lesions observed at baseline and the number seen in subsequent examinations was used to evaluate the efficacy of therapy. At every check-up we assessed the clinical response to azithromycin, any adverse events, and patient tolerance. The exclusion criteria were pregnancy, a history of macrolide sensitization and retinoid therapy. Patients with relapsing acne previously treated with antimicrobials such as doxycycline, minocycline and erythromycin were eligible to be enrolled in the study after a six-month wash-out period. No topical therapy was associated. Patients were advised not to undergo any beauty procedures, such as chemical peels, bleaches during the study period. All patients were also evaluated at 2 months, post-treatment follow-up visit. 100 hundred patients 50 male and 50 female 17-25 yrs of age and with mild to severe acne (score of acne 19-38), in the Global Acne Grading System (GAGS), were included in the study.9 Every patient was being exact physical examination and graded by GAGS. In GAGS: Acne patients were assigned into 4 grades.

- Mild = 1 – 18 Score
- Moderate = 19 – 30 Score
- Severe = 31 – 38 Score
- Very Severe > 39 Score

In this study patients were excluded if: Global acne score was greater than 39 or lower than 19. Concomitant use of anti-androgenic drugs Isotretinoin use in the last six months Participants were awarded and investigators got written informed consent from them. After that, they were allocated to four groups as a grading system. We prescribed Azithromycin in these groups as follow:

Grade I: 500 mg Azithromycin as initial dose followed by 500 mg weekly pulse doses for 12 weeks.

Grade II: 500 mg Azithromycin as initial dose followed by 500 mg weekly pulse doses for 12 weeks.

Grade III: 500 mg Azithromycin as initial dose followed by 500 mg weekly pulse doses for 12 weeks. Grade IV: 500 mg Azithromycin as initial dose followed by 500 mg weekly pulse doses for 12 weeks.

We followed patients over a 12-week period and visited them monthly. At each visit, acne lesions were assessed by blinded dermatologist to treatment protocols and GAGS was used to evaluate the response of patients to treatment. The patient visits were done at the end of first, second and third month.

Grading of acne vulgaris using visual analogue Scale :

Grade	Score	Observation
Grade 1 (Mild)	1 – 18	Microcomedone
Grade 2 (Moderate)	19 – 30	Comedone
Grade 3 (Severe)	31 – 38	Inflammatory Papule/Pustule
Grade 4 (Very-severe)	> 38	Nodule Nodulo-Cystic

Result

At this open therapeutic trial 100 patients were enrolled (50 males, 50 females) all of them were teenagers and adolescents (ages 17-50 years) with moderate-sever papulo-pustular acne. **Grade 1** patient were achieved good excellence effect 80%. Grade II is also effective as 90% recovery. Grade III is also effective as a 90% recovery. But Grade 4 were not much effective only 65% recovered **(Table-1).**

Table I: Evaluation of efficacy of therapy

Grade of Response%	Reduction of Acne
Grade I	Up to 80%
Grade II	Up to 90%
Grade lll	Up to 90%
Grade IV	Up to 65%

Table II: Overall distribution of all acne patients (%)

Grade	Male	Female	Recovered Patient	Recovered Patient (%)
Grade 1	3	7	8	80%
Grade 2	7	3	9	90%
Grade 3	20	20	36	90%
Grade 4	20	20	22	65%
Total	50	50	85	85%

Discussion

Acne is multifactorial disease primarily of teenagers with follicular plugging and inflammation. It is the most common skin disease; affecting almost every individual during puberty[4,5].

Our patients achieved over all response (85%). Federico who reported a good excellent response of 90.9% after 4 weeks of therapy[6] and slightly higher than Singhi[7] comparative clinical trials have shown that the tolerability profile of azithromycin is superior to that of erythromycin and doxycycline[8] which is similar to the results conducted in our study. Moreover, tetracyclines can cause both mucocutaneous and systemic adverse effects. Azithromycin has many advantages compared to other antibiotics. It is more stable than erythromycin in low gastric pH, it produces fewer gastrointestinal side-effects and does not present any major drug interaction[9].

Gruber et al[10] compared azithromycin with minocycline and observed a satisfactory clinical response (70-75%) with both the drugs. These findings suggest that azithromycin is a better alternative in patients with moderate to severe acne and has no serious side effects.

Our study conveyed that Azithromycin had a less frequent dose, was easy to administer and was effective in controlling and clearing acne. The ease of this pulse regimen contributed to patient and parental compliance and cost-effectiveness which was comparable to the study conducted by Federico Bardazziet al in Italy[11].

