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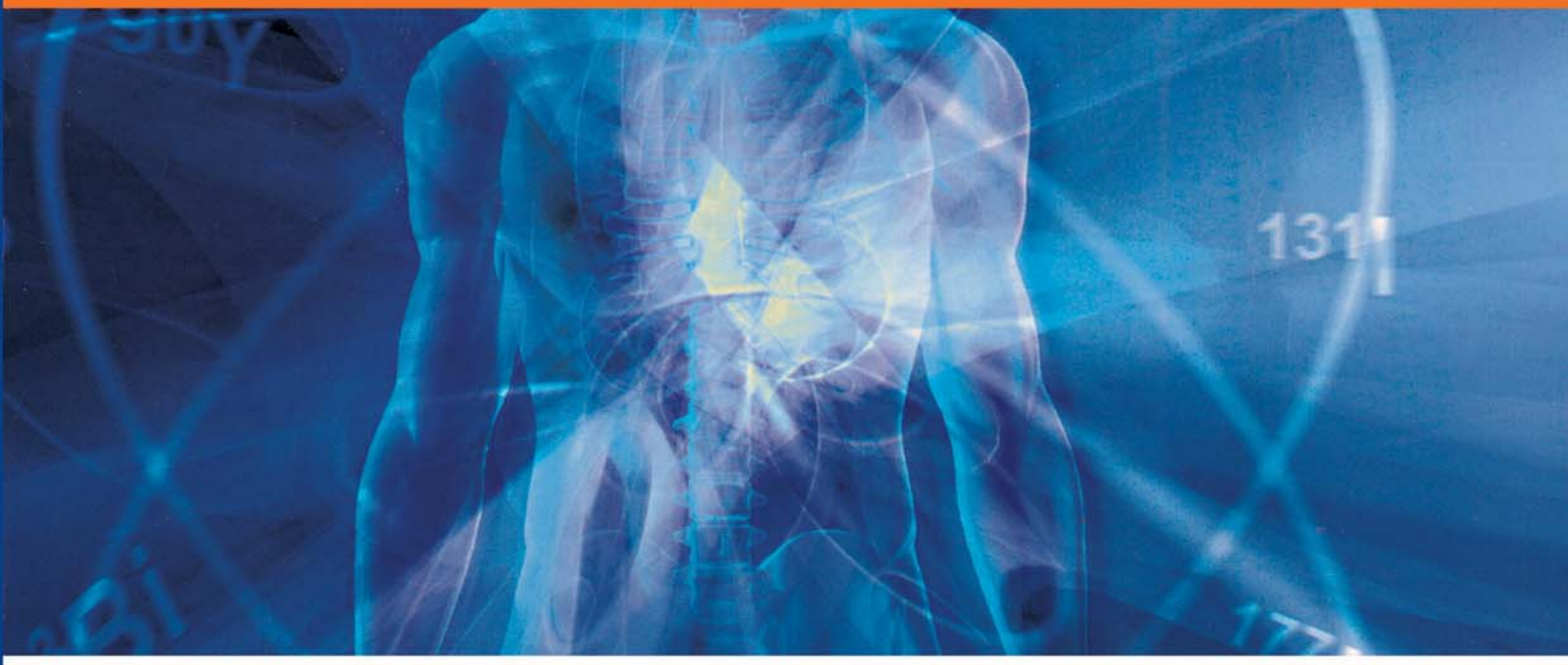

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EDITORIAL

Ebola- New Vampire of Modern Era

Irfan Mirza

Gone are the days when we used to watch horror movies of Vampire Count Dracula who used to suck and bleed individuals to death. We now have a disease which is bleeding the mankind and is much more terrifying, frightening and horrifying than any of the horror movies. During last few months this disease has literally made hostage to whole of the medical community across the world. It is proving to be one of the most fatal diseases in the history of mankind. It is a tragedy, the rate at which Ebola Virus is spreading in West Africa. The exponential rate at which this disease has been spreading in the last couple of months has jolted even the superpowers of the world. God has been very kind that we in Pakistan are not exposed to this deadly disease but we need to know and beef up our preventive and preparedness level, should we encounter any such case in future.

