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Healthcare Associated Infection with Rapidly Growing Mycobacteria : An Emerging Health Problem

Rapidly growing mycobacteria (RGM) are nontuberculous species of mycobacteria having ability to grow on culture media within 7 days of post-inoculation. These atypical mycobacteria are widely distributed in nature and have been isolated from soil, tap water and natural water.¹ Among RGM, *M. fortuitum*, *M. chelonae* and *M. abscessus* have emerged as important human pathogens being responsible for a number of healthcare associated infection (HAI).^{2,3,4,5} These bacteria are not a part of skin commensal, yet loss of skin integrity is very important in infection.² These hydrophobic RGM have the ability to form biofilm in the environment for their survival. Hence, these are difficult to eradicate with regular disinfectants like glutaraldehyde, chlorine etc. Shedding of these organisms from biofilm in water pipe or device may contaminate them.¹ Improper sterilization of endoscopes and laparoscopic and surgical instruments thus may cause post-procedural wound infection. Contaminated gentian violet, rinsing solution, antiseptic solution, injectable medications, unsterile surgical instruments or poor wound care, like cleaning post-operative wound with contaminated tap water may be the source of infection in hospital settings.⁶ Clinical categories of HAI by RGM includes respiratory tract infections, infections related to hemodialysis, peritonitis associated with CAPD, injection associated cutaneous and joint infections and post-surgical infections.⁷ Post-operative wound infections are the most predominant category. Such infections caused by RGM generally appear 4-6 weeks after the procedure, because of their longer incubation period, with painful, draining subcutaneous nodules at the infection sites, not responding to antibiotics used for pyogenic infection. Diagnosis is delayed due to relatively mild and indolent symptoms⁴ and also due to the fact that Ziehl – Neelsen staining and mycobacterial culture are not routinely done for surgical wound.² Laboratory diagnosis of RGM can be done by Ziehl-Neelsen staining and mycobacterial culture of specimen collected from infection site. Collection of specimens should be done by avoiding potential sources of contamination, like tap water. Successful treatment of RGM requires administration of antibiotics as determined by susceptibility testing and in some cases addition of surgical debridement.⁵ It has been reported that conventional anti-tubercular drugs are ineffective against RGM. Studies shows susceptibility of several RGM species to clarithromycin, cefoxitin, amikacin, sulphonamides ranges from 96-100%.⁸ To prevent recurrence, antibiotic treatment should be continued for at least 3-6 weeks after the wound heals.^{8,9} As because laboratory identification of RGM needs special settings and longer time and due to scarcity of data regarding antimicrobial susceptibility of these organisms in our country, prevention of infection is most important. Careful surveillance by hospital

infection control team, attention to adequate high –level disinfection of medical devices, use of sterile reagents and biologicals will prevent most outbreaks.⁷

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Original Article

Effects of Physical Exercise on Urinary Albumin Level in Type 2 Diabetic Male with Microalbuminuria

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Abstract

Background: Microalbuminuria is a microvascular complication of diabetes mellitus. Physical exercise has effects on urinary albumin level in type 2 diabetic male with microalbuminuria.

Objective: To assess the effects of physical exercise on urinary albumin level in type 2 diabetic male with microalbuminuria.

Methods: This prospective interventional study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC), Dhaka between 1st July 2015 and 30th June 2016. Total thirty (30) type 2 diabetic male with newly diagnosed microalbuminuria (urinary albumin-creatinine ratio 30-299 mg/g), age ranged from 45 to 60 years were selected by purposive consecutive sampling from Out Patient Department of Endocrinology, Sir Salimullah Medical College and Mitford Hospital, Dhaka. Previously prescribed oral hypoglycemic and antihypertensive drugs were maintained, and the participants were instructed not to change their diet habits during the study period. All the participants were asked to perform moderate aerobic physical exercise, consisting of 30-40 minutes walking/day, 5 days/week, at an intensity of 50-70% of maximum heart rate (HRmax) for a total duration of 90 days. All the subjects were studied two times: before performing physical exercise i.e. on day-1 (Phase A) and after performing physical exercise for 90 days i.e. on day-91 (Phase B). Urinary albumin level was estimated by immunometric assay method. For statistical analysis, paired sample "t" test was performed.

Results: In this study, urinary albumin level was significantly ($p < 0.001$) decreased in type 2 diabetic male with microalbuminuria after performing physical exercise for 90 days in comparison to those of their pre exercise values.

Conclusion: From this study it may be concluded that, physical exercise significantly decreased urinary albumin level in type 2 diabetic male with microalbuminuria.

Keywords: Physical exercise, Type 2 Diabetes Mellitus, Microalbuminuria, Urinary albumin.

Introduction

Diabetes mellitus is a syndrome of impaired carbohydrate, fat and protein metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissues to insulin. Type 2 diabetes, also called non-insulin-dependent diabetes mellitus, is initially caused by decreased sensitivity of target tissues to the metabolic effect of insulin.¹ Diabetes mellitus is characterized by hyperglycaemia. Symptoms of hyperglycemia include thirst, polyuria, weight loss, fatigue, sometimes with polyphagia and blurred vision.²

The World Health Organization reports on diabetes prevalence alarmed that diabetes is a serious threat to entire population of the world. Microalbuminuria is one of the most common diabetic microvascular complications. It is the earliest sign of diabetic nephropathy.³ It is a sign of abnormal vascular function and increased vascular permeability.⁴ The prevalence of microalbuminuria is 4.6 % in diabetes mellitus patients.⁵ Microalbuminuria may progress to overt nephropathy which is the most common cause of end-stage renal disease and an important cause of morbidity and mortality.

Exercise is planned, structured and repetitive bodily movement performed to improve or maintain one or more components of physical fitness.⁶ Physical activity may be associated with less albuminuria and it has protective effects on the vascular endothelium.⁷ Exercise reduces albuminuria in diabetic rats. Reduction in albuminuria and maintained podocyte numbers, with improvements in oxidative damage and chronic inflammation, might be the beneficial effects of exercise in diabetic kidney disease.⁸

A small study revealed that microalbuminuria was improved after 6 months of aerobic exercise.⁹ In another human study, after one year follow up urinary albumin level were decreased in the physical activity groups. They also found a trend toward reducing albuminuria in the macroalbuminuria group.¹⁰

There is little information about the effects of exercise on urinary albumin level in type 2 diabetes mellitus patients with microalbuminuria. So, this study has been designed to observe the effects of physical exercise on type 2 diabetic male with microalbuminuria. It is expected that the findings of this study will be beneficial for type 2 diabetic male with microalbuminuria as well as for the physician of faculty of endocrinology for better management of microalbuminuria.

Methods

This prospective interventional study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC), Dhaka between 1st July 2015 and 30th June 2016. Total thirty (30) type 2 diabetic male with newly diagnosed microalbuminuria (urinary albumin-creatinine ratio 30-299 mg/g), age ranged from 45 to 60 years were selected by purposive consecutive sampling from Out Patient Department of Endocrinology, Sir Salimullah Medical College and Mitford Hospital, Dhaka. Ethical permission was taken from the Institutional Ethics Committee (IEC) of Sir Salimullah Medical College. After proper counseling, the aim, objectives, risk and the procedure of the study were explained in details to the subjects. Written informed consent was taken from the subjects. Then their general information (personal, medical, family and occupation) and data were collected and all the information were recorded in a prefixed questionnaire. Previously prescribed oral hypoglycemic and antihypertensive drugs were maintained, and the participants were instructed not to change their diet habits during the study period. All the participants were

asked to perform moderate aerobic physical exercise, consisting of 30-40 minutes walking/day, 5 days/week, at an intensity of 50-70% of maximum heart rate (HRmax) for a total duration of 90 days. All the subjects were studied two times: before performing physical exercise i.e. on day-1 (Phase A) and after performing physical exercise for 90 days i.e. on day-91 (Phase B). Five (5) ml of first morning urine sample was collected in sterile glass test tube from each participant for estimation of urinary albumin level. Urinary albumin level was estimated by immunometric assay method in the laboratory of the Department of Biochemistry, Sir Salimullah Medical College, Dhaka. Statistical analysis was done by paired sample 't' test. P value ≤ 0.05 was accepted as level of significance. Statistical analysis was performed by using a computer based statistical program SPSS version-22.

Results

In this study, the mean (±SD) urinary albumin level was significantly (p<0.001) decreased in phase B in comparison to that of phase A (Table I and Figure-1).

Table-I: Urinary albumin in type 2 diabetic male with microalbuminuria (n=30)

Parameters	Phase-A	Phase-B	P-value
Urinary albumin (mg/L)	63.23±5.09 (55-71)	42.93±5.63 (33-50)	0.000***

Phase A: Before performing physical exercise (Control, on day-1)

Phase B: After performing physical exercise (Study, on day-91)

***= Significant at P<0.001; n= Total number of subjects

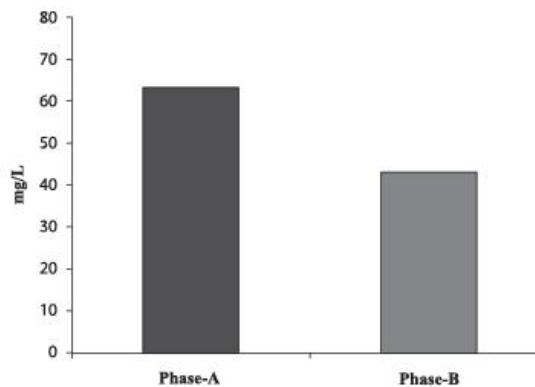


Fig-1: Urinary albumin Comparison among groups

Discussion

In the present study, mean urinary albumin level was significantly ($p < 0.001$) decreased in the subjects after performing physical exercise in comparison to that of before exercise value. This finding is in agreement with others.¹¹⁻¹⁶ Whereas, some investigators found non-significantly decreased urinary albumin level after performing aerobic exercise.¹⁷

Though exact mechanisms of these effects could not be revealed directly from the present study, several researchers of different countries proposed various suggestions on these aspects, which might be cause of our present findings. It has been suggested that exercise improves the indices of endothelial function.¹⁸ Again, exercise causes improvement of oxidative damage of the tissue and inflammation, and maintains podocyte numbers. Moreover, exercise induced withdrawal of efferent sympathetic vasoconstrictor activity to kidney contribute to decrease urinary albumin excretion.¹⁵

Conclusion

From this study it may be concluded that, physical exercise significantly decreased urinary albumin level in type 2 diabetic male with microalbuminuria. Although, further study is needed to elucidate the exact mechanism responsible for these effects.

Acknowledgement

The Authors acknowledge the department of Biochemistry, Sir Salimullah Medical College, Dhaka, for their kind cooperation to carry out the laboratory investigations and also thankful to the study subjects for their active and enthusiastic participation.

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Original Article

Pattern of Fertility in Women of Reproductive Age Suffering from Cervical Cancer

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Abstract

Background: Cervical cancer is the most common malignancy of female genital tract in Bangladesh. Though with proper screening and risk factor modification it can be prevented easily.

Objective: The major objective of the study was to find out fertility pattern in women of reproductive age group suffering from cervical cancer.

Methods: This cross sectional study was carried out in National Institute of Cancer Research and Hospital, Mohakhali, Dhaka during the period of January 2016 to December 2016. The study was performed among 105 diagnosed female patients suffering from cervical cancer available during the data collection period in the study place. Data were collected by face-to-face interview with a questionnaire and with a check list.

Results: It was found that majority of the respondents (54%) were within the age range of 46 to 50 years. Ninety percent of the respondents were found to be currently married and majority of them (86.9%) were Muslim. About 39% of the respondents were illiterate and 31% of them had primary level education. Majority of the respondents (70%) were housewife by profession and 8.6% were service holders. The monthly family income was Tk. 14247±4360. About 70% of the respondents were found to practice of different types of contraceptive methods, the most commonly used method was oral pill (73%). Mean age at menarche was 13 years and the mean age at first marriage was 15.5 years. Mean age at first childbirth of the respondents was 15.62 years. Majority of respondents were multipara and 48% of them had conceived for 3 to 4 times. Maximum proportion (48.6%) of cervical cancer patients were in grade III. Next higher group 25.7% was in grade II, 15% were at grade I and 10% were at grade IV. 55.2% of the patients had squamous cell carcinoma, 22.9% had adenocarcinoma and only 21.9%, had adenosquamous carcinoma.

Conclusion: Study showed that women who had early marriage and experience their 1st pregnancy at a young age, multiple and repeated pregnancies are at an increased risk of cervical cancer. Screening women for pre cancerous changes and treating the abnormal tissue seems to protect women from developing cervical cancer. If those factors are avoided there could be safe guarded in a significant proportion.

Keywords: Fertility, Reproductive age, Cervical cancer.

Introduction

Cervical cancer is the fourth most common cancer among the women globally with an estimated 604000 new cases and 342000 deaths in 2020, 90% of which occur in developing countries.¹ In developing countries mortality rates are reported 11.2 per 1,00,000 women on average, almost three times the rate of developed countries.² Cervical cancer is preventable and curable

when detected at an early stage. 5 year survival rate of cervical cancer when detected at an early stage is 92% and the combined 5 year survival rate for all stage is 71%.³

Cervical cancer is an important reproductive health problem in Bangladesh. It is the most common malignancy of female genital tract in Bangladesh. Cervical cancer constitutes 12% of all cancer cases in

women in Bangladesh.⁴ More than 80% of patients diagnosed with this eminently preventable cancer present in clinically advanced, inoperable stages.⁵ Most of the cancer patients in Bangladesh usually attend in the hospital in an advanced stage, resulting in decrease survival and increase morbidity and mortality rate. So it can be said that as one of the rapidly becoming growing public health problem causing a good number health and economic loss of the community and the country as a whole.