The study also highlighted that azithromycin has great advantage over that systemic antibacterials because it is long acting and can be used in single dose three times weekly which distinguishes it from other acne drugs[12].

Conclusion

This study showed that, azithromycin has greatest advantage over other systemic antibacterial in acne because it is long-acting drug and can be used in single dose three times weekly.

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Original Article:

EFFECTS OF FOLIC ACID ON PAIN AND INFLAMMATION; AN ANIMAL STUDY

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Abstract:

Background: *Folic acid's (FA) role on inflammation is still controversial. Moreover its role on painful condition is not clearly demonstrated.* ***Objective:*** *To assess the effectiveness of FA supplementation on reducing pain and inflammation.* ***Methods:*** *This prospective experimental study was conducted in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahabag, Dhaka from 1st January 2011 to 30th June 2012. For this purpose, 12 male Long Evans rats, weighing 200 to 250 grams were collected from the animal house of BIRDEM, Shahabag, Dhaka. All these rats received a single intraperitoneal injection of either FA (5mg/kg) or equal volume of normal saline. To evaluate the effects on pain, tail immersion test for nociceptive pain and formalin test for nociceptive & inflammatory pain were done. In addition, to evaluate its effects on inflammation formalin induced hind paw oedema was measured.* ***Result:*** *FA supplementation significantly lowered the variables for chemical nociceptive pain.* ***Conclusion:*** *This study revealed that, supplementation of FA is effective in lowering nociceptive pain.*

Key words: Inflammatory pain, Nociceptive pain, Pain.

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Introduction

Pain is a multidimensional sensation consisting of physical, affective and cognitive components. It is protective, as it warns the brain about actual or potential tissue damage. But relieving pain is among the major goals of healthcare profession as it is the most unpleasant sensation. Pain is classified on the basis of etiological characteristics into nociceptive, inflammatory, neuropathic and functional pain[1-3]. Nociceptive pain act as an early alarm system declaring the direct activation of the nociceptor by noxious stimuli[2]. Nonetheless, under circumstances such as during surgery or after bony fracture following a RTA; this type of pain is needed to be relieved[4]. Combination of persistent noxious stimuli, resultant peripheral inflammation and the sensitized nervous system; leads to the development of the inflammatory pain[2]. This variant of pain is unremitting in nature and the major cause of suffering and morbidity in human unless relieved[5]. Inflammation is the local reactions of vascularized living tissues to microbial invasion or injury. This protective mechanism often spiral out of control and lead to further tissue damage or even organ failure[6]. Traditional analgesic and anti-inflammatory drugs which are being used to treat painful and inflammatory conditions have many side effects. Lately, many studies are being carried out throughout the world to replace or at least to reduce the dose or duration of traditional analgesics or anti-inflammatory drugs, by inventing alternate or adjunct medications.

Recently, the analgesic and anti-inflammatory effects of several members of the Vitamin B complex such as B17, B28 and B69 have been demon-

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strated in different experimental animals.

Among the other B vitamins, Folic acid's (FA) role in pain is least explored. Though no study was found on individual effects of FA supplementation on pain, its combination with other B vitamins were found to reduce pain in 2 groups of patients with chronic cephalgia[10] & osteoarthritis11. In addition, our previous study showed that 1 week supplementation of vitamin B12 & FA can decrease inflammatory pain[12]. Moreover, supplementation of this vitamin improves the availability of NO[9] and serotonin[10] in the human brain, where they act as analgesic agents[11]. Single dose supplementation of this vitamin lowered inflammation in different cell culture studies. In addition, 1-12 weeks supplementation of FA showed anti-inflammatory effect in different animal & human models[12-14]. On the contrary, single dose & repeated 4 weeks supplementation of this vitamin was found to increase inflammation by 2 other studies[15-16].

Therefore, on the basis of this background the present study has been designed to evaluate the effects of single dose FA (5mg/kg) supplementation on nociceptive pain, inflammatory pain and inflammation in male Long Evans rats.

2014 and ultimately photograph of eye was converted into actual size. Then the interpupillary distance was measured from photograph by MB ruler software.

Results: The mean ± SD of interpupillary distance was 60.81±5.79 mm (range 33.44 - 79.52 mm) in male and 57.07±5.34 mm (range 45.75 - 71.96 mm) in female. Interpupillary distance is significantly higher in male than female ($P < 0.01$). So, interpupillary distance shows sexual dimorphism.

Keywords: Interpupillary distance, Medical students, Photo-anthropometry

Materials and Methods

This prospective experimental study was conducted in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahabag, Dhaka from 1st January 2011 to 30th June 2012. All the experiments were conducted according to the guidelines for the Animal Experimentation Ethics Committee, Institute of Cholera and Diarrhoeal Disease Research, Bangladesh (icddr,b; 2003) and was approved by the Ethical review committee, BSMMU.

Experimental animal

A total number of 12 male Long Evans rats, weighing 200 to 250 grams were collected from the animal house of Bangladesh Institute of Research and Rehabilitation for Diabetic Endocrine and Metabolic Disorders (BIRDEM), Shahabag, Dhaka. They were kept under a 12/12 hour light/dark cycle in a standard laboratory condition for 7 days prior to testing for acclimatization. The experiments were performed during the day time between 8:00 to 13:00 hours to avoid the circadian influences. All the rats had free access to standard laboratory food and cooled boiled water. The room temperature was kept around 27˚ to 28˚ C which corresponds to the thermo neutral zone of rats. All the rats were regularly inspected for their wellbeing.

Grouping

The rats received single intra-peritoneal injection of either 5mg/kg of FA (experimental group- 6 rats) or equivalent amount of normal saline (control group- 6 rats). One hour after supplementation, they were subjected to tail immersion test followed by formalin test & then formalin induced paw oedema test.

Tail immersion test

To assess the thermal nociception tail immersion test was done23, 24. For this, each rat was placed in a Plexiglas mechanical restrainer, with the tail hanging freely and kept there for initial 5 minutes for acclimatization. Then 400 ml of heated water (52±0.5˚C) was taken in a 500 ml glass beaker with a thermometer placed in it. Then the distal 10 cm

of the tail was immersed into the heated water and the tail withdrawal latency and the mean of similar 3 successive maneuvers (at 5 minutes interval) noted as baseline latency (BL) (taken before vitamin supplementation). Again, another tail immersion measurement was done 1 hour after vitamin supplemntation. The mean of similar 3 successive maneuvers at 5 minutes interval were noted as test latency (TL). To minimize tissue damage, a maximum latency of 15 seconds was considered as cut-off time. Antinociceptive effect was calculated as percentage of maximum possible effect (% MPE) as follows:

% MPE=[(TL-BL)/(Cut off time-BL)]×100

Formalin test

Formalin test25 was done to assess nociceptive & inflammatory pain just after completing the tail immersion test. The rat was restrained by a thick towel and the right hind paw was exposed. Fifty (50) µl of dilute formalin (2%) was injected subcuteneously into the planter aspect of the rats right hind paw with an insulin syringe. Then the animal was placed in the observation cage of the plexiglas formalin box and the pain behaviors were observed for consecutive 60 minutes. Within this time the first 5 minutes (1st – 5th) were considered as the early phase (nociceptive pain), middle 10 minutes (6th -15th) as the interphase and last 45 minutes (16th-60th) as the late phase (inflammatory pain)26, 27. Observation was made by counting the total frequency of jerking and total duration of flexing plus licking of the injected paw during this time through a mirror fixed below the formalin box at 45˚ angle.

Formalin induced paw oedema test

After completing the formalin test, the animal were sacrificed and formalin induced paw oedema test28 was done to measure inflammation. Both hind paws were cut at knee joint & their volumes were measured using a water plethysmometer. Paw volume was calculated as the difference of the amount of water volume after & before paw immersion. Net oedema volume was calculated by substracting the left paw volume from the right paw volume.

Drugs

FA (Mark, Germany) was purchased from the local market.

Statistical analysis

The results were expressed as mean ± SE and were statistically analyzed by independent sample't' test with SPSS (Version 21.0). In the interpretation of results $p \leq 0.05$ was accepted, as the level of significance.

Result

Nociceptive pain

The effects of intraperitoneal (i.p.) administration of FA or normal saline were observed in tail immersion test & in early phase of formalin test. In tail immersion test % MPE & in early phase of formalin test total jerking frequency as well as total duration of flexing & licking were analyzed as nociceptive pain behaviors.