Present study was designed to ascertain some risk factors such as early marriage, early age at first pregnancy, too many and repeated childbirth have been associated with the increasing risk of the carcinoma cervix. The natural history of cervical cancer is such that it seems to follow as progressive course from epithelial dysplasia to carcinoma in situ to invasive carcinoma. Fortunately, it is possible to detect it early during a pre-invasive curable stage by the Pap smear test and VIA test to take measures to prevent it from progressing into a life threatening illness.

The result of the study may guide us whether immediate necessary steps are to be taken by the government for the prevention of the spread of this dreadful disease by giving emphasis on avoiding early marriage, early child birth, multiple pregnancies, improvement of socio-economic condition, proper health education as well as by simple measure like pap smear screening. Deaths associated with cervical cancer are the most telling indicator of the disease's impact on women, their families, and their communities. A mother's death dramatically compromises the health of a family, especially the health of children. These deaths are avoidable, however. With timely screening and appropriate treatment, deaths from cervical cancer can be greatly reduced. The aim of the study is to identify some risk factors of cervical cancer which may help to diagnose this life threatening disease at an early stage via screening test and thus give early treatment.

Methodology

This descriptive type of cross sectional study was conducted to assess the correlation between some fertility related factors and the risk of developing cervical cancer in National Institute of cancer research and hospital. This place was selected purposively for it provides integrated treatment facilities both indoor and outdoor services. According to the study objectives the study was designed with description of knowledge

related factors. The study period was January to December 2016 and Total of 105 women who are diagnosed case of ca cervix between 15-49 years of age were taken as study population. Prior to data collection a semi structured pre-tested questionnaire prepared based on the objectives of the study. Respondents were selected purposively and data was collected by face to face interview. The respondents were informed about their full right to participate or refuse to participate in the study. After collection of data, entry and analysis such as frequencies, percent were done by the software SPSS (version 23).

Results

Out of 105 respondents, majority of the women (53.2%) were of 46-50 years and only 02 (1.9%) belongs 30-35 years age group. Out of 105 respondents 41 (39%) women were illiterate and the rest are educated. Most of the respondents were house-wives 73 (69.5%) followed by 32 (30%) were various type of service holder. Monthly family income of majority women 102(97.1%) was taka 1,0000-20000 taka (low socio economic background) and few of them 03(2.9%) had 20000-30000 taka (middle socio economic status). (Table-I)

The majority i.e. 77% were married when their ages between 14-17 years, 17% got married between the age of 18-21 years and very few i.e. 6% did so at the age of 22-25 years. Asked about the duration of conjugal life, majority i.e. 51% led 21-30 years of married life followed by 37% led 31-40 years, 9% led 11-20 years and 3% led 5-10 years. Among the respondents almost 73(69.5%) had regular menstrual cycle while 32(30.5%) of them gave the history of irregular cycle. About 91% of respondents had history of MR and 9% had no history of MR. About 71% of respondents had history of abortion and 29% had no history of abortion. Among them 74(70.5%) used different methods of contraceptive. Majority i.e. 54 (73%) used oral pill followed by 9(12.2%) used copper-T and 7(9.5%) used injectable contraceptive, only 4(5.4%) used barrier method and 31(29.5%) had no history of contraceptive used. Among the respondents majority i.e. 45(47.9%) conceived 3-4 times in their life followed by 39(41.5%) conceived 5-6 times and 10(10.6%) conceived 1-2 times. So mean + (SD=3.64+ (1.10). 105 respondents 65(69.1%) had 3-4 no. of children followed by 16(17%) had 5-6 no. of children and 13(13.8%) had 1-2 no of children. (Table-II)

Among the respondents about 98(93.3%) had history of cervical infection and 7(6.7%) had no history of cervical infection. About 58(55.2%) of respondents had squamous cell ca, 24(22.9%) of respondents had adenocarcinoma and 23(21.9%) had adenosquamous carcinoma. Majority of the respondents about 51(48.6%) had in grade III, followed by 27(25.7%) had in grade II, 16(15.2%) had in grade I and 11(10.5%) had in grade IV. (Table-III)

The study showed relationship between cancer types with obstetrical and gynaecological factors. There was also association of cervical cancer types with the number of conception of the respondents. But MR and abortion has no significant association between the type of cervical cancer. (Table-IV)

Table-I: Socio-demographic variables of the respondents (n=105)

Age-group (years)	Respondents (%)
30-35	02 (1.9)
36-40	18 (17.1)
41-45	29 (27.6)
46-50	56 (53.3)

Education of the women	
Non educated	41(39%)
Educated	64(60%)
Occupation of the women	
Housewife	73(69.5%)
Various type of service holder	32 (33%)
Income	
Lower income (10000-20000)	102 (97.1%)
Middle income (20001-30000)	03 (2.9%)
Age at Marriage (Years)	
14-17	77 (77%)
18-21	17 (17%)
22-25	6 (6%)
Duration of Married Life	
5-10	3 (3%)
11-20	9 (9%)
21-30	51 (51%)
31-40	37 (37%)

Table II: Reproductive variables of the respondents (n=105)

Reproductive variables	Frequency
Menstrual Cycle	
Regular	73 (69.5%)
Irregular	32 (30.5%)
History of MR	
Yes	91 %
no	9 %
History of Abortion	
yes	71%
no	29%

Delivery Conducted by	
Doctor	27 (28.4%)
Nurse	08 (8.4%)
Midwife	51 (53.7%)
Untrained Dai	09 (9.5%)
Types of delivery	
Normal	66 (69.5%)
Caesarean	22 (23.2%)
Instrumental	07(7.3%)
Birth Injury	
Yes	46(43.8%)
No	59(56.2%)
Contraceptive use	
Yes	74 (70.5%)
No	31(29.5%)
Type of contraceptive	
Oral pill	54 (73%)
Condom	04 (5.4%)
Copper T	09 (12.2%)
Injection	07 (9.5%)
Duration of contraceptive use	
3-6	47(63.5%)
7-10	26(35.1%)
11-14	01(1.4%)
Number of Conceive	
1-2	10(10.6%)
3-4	45(47.9%)
5-6	39(41.5%)
Number of children	
1-2	13 (13.8%)
3-4	65 (69.1%)
5-6	16 (17%)

Table-III: Types and staging of cervical cancer (n=105)

Variables	Frequency
Cervical infection	
Yes	98 (93.7%)
No	07 (6.7%)
Histopathological type	
Squamous cell carcinoma	58 (55.2%)
Adeno carcinoma	24 (22.9%)
Adeno squamous carcinoma	23 (21.9%)
Stage of cancer	
Grade I	16 (15.2%)
Grade II	27 (25.7%)
Grade III	51 (48.6%)
Grade IV	11 (10.5%)

Table-IV: Association between cancer types with obstetrical and gynaecological variable (n=105)

No of conceive	Cancer types			P-value
	Sq cell ca	Adeno ca	Adeno sq ca	
1-2	4 (40.0%)	2(20.0%)	4(40%)	
3-4	24(53.3%)	9(20.1%)	12(26.7%)	P=0.042*
5-6	21(53.8%)	12(30.8%)	6(15.4%)	
MR				
Yes	4(40.0%)	4(40.0%)	2(20.0%)	P= 0.038
No	54(56.8%)	20(21.1%)	21(22.1%)	
Abortion				
Yes	19(63.3%)	7(23.3%)	4(13.3%)	P=0.385
No	39(52%)	17(22.7%)	19(25.3%)	

Discussion

The current study was under taken to find out some factors associated with ca cervix, as well as to observe the fertility pattern of the women suffering from cancer cervix. In this study among 105 respondents more than half of the patients (54%) suffering from cervical cancer were within the age range of 46 to 50 years, with mean age of 44.72 ±3.84 years. These findings agree with the findings of the study done in abroad that showed the maximum age group of cancer cervix patients are within 40-50 years. 660% of the respondents were educated. In a study about 23% of total respondents were illiterate and 63% had secondary education.⁷ Study showed that about 90.5% respondents were housewife which is almost consistent with this study.^{5,6} The median monthly family income of the respondents was found to be (14247 tk ± 4360). And 97.1% of the

respondents monthly income was between 10000-20000tk. Above data are consistent with the various studies.^{8-10,13,16} Age at first marriage there by age at first coitus is recognized as a major risk factor for cervical cancer.¹¹ The mean age at first marriage of the respondents was 13.54 years, 60% of the respondents were married between 10-14 years. It supports the finding of the study which showed that marriage earlier than 17 years are at particularly high risk of developing cervical cancer.^{11,12,16} It is also consistent with another study.^{12-14,16} In a case control study revealed that patients who experience inter course at the age before 20 years the relative risk of developing, carcinomas in situ (CIS) was 2.55 times higher than that of women who were exposed to sexual activity at 21 years or earlier.¹⁵ The mean age at first child birth of the respondents was found to be 15.62 years minimum and maximum ages were 13 and 24 years respectively, More than 90% of the respondents had their first child before the age of 20 years. The findings are consistent with the findings of Kumar V where majority was within age group of 16-19 years.¹⁴

Among the respondents 48% had 3-4 parity and 42% had 5-6 parities. It indicates that multiple parity had an impact on fertility. This statement also consistent with other study where it has been seen an impact on fertility. This statement also consistent with other study where it has been seen that risk of cervical carcinoma increased with number of births.¹⁷

Almost 91% respondents had performed MR and 71% had at least experience of one abortion. This finding has similarity with the study which showed that risk increased to 2.2 for women who had undergone 2 or more abortions compared within women who had never had one abortion.¹⁸

In this study a greater number (70%) of respondents were contraceptive users. About 73% responded used oral pill only. Mean duration of use of contraceptives by respondents was 3-6 years. None of the respondent's husbands used condom for contraception. The finding are similar to the study that long term oral contraceptive uses were found to be at increased risk of carcinoma in situ. Woman with more than 6 years of oral contraceptive use had an adjusted relative risk of 2.3 compared with never users.¹⁹ The present study finding about no use of condom is supported by the study done by Barry A in Denmark that most significant risk determination of cervical neoplasia were history of non use of Condom and also risk of infection with

human papilloma virus (the potential carcinogenic virus) from male partner.¹⁸ Most (94%) of the respondents encountered cervicitis. Three histopathological type of carcinoma was found among the respondents. 55% of the respondents had squamous cell carcinoma, 23% had adeno carcinoma and only 21% had adeno squamous carcinoma. According to a study showed that 89.19% were squamous cell carcinoma and 5.68% were adeno carcinoma, which is consistent with the current study.²⁰ Almost half (49%) of the respondents were diagnosed as ca cervix Grade III. About 40% of the respondents were diagnosed 4-6 months after initial signs and symptoms. 23% were diagnosed after 1-3 months and another 23% were established 7-12 months after the initial problem.

Conclusion

Study showed that women who had early marriage and experience their first pregnancy at a young age, multiple and repeated pregnancies are at an increased risk of cervical cancer. Screening women for pre cancerous changes and treating the abnormal tissue seems to protect women from developing cervical cancer. If those factors are avoided there could be safe guarded in a significant proportion. Screening practices can preferentially be directed to the target population for optimal utilization of resources. Specific awareness programmes, health education, promotion of condom uses, and need to follow healthy hygienic practices is the most easiest approach in reducing the incidence of cervical carcinoma in resource crunched societies like Bangladesh. Cervical cancer control activities included in the existing reproductive and child health programme. As cervical cancer is one of the most common cancers among the women in most of the developing countries, substantial measures need to be taken to address such a situation.

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Original Article

Pattern of clinical presentation of bronchial carcinoma

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Abstract:

Background : Lung cancer is most common cancer world –wide, accounting for 1.2 million new cases annually in 2000, and causing 18% of all cancer deaths. The prevalence of lung cancer is second only to prostate cancer in men and breast cancer in women. The disease caused more than 158,000 deaths –more than colorectal, breast, and prostate cancers combined.

Objective : The study was carried out to evaluate the clinical presentation of bronchial carcinoma.

Methods: This observational study was carried out in the Department of Medicine (Respiratory wing), Bangabandhu Sheikh Mujib Medical University (BSMMU) and National Institute of Chest Disease (NIDCH) during the period of september 2011 to February 2012. A total of 60 admitted patients with a clinical, radiological and histological diagnosis of bronchial carcinoma were enrolled in the study. Complete sociodemographic characteristics, smoking status, radiological, and histopathological characteristics of the tumor were recorded in the study. CT scan of the chest was done in the majority of the patient. CT-guided FNAC and US guided FNAC tissue sampling from lung lesions followed by histopathological examination was done to diagnose the appropriate tumor type. After collecting the data, the statistical analyses were performed using the licensed version of Statistical Package for the Social Science Version 23 (SPSS-23).

Results: Out of 60 cases, majority 27 (45.0%) patients were belonged to age 51 to 60 years with mean age was 58.4±10.2 years Male: female ratio was 4.1. Three fourth (75.0%) of the patients were smoker. Cough (90.0%) was the most frequent pulmonary symptoms of bronchial carcinoma followed by dyspnoea (55.0%), wheeze (40.0%), chest pain (20.0%) and haemoptysis (15.0%). Loss of weight (90.0%) was the most frequent extra pulmonary symptoms of bronchial carcinoma followed by loss of appetite (85.0%), fever (70.0%), face & neck swelling (10.0%), hoarseness (5.0%) and dysphagia (5.0%). Physical findings of the patients were anaemia (35.0%), clubbing (70.0%), features of pleural effusion (50.0%), features of consolidation (25.0%), features of collapse (10.0%), palpable lymph node (10.0%) and features of SVC obstruction (10.0%). Squamous cell carcinoma (50.0%) was the most common histological pattern of bronchial carcinoma followed by adenocarcinoma (45.0%) and small cell carcinoma (5.0%). Diagnostic procedure of bronchial carcinoma was bronchoscopy & biopsy (15.0%) followed by CT guided FNAC (50.0%), US guided FNAC (5.0%), pleural biopsy (5.0%), lymph node biopsy (20.0%) and pleural fluid study (5%).

Conclusion: Thus, our analysis suggests that most of the patients were elderly and males were predominant with smoking as the principal risk factor. Squamous cell carcinoma still remains the commonest histological subtype. CT guided FNAC was most detected of bronchial carcinoma.

Keywords: Bronchial carcinoma, Clinical presentation, Histopathological findings.

Introduction

Lung cancer is most common cancer world –wide, accounting for 1.2 million new cases annually in 2000, and causing 18% of all cancer deaths.^{1,2} In 2007, primary

carcinoma of lung affected 114,760 males and 98,620 female in United states, 86% die within 5 years of diagnosis, making it the leading cause of cancer death in both men and women.³ In UK it is the 3rd most

common cause of death after heart diseases and pneumonia; about 32000 people die each year with a male to female ratio of 3:1.⁴ Cigarette smoking is by far the most important cause of lung cancer. It is directly responsible for at least 90% of lung carcinomas, the risk being proportional to the amount smoked and to the tar content of the cigarettes. The death rate from the diseases in heavy smokers is 40 times than in non smokers.³

Lung cancer is symptomatic at diagnosis in 75 to 90% patients,⁵ and may present in a number of different ways, Symptoms reflect local involvement of bronchus, spread to chest wall or mediastinum, from distant blood bone metastasis or non-metastatic syndrome.¹ The frequency of common presenting symptoms are cough (41%), chest pain (22%), haemoptysis (7%), chest infection like recurrent pneumonia or lung abscess (<5%), weight loss (<5%), no symptoms (<5%).⁴

Bronchial carcinoma fall into four major histological types: Viz. Squamous -cell carcinoma, small cell carcinoma, large-cell carcinoma and adenocarcinoma. These four types account for about 95% of all cases of primary lung cancer.⁶ Common cell types of bronchial carcinoma are small cell lung carcinoma (SCLC) – (20%) and non small cell lung carcinoma (NSCLC)- (8%). Among NSCLC, Squamous -cell carcinoma (35%), large-cell carcinoma (15%) and adenocarcinoma (20%).³ Although squamous-cell carcinoma has for many years been the most common histological type, adenocarcinoma has been increasing in incidence over last 20 years.³

A number of extra pulmonary manifestation have been described in association with bronchial carcinoma unrelated of the tumor. These may be the presenting finding or the first sign of recurrence. The most frequently encountered endocrine syndromes (inappropriate ADH secretion & ectopic ACTH secretion) are usually associated with small cell cell carcinoma. Hypocalcaemia due to secretion of PTH like peptides is usually caused by squamous cell carcinoma. Associated neurological syndromes may occur with any type of bronchial carcinoma.¹

In patients with metastatic disease the diagnosis can often be confirmed by needle aspiration or biopsy of affected lymph nodes, skin lesion, liver or marrow. CT scan of brain, radio nuclide bone scanning, liver ultrasound. Bone marrow biopsy can be reserved for patients with clinical, hematological or biochemical

evidence of tumours spread to such site.¹ Our observation is to expertise about clinical presentation and different radiological and histopathological pattern of bronchial carcinoma. So that we can optimally manage the cases of bronchial carcinoma associated with high mortality and morbidity.

Materials and methods

This observational study was carried out in the Department of Medicine (Respiratory wing) Bangabandhu Sheikh Mujib Medical University (BSMMU) and National Institute of Chest Disease (NIDCH) during the period of September 2011 to February 2012. A total of 60 admitted patients with a clinical, radiological and histological diagnosis of bronchial carcinoma were enrolled in the study. Patients age >20 years both gender and clinical and histological findings of bronchial carcinoma were enrolled in the study. Age <20 years, patients present with typical features of pneumonia like abrupt onset, duration <7 days, high fever, rusty sputum, neutrophilic leucocytosis, gm(+ve, or gm(-) ve, organisms, on sputum examination, patients presented with clinical features of tuberculosis like low grade fever, night sweating, cough with sputum, chest X-ray P/A view–patchy opacities with or without cavitations, sputum – acid fast bacilli (+)ve, tuberculin test(+ve) and when detailed history, clinical examination and roentgenographic findings and histology raised the possibility that the lung cancer is a secondary one as opposed to primary tumor were excluded from the study. Complete sociodemographic characteristics, smoking status, radiological, and histopathological characteristics of the tumor were recorded in the study. The performance status of patients was documented using the Eastern Cooperative Oncology Group scale (ECOG). CT scan of the chest was done in the majority of the patient. CT-guided FNAC and US guided FNAC tissue sampling from lung lesions followed by histopathological examination was done to diagnose the appropriate tumor type. After collecting the data, the statistical analyses were performed using the licensed version of Statistical Package for the Social Science Version 23 (SPSS-23).

Results:

Out of 60 cases, majority 27 (45.0%) patients were belonged to age 51 to 60 years. The mean age was 58.4±10.2 years with ranging from 38 to 82 years. Male patients were predominant 48(80.0%) and 12(20.0%)

patients were female. Male: female ratio was 4.1. Half (50.0%) of the patients were cultivator and 30(50.0%) were come from middle class family (Table-I). Three fourth (75.0%) of the patients were smoker among them 21(46.7%) patients used 5 to 10 sticks/day and 42(93.3%) patients used to smoke 31-30 yrs (Figure-I). Duration of clinical presentation was up to 1 month in 15.0%, 2-3 months in 43.3%, 3-4 months in 10% and 4-6 months 31.7% patients with bronchial carcinoma (Table-II). Cough (90.0%) was the most frequent pulmonary symptoms of bronchial carcinoma followed by dyspnoea (55.0%), wheeze (40.0%), chest pain (20.0%) and haemoptysis (15.0%). Loss of weight (90.0%) was the most frequent extra pulmonary symptoms of bronchial carcinoma followed by loss of appetite (85.0%), fever (70.0%), face & neck swelling (10.0%), horseness (5.0%) and dysphagia (5.0%) (Table-III). Physical findings of the patients were anaemia (35.0%), clubbing (70.0%), features of pleural effusion (50.0%), feature of consolidation (25.0%), features of collapse (10.0%), palpable lymph node (10.0%) and features of SVC obstruction (10.0%) (Table-IV). Squamous cell carcinoma (50.0%) was the most common histological pattern of bronchial carcinoma followed by adenocarcinoma (45.0%) and small cell carcinoma (5.0%) (Figure-II). Diagnostic procedure of bronchial carcinoma was bronchoscopy & biopsy (15.0%) followed by CT guided FNAC (50.0%), US guided FNAC (5.0%), pleural biopsy (5.0%), lymph node biopsy (20.0%) and pleural fluid (5%) (Table-V).

Table-I: Demographic characteristics of the study population (n=60)

	Frequency	Percentage
Age (years)		
30-40	3	5.0
41-50	15	25.0
51-60	27	45.0
61-70	9	15.0
>70	6	10.0
Mean±SD	58.4	±10.2
Range (min-max)	38	-82
Sex		
Male	48	80.0
Female	12	20.0
Occupational status		
Service	10	16.7
Business	8	13.3
Cultivator	30	50.0

	Frequency	Percentage
Housewife	12	20.0
Socio-economic status		
Lower	27	45.0
Middle	30	50.0
Higher	3	5.0

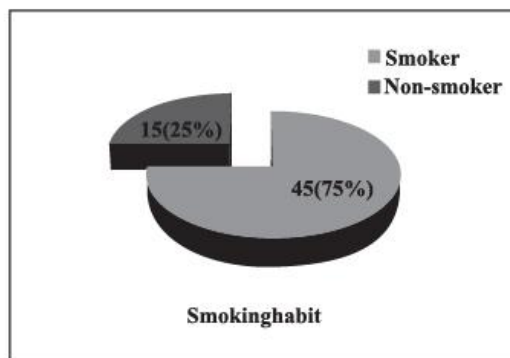


Figure-I: Smoking habit of the study population

Table-II: Duration of illness in bronchial carcinoma (n=60)

Duration of illness	Frequency	Percentage
Up to 1 month	9	15.0
2.-3 months	26	43.3
3-4 months	6	10.0
4-6 months	19	31.7

Table-III: Pulmonary symptoms of bronchial carcinoma (n=60)

	Frequency	Percentage
Pulmonary symptoms		
Cough	54	90.0
Dyspnoea	33	55.0
Wheeze	24	40.0
Chest pain	12	20.0
Haemoptysis	9	15.0
Extra-pulmonary symptoms		
Fever	42	70.0
Loss of weight	54	90.0
Loss of appetite	51	85.0
Horseness	3	5.0
Face & neck swelling	6	10.0
Dysphagia	3	5.0

Table-IV: Physical findings of bronchial carcinoma (n=60)

	Frequency	Percentage
Anaemia	21	35.0
Clubbing	42	70.0
Nicotine staining	3	5.0
Palpable lymph node	6	10.0
Features of SVC obstruction	6	10.0
Feature of consolidation	15	25.0
Features of pleural effusion	30	50.0
Features of collapse	6	10.0
Hepatomegaly	3	5.0

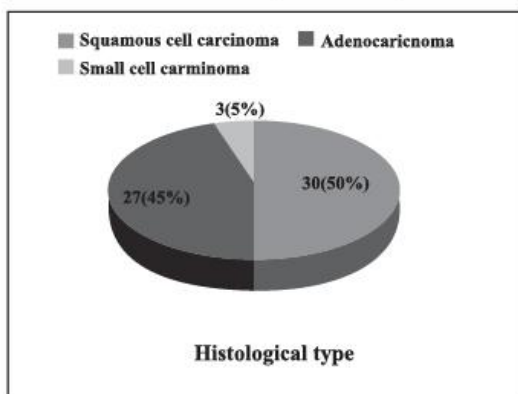


Figure-II: Histological type of the study population (n=60)

Table-V: Different methods of diagnosis of bronchial carcinoma (n=60)

	Frequency	Percentage
Bronchoscopy & biopsy	9	15.0
CT guided FNAC	30	50.0
US guided FNAC	3	5.0
Pleural biopsy	3	5.0
Lymphnode biopsy	12	20.0
Pleural fluid study	3	5.0

Discussion

Lung cancer is most common cancer world –wide, accounting for 1.2 million new cases annually in 2000, and causing 18% of all cancer deaths.^{1,2} The prevalence of lung cancer is second only to prostate cancer in men and breast cancer in women.⁶ In 2006, the disease caused more than 158,000 deaths –more than colorectal, breast, and prostate cancers combined.⁷ In

2007, primary carcinoma of lung affected 114,760 males and 98,620 female in United states, 86% die within 5 years of diagnosis, making it the leading cause of cancer death in both men and women.³

The age of the patients was ranging from 38 to 82 years with means age of 58.40(±10.20) years (mean ±standard deviation) table shows the distribution of age group., Forty -five percent of the patients were in the age group of 51 to 60 years, 25.0% were in the age group of 41 to 50 years, 15.0% were in 61-70 years, 10.0% were >70 years and 5.0% were in the age group of 30 to 40 years. In a study done by Sarfraz et al.⁸ reported that the mean age of lung carcinoma patients were 59.9 years. Akl et al.⁹ described that the incidence declined before the age of 40 with 5.9% of cases and after the age of 70 with 7.7% of cases, and no cases were found before age of 26 years, indicating that bronchogenic carcinoma was less common in these age groups. This showed that lung cancer mostly occur in older age. Age group in the present study is comparable to the study conducted by Mandal et al.¹⁰ which showed that age ranged between 39 to 85 years.

In this study out of 60 patients 48 (80.0%) patients were male and 12(20.0%) patients were female. Male: female ratio was 4.1: Similarly, Sarfraz et al.⁸ revealed that 67 (83.7%) were males and 13 (16.3%) were females. Male to female ratio was 5.15:1. Akl et al.⁹ obtained that male patients were predominant 82.2% and female was 17.8%. The sex ratio reported in various Indian studies ranged from 4.2:1 to 7:1.¹¹⁻¹³

In this study 75.0% percents of the patients were smoker and ex-smoker and 25.0% were non-smoker. Thirty –five percent of the patients used 05 to 10 sticks/day, 25.0% of the patients used 11 to 20 sticks/day, 05.0% of the patients used 21 to 30 sticks/day, 10.0% of the patients used 30 to 40 sticks/day and another 25.0% were non smoker. Sixty percents of the patients used to smoke 31-30 yrs, 20% of the patients used to smoke 11-20 yrs, 13.3% of the patients used to up to 10 years and 6.7% of the patients used 31-40 yrs. Sarfraz et al.⁸ described that seventy one (88.75%) patients were smokers. The smoker to non-smoker ratio was 7.8:1. The smoker to non-smoker ratio in the study was 7.8:1 which is comparable with the study by Rawat et al.¹⁴ and Khan et al.¹⁵

In this series cough (90.0%) was the most frequent pulmonary symptoms of bronchial carcinoma, followed by dyspnoea (55.0%), wheeze (40.0%), chest pain

(20.0%) and haemoptysis (15.0%). This finding was similar to the study of Spiro et al.¹⁶ that 60.0% patients of bronchial carcinoma were presented as dyspnoea. Sarfraz et al.⁸ study showed that the commonest symptom was cough present in 87.5% patients. This is comparable to various other studies.^{13,17,18} Chest pain was present in 46.25% patients in our study. This is also comparable to various studies.^{17,18} Various studies have reported haemoptysis in 11% to 24% lung cancer patients.^{14,19} Akl et al.⁹ reported that cough was the most common symptom (347 patients; 85.9%) and was followed by dyspnea (276 patients; 68.3%), expectoration (270 patients; 66.8%), chest pain (241 patients; 59.7%), hemoptysis (142 patients; 35.1%).