All the nociceptive pain variables were improved in experimental group compared to control. Moreover, the results were significant for formalin test **(Figure 2)** but not tail immersion test **(Figure 1)**

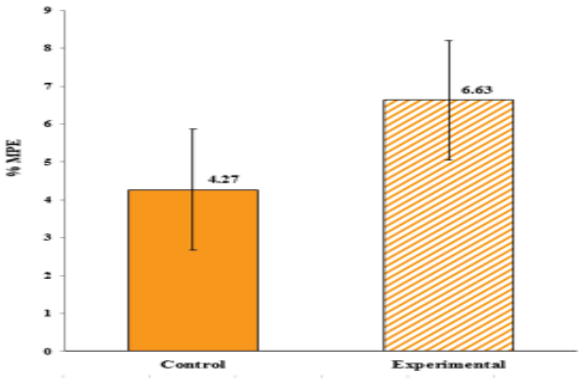

Figure 1: %MPE in tail immersion test in different groups of rats. Each bar symbolizes for mean ± SE for 6 rats.

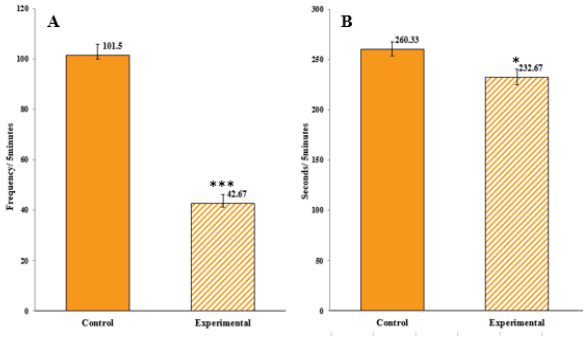

Figure 2: Frequency of jerking (A) & duration of flexing & licking (B) in early phase of formalin test in different groups of rats. Each bar symbolizes for mean ± SE for 6 rats. *** = p≤0.001 & *= p≤0.05, compared to control.

Inflammatory pain

Inflammatory pain behaviors were observed as frequency of jerking & total duration of flexing & licking in the late phase of formalin test.

All the inflammatory pain variables were lower in the study group than that of controls, though the results were statistically non-significant (Table I).

Table I: Inflammatory pain variables in different groups (n=12)

Variables	Control	Experimental
Jerking in late phase of formalin test (frequency/ 5min)	75.44±1.26	72.57±1.32
Flexing & licking in late phase of formalin test (seconds/ 5min)	288.85±2.59	284.98±1.94

Data were expressed as mean±SE. Independent sample 't' test was done in between control & experimental groups.

Inflammation

The amount of oedema in the formalin injected paw was measured as inflammatory variable at the end of formalin test. No difference was observed between the control & experimental group for this variable (Table II).

Table II: Inflammatory variable in different groups (n=12)

Variables	Control	Experimental
Paw oedema volume (ml)	0.23±0.02	0.23±0.02

Data were expressed as mean±SE. Independent sample 't' test was done in between control & experimental groups.

Discussion:

Pain & inflammation, though protective; are the major causes of physician consultation worldwide[29]. The annual cost for their management exceeds billions of dollars in developed countries[30]. Combinations of water soluble vitamins are commonly prescribed as an adjunct to traditional analgesic. But their individual effects in relieving painful or inflammatory conditions are least explored. With this view, the present study was undertaken to assess the effects of FA on pain & inflammation.

Hot water tail immersion test & early phase of formalin test are amongst the common & standard methods for elicitation of nociceptive pain in rodents[23]. Our study demonstrated significant decrement of nociceptive pain after single dose FA supplementation. However, no study was available to compare with this finding. Although mechanism of this decrement of nociceptive pain can't be explained from our study but increased production of NO[13], serotonin[14] or Noradrenaline[31, 32] by FA in the brain may be responsible its antinociceptive effect.

Late phase of formalin test is the commonest method for the study of inflammatory pain in rodents[23]. In this study, non-significant decrement of inflammatory pain were observed; though no study was found demonstrating the effect of FA on inflammatory pain alone; our previous studies

showed that the combination of B12 & FA lowers inflammatory pain in similar animal models[12,33]. Further study with larger group size, different animal models or administering FA for longer duration is required for further exploration.

Formalin induced paw oedema test is a simple but accurate method for inducing inflammation in experimental animal[34]. No effect of FA was observed on inflammation in our study. Literature review revealed FA to possess both anti-inflammatory as well as pro-inflammatory effects in different studies[16-22]. Further studies with longer duration of FA supplementation may yield clues to its effect on inflammation.

Conclusion

From this study, it may be concluded that supplementation of FA alleviates formalin induced nociceptive pain.

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