In this series loss of weight (90.0%) was the most frequent extra pulmonary symptoms of bronchial carcinoma, followed by loss of appetite (85.0%), (70%) fever, (10%) face and neck swelling, (05%) hoarseness and dysphagia (5.0%). Patients were anaemia (35.0%), clubbing (70.0%), features of pleural effusion (30.0%), feature of consolidation (25.0%), features of collapse, palpable lymph node and features of SVC obstruction (10.0%) each. Nicotine staining and hepatomegaly (5.0%) each. Akl et al.⁹ revealed that weight loss (115 patients; 28.5%), and hoarseness of voice (85 patients; 21%) was also a frequent symptom. Other symptoms, as fever (16.3%), dysphagia (9.2%) and supraclavicular lymph node (1%) were not so frequent clinical presentations.

In this study squamous cell carcinoma (50.0%) was the most common histological pattern of bronchial carcinoma, followed by adenocarcinoma (45.0%), small cell carcinoma (5.0%) and no any large cell carcinoma was found. Sarfraz et al.⁸ revealed that squamous cell carcinoma was found to be the most common type of carcinoma lung and was found in 40 (50%) patients, followed by small cell carcinoma which was present in 12 (15%) patient. Gupta et al.¹³ also found that most common location of small cell carcinoma was central (50%). Adenocarcinoma most commonly manifests as peripheral mass or a malignant pleural effusion. In present study adenocarcinoma constituted 45% of lung cancer, mostly present in upper zone (66.7%) and most commonly associated with pleural effusion. This is comparable with the study conducted by Rawat et al.¹⁴ which observed that adenocarcinoma commonly manifested as peripheral mass or a malignant pleural effusion. In the cell type distribution reported by Radzikowska et al.²⁰ squamous cell carcinoma had the

highest cell type incidence (52.1%) followed by small cell carcinoma (20.8%) while adenocarcinoma represented only 11.3% of the cases. According to Shetty et al.²¹ study, squamous cell carcinoma also presented 44.5% of cases followed by adenocarcinoma (18.5%) and small cell carcinoma (17.2%).

In this series diagnostic procedure of bronchial carcinoma was bronchoscopy and biopsy (15.0%), followed by CT guided FNAC (50.0%), US guided FNAC (5.0%), lymph node biopsy (20.0%) and pleural biopsy (50%). Akl et al.⁹ reported that bronchoscopic biopsy was positive in 107 of 151 patients (70.9%) of the squamous cell carcinoma cases. The cases of bronchogenic carcinoma that was diagnosed by CT guided biopsy were 86 cases (21.3% of all cases).

This study was conducted in a tertiary hospital only and may not reflect the actual situation of the country. This was an observational study and sample size was small, may not give the actual conclusion.

Conclusion

Thus, our analysis suggests that most of the patients were elderly and males were predominant with smoking as the principal risk factor. Squamous cell carcinoma still remains the commonest histological subtype. CT guided FNAC was most detected of bronchial carcinoma. Early detection and early treatment to reduce the morbidity and mortality associated with lung cancer in addition to imparting awareness on harmful effects of smoking and how to prevent the disease in general population is the need of this region. Furthermore, a longitudinal study using large sample size should be conducted to find out the magnitude of the lung cancer in our country.

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Original Article

A Comparative Study on Fatigue Resistance Between Cobalt-Chromium and Nickel-Chromium Occlusal Rest

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Abstract:

Background: Fatigue failure in a removable cast partial denture framework includes fracture of the occlusal rest at the rest-minor connector angle.

Objective: To evaluate the fatigue resistance of 0.7mm-thick occlusal rests casted with Cobalt-Chromium (Co-Cr) and Nickel-Chromium (Ni-Cr) alloy.

Materials and Method: It was a comparative observational in vitro study was carried out in the Department of Prosthodontics, Faculty of Dentistry, Bangabandhu Sheikh Mujib Medical University & Material & Metallurgy Department, Bangladesh University of Engineering & Technology (BUET). The study was carried out during the period of January 2006 to December 2007. Total 70 casted metals with no porosity, no cracks and metal thickness 0.7 mm were included. This divided into two groups, Group-A consisted of 35 occlusal rest casted with Ni-Cr alloy and Group-B consisted of 35 occlusal rest casted with Co-Cr alloy.

The specimen consisted of occlusal rest (0.7x2.0x10 mm), vertical minor connector (0.9x2.0x5.0 mm), and denture base connector (1.5x5.0x25 mm). Thirty-five specimens of each group were casted with Co-Cr and Ni-Cr alloy. Five specimens from each group were subjected to a load-deflection test conducted to determine the amount of deflection to be used in fatigue test. The fatigue test was performed such that the occlusal rest component was deflected by displacing the denture base component in a tissue ward direction. Predetermined denture base displacement values of 0.25 and 0.49 mm were applied for Co-Cr and Ni-Cr alloy specimens respectively, and repeated at a rate of 500 cycles/min by use of a displacement-controlled fatigue-testing machine, until occlusal rest failure occurred or a preset limit of 2 million cycles was achieved. The survival rates of the occlusal rests were calculated assuming a chewing cycle of 2×10^2 per year. All data of the study were collected and recorded in specific parameters of fatigue resistance and survival rate of occlusal rest. Data were analyzed by using computer based programmed statistical package for social science (SPSS) for windows version 15. Student's t-test was done to find out the statistical significance. P-value <0.05 was considered as significant.

Results: The mean fatigue resistance of Co-Cr alloy was 1559066 cycle, Ni-Cr alloy was 383300 cycles. The mean load deflection of Co-Cr alloy was 0.25mm; Ni-Cr alloy was 0.49mm.

Conclusions: Co-Cr occlusal rest is more rigid and resistant to fatigue than Ni-Cr occlusal rest.

Keywords: Fatigue resistance, Cobalt-Chromium, Nickel-Chromium, Occlusal rest.

Introduction

Usually mechanical failures in removable cast partial denture (RPD) frameworks do not occur immediately, but after years of service some failures have been reported.^{1,2} These reports indicate that the components of the framework undergo fatigue, a mode

of failure whereby a material or structure eventually fails after being subjected to repeated stresses. Studies have shown that normal mastication can produce thousands of stress cycles per day.³ Thus fatigue resistance is an important factor in the clinical durability of dental materials.

Among cast RPD components, greater attention has been given to studies and experiments on fatigue behavior of clasp arms.⁴⁻⁶ Ben-Ur et al.⁷ studied the rigidity of major connectors when subjected to bending and torsion forces, whereas Ohkubo et al.⁸ compared the fatigue strengths of different denture base designs for RPDs.

The occlusal rest is an integral part of cast RPD design. Its primary function is to provide vertical support for the denture. In doing so, it also serves to maintain stability of the denture, protects the underlying mucosa from impingement, and distributes occlusal loads to the abutment teeth. Kratochvil⁹ has stated that the occlusal rests receive the greatest force produced in the mouth during function and that the first consideration for these rests is rigidity, so they will not flex under masticatory loads. A rest that is too thin will deform elastically, a greater proportion of the load will be transferred to the residual ridge, and the rest will fracture as a result of fatigue.¹⁰

Clinically, fatigue failures in cast RPD's include the breakage of the occlusal rest, which usually occurs at the angle formed by the minor connector and the rest as it crosses the marginal ridge of the abutment tooth.⁷⁻⁹ Sometimes the fracture occurs sooner than could be expected after placement of the prosthesis.

The reasons often cited include the following: Thin metal alloy because of insufficient rest seat preparation, internal defects including porosity in the framework and accidental distortion.^{7,9,11}

To provide the required rigidity and resistance to fracture, the occlusal rest should be 1.0 to 1.5 mm thick^{7,12} and 2.0 to 2.5 mm wide where it crosses the marginal ridge of the abutment.¹³ This is made possible when an adequate rest seat is prepared on the abutment tooth. In spite of this guideline, however, rest seats with depths less than 1.0 mm has been observed among general dentists, postgraduate students, and faculty Culwick et al.¹⁴ To date, the longevity of the occlusal rests intraorally or the actual dimensions of rests that have failed clinically have not been reported.

Fatigue test is believed to simulate the clinical situation. Studies have shown that some materials and RPD designs possess greater fatigue resistance than others.^{15,16} Thus, information on the fatigue behavior of materials and structures would guide dentists and dental technicians during RPD design, material selection, and fabrication.

Co-Cr and Ag-Pd-Cu-Au alloys are used to fabricate denture frameworks. Both are alternatives to the more expensive gold alloys. Co-Cr alloy as a standard alloy and Nickel-chromium alloy were used for in vitro studies and fabrication of cast RPD frameworks.

Co-Cr and Ag-Pd-Cu-Au alloys are used to fabricate denture frameworks. Both are alternatives to the more expensive gold alloys. Co-Cr alloy as a standard alloy and Nickel-chromium alloy were used for in vitro studies and fabrication of cast RPD frameworks.

Previously a study was done to evaluate the fatigue resistance of 0.8-mm-thick occlusal rests cast with Co-Cr and Ag-Pd-Cu-Au alloys.¹⁷ This in vitro study was designed to evaluate the fatigue resistance of 0.7mm thick occlusal rests casted with Co-Cr alloys and Ni-Cr alloy.

Materials and methods

It was a comparative observational in vitro study was carried out in the Department of Prosthodontics, Faculty of Dentistry, Bangabandhu Sheikh Mujib Medical University & Material & Metallurgy Department, Bangladesh University of Engineering & Technology (BUET). The study was carried out during the period of January 2006 to December 2007. Total 70 casted metals with no porosity, no cracks and metal thickness 0.7 mm were included. This is divided into two groups; Group-A consisted of 35 occlusal rest casted with Ni-Cr alloy and Group-B consisted of 35 occlusal rest casted with Co-Cr alloy.

Study procedure: An experimental structure was designed with 3 components: occlusal rest, vertical minor connector, and denture base connector. The specimen consisted of occlusal rest (0.7 x 2.0 x 10 mm), vertical minor connector (0.9 x 2.0 x 5.0 mm), and denture base connector (1.5 x 5.0 x 25 mm). Although clinically the occlusal rest should be spoon-shaped and form an acute angle with the adjoining vertical minor connector. Data on the mechanical importance of these design principles were not found. Thus a simple design, which also facilitated the evaluation of cast specimens, was fabricated. The occlusal rest length was extended to 10 mm so that the specimen could be properly supported in the fatigue- testing machine. The 0.7-mm thickness was chosen.¹⁷ A wax pattern of the master split mold of the model structure was made. After the wax elimination was completed at 800°C, fresh Co-Cr ingots were melted by use of Oxy acetelin flame and

filled into the molds by casting machine with centrifugal force. For Ni-Cr alloy, wax patterns were sprued and invested in a phosphate-bonded investment material (Investment: GC Corp). After the wax elimination was completed at 700°C, fresh Ni-Cr alloy ingots were melted by use of Oxy acetelin flame and filled into the molds by casting machine with centrifugal force. The specimens were deinvested after 1 hour of bench cooling, and residual investment material was removed. Polishing the specimens would closely resemble the clinical condition. Cantilever-type bending test was performed to determine the load and deflection to be applied to the fatigue test specimens. Five specimens from each group were randomly selected and tested using a universal testing machine. The denture base component was tightly gripped by a jig connected to a load cell. The occlusal rest component, held by 2 metal rollers, was deflected at a speed of 1 mm/min. The generated load (kgf) was recorded until the proportional limit of the tested alloy was reached. The flexural rigidity of the latter was estimated to be 8.07 times that of the former.^{16,18}

Two factors were considered for the fatigue test: (1) the cyclical load/stress applied was within the proportional limit of the specimen; and (2) the maximum occlusal rest deflection/denture base displacement was within 0.5 mm, representing the reported resiliency of the residual ridge tissues.¹⁹ Hence, on the basis of the results of the load-deflection test, a load of 1.3 kgf and its corresponding deflection values were selected: 0.25mm and 0.49mm for Co-Cr and Ni-Cr alloy specimens, respectively.

A motor-driven fatigue-testing machine (Fatigue testing machine-Terco) was used for this experiment. The machine had- (a) five 10-mm diameter rollers for holding the specimen; (b) a fixed loading frequency of 500 cycles/min; (c) a constant-displacement mechanism; and (d) a counter to record the number of fatigue cycles automatically. With a dial gauge, the denture base displacement value was set in the machine. The denture base component was held by the moving roller grips and the occlusal rest component was put on a fixed roller. The denture base was displaced cyclically effecting the pulsative sinusoidal deflection of the occlusal rest, until complete fracture was observed at the rest-vertical connector angle, or a preset limit of 2 million cycles was reached.

Data were collected on a predesign data collection sheet. All relevant data of the study were collected and

recorded in specific parameters of Fatigue test and Survival rate analysis. Data were analyzed by using computer based programmed statistical package for social science (SPSS) for windows version 15. Student's t-test was done to find out the statistical significance. P-value <0.05 considered as significant.

Results

Table-I: Fatigue resistance in between the two groups (n=70).

Groups	N	Mean±SD (cycle)	P-value
Group A	35	383300±72291	0.001
Group B	35	1559066±610089	

Data were analyzed by using student 't' test

n- total number of specimen.

N-total number of specimen in each group.

Group A- Ni-Cr alloy.

Group B- Co-Cr alloy.

SD- Standard deviation.

Table-II: Mean Survival year in relation to survival cycle (n=70).

Groups	N	Mean±SD (year)	P-value
Group A	35	1.91±0.36	0.001
Group B	35	7.79±0.30	

Data were analyzed by using student 't' test

n- total number of specimen.

N-total number of specimen in each group.

Group A- Ni-Cr alloy.

Group B- Co-Cr alloy.

SD- Standard deviation.

Discussion

Fatigue fracture of the cast RPD framework occurs at specific sites that are determined by the design of the castings. Fracture usually occurs in areas where stress concentration is greater. With the occlusal rest, fatigue may occur at the angle where it joins the vertical minor connector, and fracture may be facilitated by inadequate alloy thickness and casting defects. This study was limited to the evaluation of fatigue resistance of an experimental 0.7-mm-thick occlusal rest, which was arbitrarily chosen to represent "inadequate rest seat depths" Culwick et al.¹⁴ prepared by dentists. The 2-mm width represented the minimum recommended

dimension. A comparison with a 1-mm-thick occlusal rest was not made because adherence to textbooks' recommendations regarding occlusal rest dimensions would undoubtedly provide a more rigid and fatigue resistant structure. The occlusal rest length of 10 mm was designed so that the specimen would be properly supported in the fatigue-testing machine. Furthermore, an extended length was needed so that a wire, which was connected to the automatic stop-on-failure terminal button of the machine, could be attached to the occlusal rest component. A rigid occlusal rest is favorable since it should prevent the tissue-ward movement of the denture and eventual impingement of the underlying mucosa. In this regard, the fabrication of Co-Cr occlusal rest is more advantageous.

Kratochvil⁹ and McGivney et al.¹² stated that to provide the required rigidity and resistance to fracture, the occlusal rest should be 1.0 to 1.5 mm thick; and 2.0 to 2.5 mm wide.¹³ where it crosses the marginal ridge of the abutment. This is made possible when an adequate rest seat is prepared on the abutment tooth. In spite of this guideline, however, rest seats with depths less than 1.0 mm have been observed among general dentists, postgraduate students and faculty Culwick et al.¹⁴ To date, the longevity of the occlusal rests intraorally or the actual dimensions of rests that have failed clinically have not been reported.

Different types of alloys are recommended for the construction of occlusal rest. Of them, we choose Co-Cr alloy as our study material because of its high properties corrosion resistance, high fracture toughness & ability to take high polish. A rigid occlusal rest is favorable since it should prevent the tissue-ward movement of the denture and eventual impingement of the underlying mucosa. In this regard, the fabrication of Co-Cr occlusal rest is more advantageous. This observation may be explained by the higher elastic modulus of this alloy. The higher the modulus of elasticity, the more rigid the material, resulting in its greater ability to resist deflection and distortion. Because the flexural rigidity of a bar is proportional to its modulus of elasticity and the cube of its thickness,^{3,16} The use of Ag-Pd-Cu-Au occlusal rest necessitates a metal thickness of approximately 1.0 mm to provide the same rigidity as the 0.8- mm-thick Co-Cr occlusal rest. Thus, the choice to make thin rests may be compensated for by use of more rigid alloys.

In our study we have used Co-Cr alloy of 0.7 mm thickness for the construction of occlusal rest. The

reduction of thickness in occlusal rest construction facilitated us in conserving more amount of dentine than 1 mm occlusal rest. Besides that it reduced the risk of tooth fracture, pulpal damage, and dentinal sensitivity as well as lessens the risk of developing secondary caries by saving more amount of dentine. Lot of researches has been done with the reduction of the thickness of occlusal rest. Culwick et al.¹⁴ studied on occlusal rest made of Co-Cr alloy with 0.8 mm thickness. That study was limited to the evaluation of fatigue resistance of an experimental 0.8-mm-thick occlusal rest, which was arbitrarily chosen to represent "inadequate rest seat depths" prepared by dentists. The 2-mm width represented the minimum recommended dimension. A comparison with a 1-mm-thick occlusal rest was not made because adherence to textbooks' recommendations regarding occlusal rest dimensions would undoubtedly provide a more rigid and fatigue resistant structure. The use of a 0.8-mm-thick and 2.0-mm-wide occlusal rest may be adequate if fabricated with Co-Cr alloy.¹³

In our study we followed the similar method to see the fatigue resistance test of Co-Cr alloy. We have used the thickness of 0.7 mm instead of 0.8-1 mm to see the prognosis of the rest. In addition to that we have also used Ni-Cr alloy as the alternative alloy to construct occlusal rest. The above-mentioned author has used silver palladium alloy as the alternative to Co-Cr alloy. Our study has shown the higher load deflection and high efficacy to fatigue resistance cycle of Co-Cr alloy compared to Ni-Cr alloy. Even with the use of 0.7mm thickness of Co-Cr alloy in our study, the alloy was proved to be efficient and worthy.

Conclusion

Co-Cr occlusal rest is more rigid and resistant to fatigue than Ni-Cr occlusal rest. 0.7mm thick and 2.0mm wide occlusal rest casted with Co-Cr alloy are recommended to use for the fabrication of removable partial denture rather than 0.7mm thick and 2.0mm wide occlusal rest casted with Nickel-chromium alloy, but according to survival rate analysis the present limit of 2 million cycles represented 10 years of simulated clinical use, which was not satisfactory. Increased number and size of internal defects may increase the fatigue failure of cast occlusal rests. Further study with some other functional parameters with the same thickness of same metal.

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Original Article

Effect of Green Tea (*Camellia Sinensis*) on Paracetamol Induced Liver Damage In Long Evans Male Rats

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Abstract:

Background: Liver is an essential organ of our body that can be damaged by poisonous effects of chemicals, toxins, prolonged and uncontrolled use of drugs. Green tea is a popular beverage which may have hepatoprotective effect.

Objective: To observe the effect of green tea (*Camellia sinensis*) on paracetamol induced liver damage in Long Evans male rats.

Methods: This study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC), Dhaka from July 2018 to June 2019. A total number of thirty (30) apparently healthy Long Evans male rats, 90-120 days old, weighing between 150-200g was taken for the study. After acclimatization for 14 days, they were divided into two groups, control group (Group A) and experimental group (Group B – green tea pretreated and paracetamol treated group). Control group was subdivided into group A1 (baseline control group) and group A2 (paracetamol treated control group). Each of this group was consisted of ten rats. All the rats received basal diet for 28 days. In addition to basal diet, baseline control group also received normal saline (20 ml/kg/day) orally daily for 28 days. Paracetamol treated control group received paracetamol orally (1.5 g/kg/day) for last 3 days (26th to 28th days) of the study period. Again experimental group received ethanolic extract of green tea orally (500 mg/kg/day) for 28 days and paracetamol orally (1.5g/kg/day) for last 3 days (26th to 28th days) of the study period. All the rats were sacrificed on 29th day. After sacrifice blood and liver sample was collected. Blood sample was collected from heart. Serum levels of total bilirubin, ALT and ALP were measured.

One way ANOVA test, post hoc-Bonferroni test and Chi-square test were done to compare the data as applicable.

Result: The mean serum total bilirubin, ALT and ALP levels were significantly higher in paracetamol treated control group and green tea pretreated and paracetamol treated group in comparison to those of baseline control group. Again, mean serum total bilirubin, ALT and ALP levels were significantly lower in green tea pretreated and paracetamol treated group than those of paracetamol treated control group.

Conclusion: This study revealed that green tea has hepatoprotective effect against paracetamol induced liver damage in Long Evans male rats.

Keywords: Green Tea, Liver Damage, Long Evans Male Rats.

Introduction

Liver is the largest organ in the body. It is essential for life for its many biochemical and metabolic functions. Among many complex functions of liver, production

and secretion of bile, nutrient and vitamin metabolism, detoxification of drugs and toxins, synthesis of clotting factors and plasma proteins are the most important.¹

Liver disease is very common worldwide and is one of the leading causes of mortality. The continuous exposure to some factors like virus, alcohol, fatty diet and bio transformed metabolites can cause liver injury leading to inflammation and liver degeneration. Liver damage can also lead to steatosis, steatohepatitis, fibrosis, cirrhosis and hepatocellular carcinoma.² Severe acute liver disease may lead to fulminant or acute liver failure (Anstee and Jones, 2018). In Bangladesh, about 13.2% patients visiting hospital OPD are suffering from liver diseases (Rahman et al. 2014). Among the liver diseases fulminant hepatic failure has the worst prognosis with a mortality rate of around 73.1%.³ Certain medicinal agents, when taken in overdoses and sometimes even when introduced within therapeutic ranges, may cause of liver injury. Reactive oxygen species are involved in liver damage caused by several conditions such as alcohol abuse, fibrosis/cirrhosis of various etiologies, hepatocellular carcinoma, paracetamol overdose and viral hepatitis.⁴ Drug induced liver injury is a common adverse event encountered in clinical practice. Paracetamol is a widely used antipyretic and analgesic drug which is used for treatment of fever, headache and other pains. Despite having beneficial effects misuse of paracetamol through uptake of supratherapeutic doses may lead to hepatic, renal⁴ and brain adverse side effects in humans and experimental animals.⁵

Paracetamol is a widely used drug to induce hepatic damage in experimental models. Acute liver failure caused by paracetamol is due to the metabolic activation of this drug to a toxic metabolite named N-acetyl-p-benzoquinone imine (NAPQI) in the liver by cytochrome p450 isoenzyme especially CYP2E1. It is known that NAPQI depletes liver glutathione thereby induces oxidative stress.⁶ As a result excess production of reactive oxygen species (ROS) like superoxide radicals, hydrogen radicals and hydroxyl radicals may invade the biological molecules such as DNA, protein, phospholipids etc. It also may lead to lipid peroxidation and depletion of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx).⁷ On the basis of these facts researchers across the world are now showing interest in the use of alternative medicines for the treatment of hepatic disease. Natural products received great attention as they are potentially antitoxic and antioxidants agents.⁸

Green tea is a popular beverage across the globe. Polyphenols found in green tea are proven antioxidant and anti-inflammatory agent.⁹ Green tea is produced from the dried leaves of the plant *Camellia sinensis* and contains several polyphenolic compounds. Most of these polyphenols are flavonols. They are usually called catechins. Epigallocatechingallate (EGCG) is the most abundant catechin, comprising for about 65% of green tea catechin content. It is also the component with the highest antioxidant properties. Oxidative stress due to generation of reactive oxygen species can be prevented by catechins. The protective effect of green tea is due to the ability of its catechins to prevent the production of oxygen radicals and also scavenge free radicals such as peroxy, hydroxyl and superoxide anions.¹⁰ Many previous journals also documented many other beneficial effects of green tea such as anti-obesity, anticarcinogenic,¹¹ hypocholesterolemic,¹² anti-neurodegenerative¹³ properties. Green tea also protects against MTX,¹⁴ cyclophosphamide,¹⁵ Tamoxifen,¹⁶ Azathioprine¹⁷ induced hepatotoxicity. Green tea extract is considered to be safe for clinical use in many studies.¹⁸ Green tea also has preventive action on paracetamol induced hepatotoxicity in Long Evans rats.¹⁹

Materials and methods

This Experimental study was conducted in the Department of Physiology, Sir Salimullah Medical College, Dhaka from 1st July 2018 to 30th June 2019. The study was approved by Institutional Ethics Committee of SSMC. Purposive sampling followed by randomization was done. A total number of thirty (30) apparently healthy Long Evans male rats, 90 to 120 days old were selected on the basis of inclusion and exclusion criteria. Rats were purchased from animal house of Department of Pharmacology, Bangabandhu Sheikh Mujib Medical University (BSMMU).

Grouping of the rats:

After acclimatization for 14 days all the animals were divided into 2 groups after randomization, Group: A (Control group) and Group: B (Experimental group).

Group A: Control group

Consisted of 20 rats. This group was subdivided into group A₁ and A₂.

• **Group A₁:** baseline control group consisted of ten (10) rats. In addition to basal diet they received normal saline (20ml/kg/day) orally for 28 days.

- **Group A₂:** paracetamol treated control group consisted of ten (10) rats. In addition to basal diet they received paracetamol orally (1.5g/kg/day) for last 3 days (26th to 28th days) of study period.

Group B: Experimental group:

Green tea pretreated and paracetamol treated group

- Consisted of ten (10) rats. In addition to basal diet they received ethanolic extract of green tea orally (500mg/kg/day) for 28 days and paracetamol orally (1.5g/kg/day) for last 3 days (26th to 28th days) of study period.

Doses and duration:

Paracetamol

- **Dose:** 1.5g/kg body weight orally by gastric gavage.
- **Duration:** Daily in the morning between 09:00 AM to 10:00 AM for last 3 days (26th to 28th days) of study period.

Green tea

- **Dose:** 500 mg/kg body weight orally by gastric gavage.
- **Duration:** Daily in the morning for twenty eight (28) consecutive days (from day 1 to day 28).

According to selection criteria all the rats were purchased from animal house of Department of Pharmacology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. They were kept in the animal house of Institution of Nutrition and Food Science, University of Dhaka where the experiment was carried out. All the animals were acclimatized for 14 days prior to intervention at 23±2 °C room temperature under 12 hours light/12 hours dark cycle. During this period, the animals had free access to standard food pellets and allowed drinking water as desired. After 14 days acclimatization the total study period was twenty eight (28) days. At the beginning of the study period (day 1) initial body weight of all the rats were measured and at the end of the study period their final body weight were measured. Blood samples were collected on day-1 from the tail vein of all rats to assess the liver function. The serum level of alanine aminotransferase (ALT) was measured and rats with normal level of ALT (10-40 U/L) were included in this experiment.

All the rats received basal diet. In addition to basal diet, rats of baseline control group received normal saline (20 ml/kg body weight) orally daily. Hepatotoxicity was induced by administration of single daily morning dose

of paracetamol (1.5g/kg body weight) orally by gastric gavage on day 26, 27 and 28 after overnight fasting in all groups of rats except baseline control group. Green tea extract (500 mg/kg/day dissolved in 1ml distilled water) was given to experimental group (group B) orally in the morning between 9:00 AM to 10:00AM for 28 consecutive days.

At the end of the study period, all rats were sacrificed on day 29 (after 24 hours of last dose of paracetamol administration on day 28). They were anesthetized with the help of chloroform (30%). Then blood samples (5ml) were collected from the heart by using disposable syringe and were taken in separate clean and dry test tubes with proper identification numbers and were kept in standing position till formation of clot. Then blood was centrifuged at a rate of 3000 rpm for 10 minutes. After that supernatant serum were collected in labeled eppendroff tube and preserved in the refrigerator for estimation of all the biochemical parameters. Liver was also removed from each rat and weighed. Serum levels of total bilirubin, alanine aminotransferase (ALT) and alkaline phosphates (ALP) were measured in Department of Physiology, SSMC by semi automated analyzer machine. Statistical analysis was done by using Statistical Package for Social Science (SPSS) for windows version 22. Data were expressed as mean ± SD. For statistical analysis, ANOVA, post hoc-Bonferroni test and Chi-square test were done as applicable. p value ≤0.05 was considered statistically significant.

Results

Serum total bilirubin, ALT and ALP levels in different groups of rats (N=30) are shown in table-I

Table-I shows that the mean (±SD) serum total bilirubin level was significantly higher in group A₂ (p<0.001) and B (p<0.05) in comparison to that of group A₁, whereas this level was significantly (p<0.001) lower in group B than that of group A₂. On the other hand, the mean (±SD) serum ALT was significantly higher in group A₂ and B (p<0.001 and p<0.01 respectively) in comparison to that of group A₁, whereas ALT level was significantly (p<0.001) lower in group B than that of group A₂.

Again, the mean (±SD) serum ALP was significantly (p<0.001) higher in group A₂ in comparison to that of group A₁, whereas ALP level was significantly (p<0.001) lower in group B than that of group A₂. ALP level in group A₁ and group B was almost similar and the difference was not statistically significant (table-I).

Table-I: Serum total bilirubin, ALT and ALP level in different groups of rats (N=30)

Group	Serum Total Bilirubin (mg/dl)	Serum ALT (U/L)	Serum ALP (U/L)
A ₁ (n=10)	0.67 ± 0.27 (0.25 - 1.05)	37.00 ± 3.37 (31 - 42)	88.60 ± 11.63 (73 - 110)
A ₂ (n=10)	2.42 ± 0.52 (1.72 - 3.33)	83.20 ± 17.50 (66 - 118)	141.30 ± 6.41 (133 - 151)
B (n=10)	1.17 ± 0.20 (0.87 - 1.52)	53.50 ± 6.36 (46 - 64)	89.80 ± 6.81 (79 - 100)

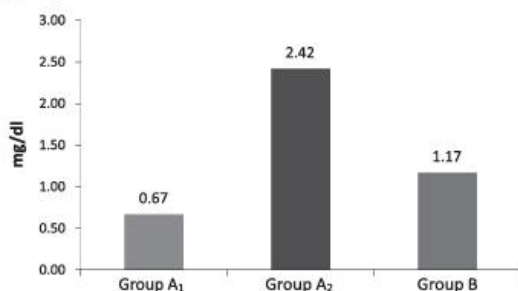
Multiple comparison

	Serum Total bilirubin p-value	Serum ALT p-value	Serum ALP p-value
A ₁ vs A ₂ vs B	0.000***	0.000***	0.000***
A ₁ vs A ₂	0.000***	0.000***	0.000***
A ₁ vs B	0.013*	0.007**	1.000ns
A ₂ vs B	0.000***	0.000***	0.000***

Data are expressed as mean ± SD. For statistical analysis, ANOVA test was performed for comparison among the groups and then post hoc-Bonferroni test to compare between groups. Figures in parentheses indicate ranges.

Group A₁: Baseline control group, **Group A₂:** Paracetamol treated control group, **Group B:** Experimental group (green tea pretreated and paracetamol treated group), N=Total number of rats; n= number of rats in each group; ns = not significant; * = significant at p-value < 0.05; ** = significant at p-value < 0.01; *** = significant at p-value < 0.001

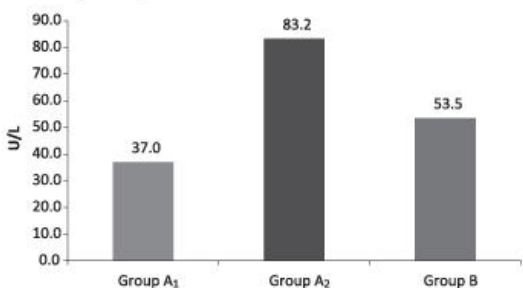
Figure-I: Mean serum total bilirubin level in different groups of rats (N=30)



Group A₁: Baseline control group, **Group A₂:** Paracetamol treated control group, **Group B:** Experimental group (green tea pretreated and

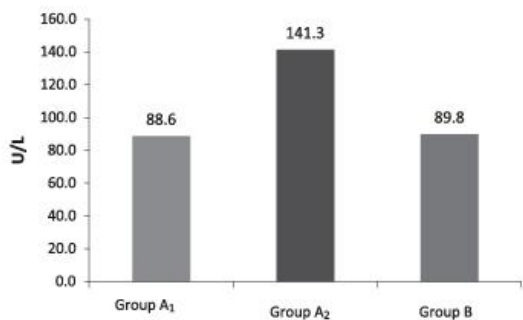
paracetamol treated group), N = Total Number of rats

Figure-II: Mean serum ALT level in different groups of rats (N=30)



Group A₁: Baseline control group, **Group A₂:** Paracetamol treated control group, **Group B:** Experimental group (green tea pretreated and paracetamol treated group), N = Total Number of rats

Figure-III: Mean serum ALP level in different groups of rats (N=30)



Group A₁: Baseline control group, **Group A₂:** Paracetamol treated control group, **Group B:** Experimental group (green tea pretreated and paracetamol treated group), N = Total Number of rats

DISCUSSION

The present study was carried out to evaluate the hepatoprotective effect of green tea on paracetamol induced hepatotoxic rats. For the purpose of the study serum levels of total bilirubin, alanine aminotransferase (ALT), alkaline phosphatase (ALP), malondialdehyde (MDA) in liver homogenate were measured to assess liver function. Moreover, histological examination of liver was also done to observe the microscopical findings of the liver. In the present study, thirty (30) Long Evans male rats, 90 to 120 days old, weighing between 150-200 grams were taken. After acclimatization for 14

days, all the rats were randomly divided into three (3) groups such as baseline control group (A₁), paracetamol treated control group (A₂) and green tea pretreated and paracetamol treated group (B). All groups of rats received basal diet for 28 days. To produce hepatotoxicity, paracetamol treated control group (A₂) and green tea pretreated and paracetamol treated group (B) were given paracetamol orally (1.5g/kg/day) for last 3 days (26th to 28th days) of study period. In addition to this, green tea pretreated and paracetamol treated group (B) also received ethanolic extract of green tea orally (500mg/kg/day) for 28 days (day 1 to day 28).

In this study, values of the study parameters such as serum total bilirubin, ALT, ALP levels of all the rats of baseline control group were within physiological limit and the histological findings of liver revealed normal histological architecture. These findings were almost similar to those reported by various researchers of different countries.¹⁹

In this study, serum total bilirubin level was significantly higher in paracetamol treated control group ($p < 0.001$) and green tea pretreated and paracetamol treated group ($p < 0.05$) in comparison to that of baseline control group. Similar finding was also observed by Lodhi²⁰ and Abolfathi.²¹

Again serum total bilirubin level was significantly ($p < 0.001$) lower in green tea pretreated and paracetamol treated group than that of paracetamol treated control group. Almost similar finding was observed by different researchers Adel²² and Hamden.²³

In this study, serum ALT was significantly ($p < 0.001$) higher in paracetamol treated control group and green tea pretreated and paracetamol treated group ($p < 0.001$ and $p < 0.01$ respectively) in comparison to that of baseline control group. Almost similar finding was observed by Saad,²⁴ Deib and Ahmed.²⁵

Again serum ALT level was significantly ($p < 0.001$) lower in green tea pretreated and paracetamol treated group than that of paracetamol treated control group. Almost similar finding was observed by El-kholy²⁶ and Mehri.²⁷

In this study, serum ALP was significantly ($p < 0.001$) higher in paracetamol treated control group in comparison to that of baseline control group. Almost similar finding was also observed by Issabeagloo,²⁸ Jweid²⁹ and El-Beshbishy.³⁰

Again serum ALP was significantly ($p < 0.001$) lower in green tea pretreated and paracetamol treated group than that of paracetamol treated control group. Almost similar finding was observed by Mohammed.³¹

Conclusion

In this study it was observed that green tea has hepatoprotective effect against paracetamol induced liver damage in Long Evans male rats.

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Original Article

Screening Of Cervical Precancer in a Tertiary Care Hospital in Bangladesh

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Abstract:

Background: Cervical cancer is the second most common cancer among women in Bangladesh. Cervical cancer is a preventable disease as it has a long precancerous stage. Routine and effective screening detects the disease at its precancerous stage and can reduce the incidence of cervical cancer by almost 80%. Visual Inspection of the cervix with 5% acetic acid allows for inspection of the acetowhite area (VIA Positive).

Objective: To evaluate cervical precancer screening in tertiary level hospital of Bangladesh.

Methods: This cross-sectional study was conducted in the gynecology Department of Sir Salimullah Medical College and Mitford Hospital, Dhaka from January 2018 to December 2019. Women who came for cervical cancer screening by VIA were included in this study. A total of 1023 women were included in this study. VIA-positive cases were evaluated in colposcopy clinics where the 'see and treat' policy applied. The specimen was sent for a Histopathology examination.

Results: Among 1023 women, 92 were VIA positive (8.99%). Colposcopy test among VIA positive women, 21 (22.82%) were normal, 39 (42.39%) were CIN-1 and 29 (31.52%) were CIN-2 & CIN-3, 3 were unsatisfactory (3.26%). In CIN-1, cryotherapy was given to 21 patients. LEEP was done in 18 patients of CIN-1, all 29 patients of CIN-2 & CIN-3. The histopathology report showed chronic cervicitis with squamous metaplasia in 15 patients, CIN-1 in 20 patients, CIN-2 in 8 patients, CIN-3 in 3 patients and invasive cancer in 1 patient.

Conclusion: VIA is safe and feasible in our country. The hopeful news is that women are eager to gather knowledge about carcinoma cervix. We will achieve the goal of reducing the mortality rates associated with cervical cancer.

Keywords: Cervical precancer, VIA, Colposcopy.

Introduction

Cervical cancer is the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women, with an estimated 604,000 new cases and 342,000 deaths worldwide in 2020.¹ Cervical cancer is the second most prevalent cancer among Bangladeshi women with approximately 8068 new cases detected every year and 5214 deaths.² Approximately 90% of deaths from cervical cancer occurred in low and middle-income countries. Rate of cervical cancer have been estimated to be at least four-fold higher in countries with a "Low" ranking Human Development Index compared to those with a "Very high" Human Development Index.³ Effective primary prevention is by education and HPV

vaccination at the age 9-13 years. Secondary prevention approaches by screening among women 30-60 years and tertiary prevention by treatment of precancerous lesions in women of 30-60 years of age will prevent most cervical cancer cases. According to World Health Organization (WHO) estimates, cervical cancer is expected to kill more than 443,000 women by 2030, with a high rate (over 98% of deaths) believed to occur in developing countries (especially in Sub-Saharan Africa (SSA)). Non-communicable diseases such as cervical cancer cause devastating effects in developing countries.⁴ It can be prevented, unlike other reproductive cancers through effective screening programs.⁵ CIN represents a spectrum of neoplastic changes of the squamous epithelium of the cervix that

has been recognized as precursors of invasive squamous cell carcinoma. Diagnosis of CIN is established by histopathological examination of a cervical punch biopsy or excision specimen. Consequently, CIN is histologically graded on a scale from I to III.⁶ Progression through different grades of CIN to CIS or CC may take several decades. The time lag between infection and development of CC is probably on average more than 15 years.⁷ Due to importance of high grade cervical intraepithelial neoplasia (CIN), as precursor to invasive cervical cancer, it is the vital to accurately screen patients for the risk of this lesions. Human papillomavirus is causative factor of carcinoma cervix. It has more than 100 subtypes among them type 16 & 18 are the major risk factor.

Based on gynaecology guidelines, colposcopy examinations are performed in women with abnormal cervical screening report to evaluate the cervical histopathology.⁸ All the tertiary level hospitals are caring a large load of cervical cancer patient. Visual inspection of the cervix with 5% acetic acid allows for inspection of the aceto-white area (VIA Positive). Women with VIA positive tests are referred for colposcopy. Successful screening program is one of the effective way for early diagnosis and prevention of this cancer. Treatment of Pre-cancerous lesions in women will prevent most cervical cancer cases. Visual inspection by Acetic Acid (VIA) is our national program. It is cheap, widely available and easy to perform.

Materials & Methods

This was a cross sectional study that was conducted in the Gynaecology Department of Sir Salimullah Medical College and Mitford Hospital, Dhaka from January 2018 to December 2019. Women who came for cervical cancer screening by VIA were included in this study. Women who have previous surgery, chemotherapy or radio therapy for cervical disease or neoplasia, pregnant women, confirmed diagnosis of invasive cervical cancer were excluded in this study. A total number of 1023 women age group 20-60 years were included in this study.

All women were counseled. There informed written consent was taken for VIA, colposcopy and colposcopy directed procedure. Data was collected in a pre-designed data collection sheet. VIA-positive cases were evaluated in colposcopy clinic where the 'see and treat' policy applied. The specimen was sent for histopathological examination.

Result

Out of 1023 patient, 495 (48.38%) were the age group of 30-39 years.

Table-I: Age distribution of the study population

Age in years	Frequency	Percentage
20-29	89	8.69%
30-39	495	48.38%
40-49	275	28.88%
59-60	164	16.03%

Early age of marriage, early sexual activity is one of the major risk factor for ca-cx, 190 (18.57%) got married before the age of 15 years, 614 (60.01%) at 15-20 years of age.

90 (8.79%) had their first child before 15 years, 601 (58.74%) between 15-20 years. 421 (41.15%) had 1-2 child and 302 (29.52%) had 3-4 child.

Table-II: Regarding the risk factors of cervical cancer

Age of marriage	Frequency	Percentage
<15	190	18.57%
15-20	614	60.01%
>20	219	21.40%

Age of first pregnancy	Frequency	Percentage
<15	90	8.79%
15-20	601	58.74%
>20	332	32.45%

Number of parity	Frequency	Percentage
Nulliparous	5	.48%
1-2	421	41.15%
3-4	302	29.52%
>4	88	8.60%
Abortion	77	7.52%
MR	130	12.70%

Visual inspection by Acetic Acid shows 92 (8.99%) VIA positive and 931 (91%) VIA negative.

Table – III: Screening by VIA

Screening by VIA	Percentage
VIA Positive	92 (8.99%)
VIA Negative	931 (91.00%)

Out of 92 VIA+ve cases, colposcopic evaluation revealed normal colposcopic finding in 21 (22.82%), CIN-1 in 39 (42.39%), CIN-2 & CIN-3 in 29 (31.52%) cases and unsatisfactory in 3 (3.29%) cases.

Table – IV: Colposcopic findings of VIA positive cases

Findings	Numbers	Percentage
Normal	21	(22.82%)
CIN-1	39	(42.39%)
CIN-2, CIN-3	29	(31.52%)
Unsatisfactory	3	(3.26%)

Cryotherapy was given in 21 patient in CIN-1. LEEP was done in 18 cases of CIN-1, 29 cases of CIN-2 & CIN-3.

Table – V: Treatment given

Treatment	Number of Patient
Cryotherapy	21
LEEP done in CIN-1, 2, 3	47

Histopathological report showed, chronic cervicitis with squamous metaplasia in 15 patient, CIN-1 in 20, CIN-2 in 8, CIN-3 in 3 patients, and invasive cancer in 1 patient.

Table – VI: Histopathology report of specimen

Biopsy finding	Number
Chronic cervicitis with squamous metaplasia	15
CIN-I	20
CIN-II	8
CIN-III	3
Invasive cancer	1

Discussion

Colposcopy is an excellent method for evaluation of cervix.⁹ World health organization suggested the priority age group 35-45 years for the CIN screening.¹⁰ In this study 495 (48.38%) were in the age group 30-39 years. Early age of marriage is one of the risk factor of ca-cx. In this study 614 (60.01%) were married between the age of 15-20 years which correspond with the study of RotKIN ID.¹¹ Multiparty is also a risk factor for CIN of the cervix. This observation correlates with the study of schiffman MH et al. and RotKIN ID.^{11,12} Among 92 VIA positive cases, colposcopic evaluation revealed normal colposcopic finding in 21 (22.82%) patient, CIN-1 39 (42.39%), CIN-2, CIN-3 29 (31.52%), unsatisfactory in 3 (3.26%).

Cryotherapy was given in 21 patient of CIN-1. Loop electro surgical excision procedure (LEEP) was done in 47 cases of CIN-1, CIN-2, CIN-3 cases.

Histopathological report showed chronic cervicitis with squamous metaplasia in 15 patients. CIN-1 in 20 patients, CIN-2 in 8 patients, CIN-3 in 3 patients and

invasive cancer in 1 patient. Many studies are comparable to my study.^{13,14,15}

Conclusions

Precancerous cervical lesions continue to be a significant public health concern in Bangladesh. It will remain a cause of death of women unless effective screening methods like VIA. This implies that clinicians can play a pivotal role in the prevention of advancement of the lesion to cancer as majority of the factors can be identified during early. Therefore, effective prevention approaches have to consider these factors for the control of cervical cancer in early phase of lesions.

The majority of cervical precancerous lesion cases were diagnosed among women who were between her third and fourth decade of life, had low education level, multiparous, had a sexual debut at a younger age. HPV Vaccination, proper screening and early diagnosis can save the life of women in our country.

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Review Article

Zinc therapy: An emerging hope in the management of COVID-19

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Abstract:

COVID-19 global pandemic creates a great threat to entire healthcare system & disrupts the whole economy worldwide. There is no specific antiviral therapeutic option available for COVID-19 management still now. So, there is an urgent need to discover effective medicines, prevention and control measures to combat this novel corona virus infection. The preventive measure has been the mainstay to fight back the current COVID-19 infection. The host immune system plays pivotal roles against COVID-19 disease progression, similar to many other viral infections. The role of trace elements in boosting the human immune system are well established. Several vitamins such as vitamin A, B6, B12, C, D, E and folate; trace elements including zinc, iron, selenium, magnesium and copper play essential physiological roles in promoting the immune system. Zinc is a trace element that plays a role in stimulating both innate and acquired immunity. It is an indispensable trace element essential for a thorough enzymatic physiological process. Zinc, together with natural scavenger cells and neutrophils, are also involved in developing cells responsible for regulating nonspecific immunity. The benefit of zinc supplementation on the immune system function has been previously observed in non-COVID-19 patients. However, there is inadequate evidence to support the use of zinc in treatment of COVID-19. Therefore, this review will discuss about the efficacy and safety of zinc supplementation as preventive & therapeutic agent as well as adjunctive therapy in treating patients with COVID-19.

Keywords: Zinc therapy, COVID-19, Trace elements, Immunity, Pandemic.

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) creates a panic situation by producing 'The Coronavirus Disease 2019' (COVID-19) and emerged as a threat to public health worldwide.¹ Symptoms of COVID-19 manifest as a cluster of mild to severe respiratory symptoms. Severe COVID-19 amplifies the overall systematic inflammatory response in critically ill patients, increasing the risk of multi-organ dysfunctions, acute respiratory distress syndrome (ARDS), and mortality.² This inflammatory response is caused by the hyperactivation of chemokines and cytokines, prominently interleukin-6 (IL-6). Therefore, the dysregulation of cytokines was one of the targets for many treatment strategies in treating patients with severe COVID-19.³

To date, no specific pharmacological agents have proven efficacy against SARS-CoV; instead, host-directed therapies and supportive therapy are used.⁴ The current treatment options for critically ill patients with COVID-19 include anti-viral agents,

immunosuppressive agents, and immunomodulators.⁵ However, the evidence about these treatment options' mortality benefit in critically ill patients with COVID-19 is conflicting.⁶ Moreover, some mineral supplements and vitamins with immunomodulatory activity and antioxidant effects such as thiamine, vitamins C and D, zinc, and selenium use in patients with COVID-19 are investigated.⁷

Zinc is essential in maintaining human physiology and was first identified in an Iranian patient in 1961.⁸ Zinc is a trace element; however, it remains a vital micronutrient for maintaining cellular physiology such as vision, taste perception, cognition, cell reproduction, growth, and immunity. Zinc deficits dampen equally innate and adaptive immune responses.⁹ Zinc deficiencies are evident by oxidant stress, increased inflammatory process, and life-threatening situations, as well as premature cell death at the cellular and sub-cellular levels.¹⁰ It has been reported that over 300 regulatory enzymes require zinc for their inhibition-activation processes.¹¹

Furthermore, the sepsis process's signal transduction pathways are positively correlated to zinc deficiency.¹² Nuclear Factor Kappa B (NF- κ B), a transcription factor known as the principal controller of the proinflammatory process, especially in infectious diseases, is also affected by zinc deficiency.¹³ Additionally, NF- κ B controls several characteristics of innate and adaptive immune purposes.¹⁴ Moreover, common pathogenic microbes, including viruses, activate NF- κ B, are remain raised among infected individuals. High NF- κ B is related to marked pro-inflammatory effects, and high death rates among infected patients, especially aggressive infections, were instigating sepsis and septic shock, which could minimize with dietary zinc.¹⁵

Zinc is a trace element that plays a role in the development and function of the immune system exhibiting direct or indirect anti-viral properties.¹⁶ High intracellular zinc levels were reported to stall the replication of coronavirus (SARS-CoV-2) and influenza virus that caused the severe acute respiratory syndrome. Some reports demonstrate the synergistic effect of zinc with anti-viral therapy in SARS-CoV-2.¹⁷

Zinc and Viral Infection

Zinc is an essential trace element that significantly impacts health, especially in maintaining immune physiology, growth, and development. Zinc is also considered an agent of antiviral immunity and an enhancer of both innate and acquired immunity.¹⁸ Earlier studies reported that high dose zinc consumption has effectively boosted patients' immune systems with several viral diseases, including torquetenovirus (TTV), common cold (rhinovirus).¹⁹ Apart from its effect on cellular division, differentiation, and rapid growth in humans, its role in preventing common cold and viral infections is underscored to date.²⁰ Increased susceptibility of viral infections has significantly been associated with zinc deficiency in the human body. Zinc-deficient individuals are more prone to severe viral infections like HIV and devastating outcomes in viral and bacterial co-infections. These include influenza-MRSA bacterial superinfection, *S. aureus* infections, and many more.²¹ In light of the sudden onset of the COVID-19 global pandemic, there has been an increasing interest in searching for potential protective and therapeutic measures necessary to curb the uncontrollable spread of this virus.²² Respiratory system pathology and oxygen saturation have improved with zinc supplements in

clinical trials.²³ Notably, the elderly population that usually develops acute respiratory syndrome has lower serum Zinc levels. Similarly, 80% incidence of pediatric pneumonia is associated with low serum zinc levels.²⁴

Anti-Viral Effects of Zinc on COVID-19

A possible clarification for the relevance of zinc in the treatment of COVID-19 conditions has been attributed to its immunomodulatory effect, antiviral property, as well as its ability to regulate the inflammatory response.²⁵ The possible mechanisms by which zinc might be effective in the therapy of COVID-19 are based on the previous evidence with other common viral infections and limited experience with COVID-19. Zinc has been found to refine and improve cilia's morphology and increase its length and beating frequency. It is also considered as a membrane stabilizer and helps to maintain cytoskeletal integrity.²⁶

Zinc is proposed to prevent viral entry and block its replication by inhibiting the RNA dependent RNA polymerase (RdRp) of the virus. Zinc also minimizes the Sirtuin 1 (SIRT-1) induced angiotensin-converting enzyme 2 (ACE-2) receptors expression, decreasing the probability of viral binding ACE2 receptors.²⁷ Zinc also modulates the immune system and increases the production of IFN α production by leucocytes. Zinc, by increasing the levels of IFN α production, indirectly increases the synthesis of antiviral proteins like latent ribonuclease and protein kinase RNA-activated, which can degrade viral RNA.²⁸ Zinc has a well-known antioxidant action with reduced reactive oxygen species production and reactive nitrogen species.²⁹ It also exhibits anti-inflammatory action by inhibiting NF- κ B signaling leading to decreased production of proinflammatory cytokine.³⁰ Zinc has been found to increase Natural Killer cells' activity, Cytotoxic T cells activity, and B Cell Receptor Signaling, along with increased production of antibodies. It also modulates regulatory T-cell functions and preventing hyperactivation of the immune system's hyperimmune response by modulating and balancing the cytokines.³¹

Generally, the role of Zinc as a stimulant of antiviral immunity coupled with its negative repercussions if deficient in the elderly persons or individuals with certain metabolic diseases like diabetes, obesity, or cardiovascular diseases has buttressed several hypotheses that claimed the use of zinc compounds might serve as an adjunct therapy in COVID-19 treatment.³² However, some critics have challenged its consumption rate notwithstanding the positive effects

of using Zinc. It was suggested that 25–50 mg zinc per day is affordable and would not cause adverse effects than a higher intake of 200 to 400mg per day, triggering epigastric pain, lethargy, vomiting, nausea and fatigue.³³ Interestingly, zinc supplementation has been influential in reducing the replication of influenza virus, reduction of hepatitis in HCV infected patients, enhancement of response to antiviral treatment, improvement of both cutaneous and genital warts which are induced by human papillomavirus (HPV), and most notable is the significant reduction of prevalence in pneumonia, especially in developing countries.³⁴ Overall, these observations strengthen the fact that adequate zinc balance is essential to protect an individual from microorganisms, including viral infections. An uptake of up to 40mg per day of zinc as recommended will likely reduce the potential threat of the COVID-19 pandemic, resulting from the rise in the host resistance to viral infections. The efficacy, tolerability, and safety of combining zinc with CQ remain a viable option in conquering COVID-19.³⁵

Evaluation of Zinc effectivity & toxicity in COVID-19 management

There are quite a few published studies that illustrate the efficacy of zinc therapy in managing COVID-19 patients. Many individuals globally consume zinc tablets, vitamin C and B because of immune booster effects and combating COVID-19 and its antiviral effect.³⁶

However, a recent pre-print United States-based retrospective analysis utilizing electronic medical records found that patients treated with hydroxychloroquine and azithromycin with the addition of zinc sulfate had a higher recovery rate. Interestingly, additional input of zinc sulfate was claimed to be associated with lower mortality rate, need for hospital care, and less invasive ventilation requirements. However, this association remained null when observed among Intensive Care Unit (ICU) patients.³⁷ These associations should further be studied in different clinical trials and laboratory tests to provide more robust shreds of evidence. Preventive measures by zinc supplement should be accompanied by a standard of care among COVID-19 patients. Henceforth more double-blind controlled clinical trials should be conducted to confirm the effectiveness. Generally, zinc should be prescribed as an optimal zinc supplement. This is because the recommended intake depends on particular conditions or specific illnesses. Acute zinc

toxicity could lead to nausea, vomiting, abdominal cramps, persistent diarrhea, and other gastrointestinal abnormalities like hematemesis, haematuria, and renal syndromes. At the same time, chronic overdose manifests as sideroblastic anemia, neurological disorders, granulocytopenia, myelodysplastic syndrome, and copper deficiency.³⁸

Furthermore, there have been no reports of deaths or significant life-threatening adverse drug reactions related to zinc supplementation.³⁹ Therefore, both preventive and therapeutic doses should be determined for COVID19 patients considering age, gender, and comorbidity to avoid further consequences. As there is some zinc-related toxicity; thereby, an individual should seek health professional advice before zinc supplementation. However, these supplementary medicines are sold as over-the-counter products without prescription. Oral zinc supplements are likely to be recommended in arresting the burden of COVID-19. This is due to its oral bioavailability and because zinc participates in protecting the body from viral and bacterial infections and improving immunity.⁴⁰

Therefore, vigorous clinical studies should commence urgently to validate the therapeutic efficacy of orally administered dose and investigate its limitations. It is noteworthy, although SARS-CoV-2, influenza, and rhinoviruses employ distinct cellular receptors, angiotensin-converting enzyme-2 (ACE2) present in the oral cavity and upper airway's epithelium further suggests reasons to initiate oral zinc therapy. Unless a comprehensive study is conducted with scientific approval of oral zinc therapy for COVID-19 patients, nobody should take it as self-prescribed. This is to avoid overdose leading to substance abuse and worsen the patient's condition.⁴¹ It should also be investigated and see if the elevated level of oral zinc helps combat SARS-CoV2 and mitigate the intensity, complications, and duration of COVID-19. All efforts should continue until the globally approved vaccination process is concluded. The nutritional therapy, particularly zinc considering its antiviral and immunity-boosting potency, should be further investigated in order to recognize its possible role in prophylactic as well as an adjuvant during treatment against SARS-CoV-2.

Conclusion

COVID-19 is a great challenge to the entire healthcare system as there is no specified antiviral treatment option to date. That's why, preventive and control

measures, or discovery of appropriate medicine should be available to fight the disease back. The host immune system plays pivotal roles against COVID-19 disease progression, similar to many other viral infections. The micronutrient zinc is found to strengthen both the innate and adaptive immunity. The antiviral effects of zinc have been reported in several viral diseases by boosting the immune systems. Furthermore, zinc augments the normal physiological process by facilitating epidermal, gastrointestinal, central nervous, skeletal, and reproductive systems in the human body. Altogether, zinc inhibits the entry of virus in the human cell, inhibits the viral replication process, viral interaction with human cell, and viral uncoating. However, double blind controlled clinical trials should be conducted on zinc therapy considering its antiviral and immunity boosting potency to recognize its possible role in therapeutic, prophylactic as well as adjuvant therapy against COVID-19.

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Case Report

A case report of Becker's variety of myotonia congenita

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Abstract:

Myotonia congenita is a disease of skeletal muscle. It usually begins at childhood and problem in muscle relaxation after contraction of muscles. It involves lower limb muscles more than any other group of muscles. It causes muscle stiffness and interfere with movement like walking, running and other daily activities. Our case was a thirteen years old Muslim male presented with history of stiffness and transient weakness. On examination we found that myotonia in grip, tongue and other muscles with hypertrophy of the proximal muscle and myotonia was more marked on lower limbs. CPK was mildly raised, electro-physiological test showed typical dive bomber's myotonic discharge and muscle biopsy showed the myopathy. On later presentation, more severe disease and marked hypertrophy of proximal muscle established the recessive Becker type of myotonia. Explanation of the nature of disease with symptomatic treatment by phenytoin, improved the patient symptoms. Familial counselling about this disease had also been carried out.

Introduction

The non-dystrophic myotonia are skeletal muscle ion channel disorder traditionally considered to be distinct from myotonic dystrophy because of the absence of progressive weakness and systemic features. The non-dystrophic myotonia are now known to be caused by the dysfunction of key skeletal muscle ion channels and includes myotonia congenita, para-myotonia congenita and sodium channel myotonia.

The worldwide prevalence of non-dystrophic myotonia has been estimated to be 1 in 100000 (Emry, 1991). Prevalence may vary considerably between geographical regions. Myotonia congenita alone was estimated to have a prevalence of between 07 in 10 in 100000 in Scavadinavia.^{1,2} Myotonia congenita is basically a chloride channel myopathy CLCN-1, the gene encoding the major skeletal muscle chloride channel, is localized to chromosome 7q35 locus. The mutation of this gene can cause either dominant Thomsen or recessive becker's type myotonia.³ Myotonia; a tonic spasm of muscle after forceful voluntary contraction stands as cardinal feature of myotonia and repeated contractions wear it out and marked profound after inactivity.⁴ Myotonia affects the face, jaw, tongue, pharynx, arm and legs and is more severe than that in myotonic dystrophy.⁵



Figure-I: Figure showed Herculean appearance and difficulty from sitting to standing position.

We reported the case as because, early detection and treatment of this variety may improve the patient outcome and genetic counseling helps the further emergence of disease in this family. Myotonia congenita due to chloride channel defects can be distinguished from the sodium channel myotonia (Hyperkalemic PP, para-myotonia congenita, sodium channel myotonia) by the rather striking muscle hypertrophy and by DNA mutational screening.⁶

Case report

A thirteen years old Muslim male, gave history of consanguinity marriage, was admitted with the complaints of stiffness of both lower limbs and difficulty in walking with problem in initiating his gait. He also developed hardening of calf muscle intermittently. He also noticed recurrent fall during walking and impairment of recent memory. Patient complained difficulty from sitting to standing posture and failure to relax his hand grip easily. His oral cavity remained open during contraction of forehead. Stiffness markedly increased with exercise after initial improvement. He also stated that tongue movement abnormality after any pressure over tongue. Patient also developed weakness after playing and running. Fine works and writing could not able to do like his friends or mates. Patient attendant did not give any history of birth injury or delayed milestone and head or spine injury. He gave no history of substance abuse or use of traditional medicine. This patient's parent denied such problem in their family. There was no involvement of bladder and bowel. On examination – patient's body built was average and he was cooperative and oriented. Pulse 80/m, BP- 100/65 mmHg, Temp- Normal, Jaundice and Cyanosis – Absent, Thyroid and skin condition – revealed no abnormality and rest of the general examinations appear to be normal. On systemic examination, most of the system revealed no abnormality except locomotor and nervous system. Proximal and calf muscle were hypertrophied. There was evidence of the myotonia during grip and over tongue. No myotonia on eyelids. Myotonia improved just after exercise but patient felt weakness after heavy exercise. Speech was normal, muscle power was normal, all deep reflexes were mildly diminished and planter bilaterally flexor. Other cranial nerves examination revealed no abnormalities and sensory examination were also normal. Relevant investigations showed CBC – normal, RBS – 5.3 mmol/l, S. Creatinine – 0.9 mg/dl, S. Bilirubin – 0.2 mg/dl, S. SGPT – 60 u/l, Na – 142 meq/l, K – 3.7 meq/l, Chloride – 103 meq/l, S- Calcium – 9 mg/dl, PBF – non-specific abnormality, S. CPK – 269 u/l, Thyroid function test – normal, USG of W/A – normal, HB-electrophoresis – normal, HBsAg – Negative, X-ray chest P/A view – normal, Urine R/E – normal. ECG within normal limit and Echocardiography also normal, muscle biopsy showed the evidence of myopathy and lastly electrophysiological study showed normal nerve conduction, but EMG showed myotonic discharge – typically repetitive discharge of varying amplitude and

frequency along with classical dive bomber's sound. Genetic evaluation e.g. CTG repeat mutation in DNA is not possible in our country so these test were excluded. Considering the autosomal recessive pattern inheritance and clinical picture and the diagnosis of Becker's variety of myotonia congenita was entertained. We started the treatment by anticonvulsants, clonazepam and patient was improved. Patient referred for genetic counseling and rehabilitation. During follow up, patient did not develop further deterioration.

Discussion

Myotonia congenita typically two types – Type -1, autosomal dominant myotonia congenita and type- 2, Becker's type recessive myotonia congenita. Myotonia congenita first described by the Thomsen in 1876 in his own family. Myotonia is persistent contraction of skeletal muscle following stimulation leading to generalized muscular hypertrophy and herculean appearance. In fig-1 showed the herculean appearance and difficulty to stand from sitting position. Myotonic muscle stiffness is painless and exacerbated by anxiety, cold and fatigue. The autosomal dominant disease should be differentiated from the recessive generalized myotonia which is similar but has a later age of onset, a more severe in nature and manifest transient muscle weakness during muscle exertion after rest.⁷ In general, patient with recessive disease experience transitory bout of weakness after period of disuse and may developed progressive myopathy; in than the dominant form and becker's myotonia is more common than Thomsen disease.⁸ The age of onset is in Thomsen variety usually within first decade but recessive variety at 10 to 14 years.⁸ Our patient presented at the age of thirteen years. Some clinical finding is more common in recessive than the dominant form but considerable overlap exist, and recessive form more severe, is frequently associated with muscle hypertrophy and with diminished deep reflexes.⁹ This case manifested as hypertrophy of proximal and calf muscle and associated with diminished deep reflexes, but our case did not show any evidence of cranial nerve involvement except tongue that is usually predominantly involved in myotonic disorder.¹⁰ The brunt of the Becker's disease fall on the lower limbs, probably as a result of work hypertrophy, since the quadriceps and other muscles are in continual state of contraction.¹⁰ This case showed the marked myotonia in lower limb. Positive family history, early appearance and lack of progression of myotonia and generalized muscular hypertrophy

distinguish the myotonia congenita form myotonic dystrophy. Para-myotonia congenita is a myotonia that is precipitated by cold.¹¹ Our patient did not show any cold sensitivity. The testicular atrophy, cardiac abnormalities, frontal baldness, and cataract- the features that characterize myotonic dystrophy are conspicuously absent.⁴ Our patient did not show any systemic features but lower limb involvement was more marked than upper limbs. On relevant investigation – The CPK was mildly raised, electro-physiological test was typically showed myotonic discharge and muscle biopsy showed evidence of myopathy. Becker's type myotonia showed the features of progressive myopathy.⁸ In one study from Portugal, patients were treated with different drug to determine the therapy for optimal relief of myotonia. Five patients responded to phenytoin, one to carbamazepine, three to acetazolamide and none to quinidine or procainamide.⁷ Another double-blind study compared phenytoin and carbamazepine on myotonic patient; there was a good response to both drug but phenytoin should decreased efficiency at high-dose.¹² Dantrolene may be tried in patient who do not respond to usual drugs.¹³ This patient responded well with phenytoin. Myotonic patient sensitive to many anesthetic drugs. Spinal and epidural anesthesia safer than general anesthesia. This patient also has a higher risk of pulmonary aspiration and post-operative pneumonia.¹⁴ DNA mutational screening is not possible in our country, so we highlighted the clinical features and investigations to establish either dominant or recessive type myotonia congenita.

Progression of the disease continues to about thirty years of age and according to sun and Strib, the course of the illness thereafter remains unchanged.

Conclusion

When faced with a patient complaining of muscle weakness and stiffness, the neurologist must able to distinguish between dystrophic and non-dystrophic myotonia. If a careful medical history and neurological examination are undertaken in combination with electro-physiological studies, it is possible to determine which genetic test should be carried out to confirm clinical impression. This disease needed further

investigations, advance treatment strategy and genetic counseling for better outcome.

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