Ebola belongs to family filoviridae and is rare and deadly infectious disease caused by infection with one of the four Ebola virus strains (Zaire, Sudan, Reston & Cote d'Ivoire)[1]. Medical science has first encountered the filo viruses when Marburg virus appeared in 1967. During that time some laboratory workers were hospitalized with unusual and severe form of disease. The detailed investigations of the cases revealed that those laboratory workers were handling African green monkeys imported from Africa as part of research and vaccine production. The strange morphology of virus, high mortality rate and failure to identify natural history of virus created lot of fear and panic among the scientists. Fortunately, disease was controlled and effective quarantine measures were adopted in many countries to ward off the recurrence of disease introduced by African monkeys[2].

The international community was once again stunned and surprised by the discovery of another virus called Ebola from the family filoviridae during the late 1970's. It was in 1976, when Ebola (named after the Ebola River in Zaire) first emerged in Sudan and Zaire (Now Democratic republic of Congo). The first outbreak of Ebola (Ebola-Sudan) infected over 284 people, with a mortality rate of 53%. A few months later, second Ebola virus emerged from Yambuku, Zaire, Ebola-Zaire (EBOZ) which had the highest mortality rate of any of the Ebola viruses (88%), infected 318 people. Majority of the affected people had severe hemorrhagic manifestations.[3], [4]. Most of the medical facilities in the affected areas had to be closed due to high rate of death among health care workers. This in fact was blessing in disguise, as closure of hospitals and clinics eliminated the possibility of disease transmission through use of unsterililised syringes and lack of barrier nursing. Most of the affectees of Ebola were segregated by traditional method of Quarantine which proved to be effective source of containing the disease.

Despite tremendous efforts of experienced and dedicated researchers, Ebola's natural reservoir was never identified. The third strain of Ebola, Ebola Reston (EBOR), was first identified in 1989 when infected monkeys were imported into Reston, Virginia, from Mindanao in the Philippines[5]. Fortunately, few people who were infected with EBOR never developed Ebola hemorrhagic fever (EHF). The last known strain of Ebola, Ebola Cote d'Ivoire (EBO-CI) was discovered in 1994 when a female ethologist performing a necropsy on a dead chimpanzee from the Tai Forest, Cote d'Ivoire, accidentally infected herself during the necropsy[6].

As of October 29 , 2014, a total of 13567 confirmed and probable cases of Ebola virus disease (EVD), which include 7728 laboratory confirmed cases with 4960 deaths from the virus, had been reported from five countries in West Africa - Guinea, Liberia, Nigeria, Senegal, and Sierra Leone (Figure 1). As far as reported morbidity and mortality is concerned, current epidemic of EVD is much larger than all previous epidemics combined[7].

Figure 1

Map showing affected countries of West Africa (Adapted from and available at CDC website)

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This epidemic began in Guinea during December 2013, and the World Health Organization (WHO) was officially notified of the rapidly evolving EVD outbreak on March 23, 2014. On August 8, WHO declared this epidemic to be a "public health emergency of international concern.[8] Now after almost 11 months after the first case appeared the numbers of reported cases and deaths were still rising from week to week even with best of multinational efforts to control the spread of infection. This epidemic has now grown to such large proportions that the three most-affected countries - Guinea, Liberia, and Sierra Leone face mammoth challenges in executing control measures at the scale required to stop transmission and to provide clinical care for all persons with EVD [9].

Natural reservoir of Ebola virus has not yet been confirmed, however bats are thought to be the most likely candidate species. Bats were known to perch in the cotton factory where initial cases of the 1976 and 1979 out breaks of Ebola were observed. Out of 24 plant and 19 vertebrate species experimentally inoculated with Ebola virus, only bats became infected. The bats showed no clinical signs of disease, which is considered evidence that these bats are reservoir species of Ebola virus. It was found in Bangladesh that antibodies against Zaire and Reston viruses were present in fruit bats thus suggesting that these bats are also likely hosts of the virus and that the filoviruses are also present in Asia[10]. Bats can infect the other wild animals like monkeys and surprisingly bats are also source of food in many African countries. So, initial human infection occurs through contact with infected bat or other wild animals. Human to human transmission is a predominant feature of epidemic. The transmission of Ebola virus is primarily through close and direct contact with infected body fluids of infected person. The most infectious body fluids are blood, stool and vomit of infected persons. The virus has also been found in urine, breast milk and semen for up to 70 days but these fluids are considered to be less infectious. In addition, saliva, tears and sweat may also carry the risk of transmission. It is extremely unlikely for the virus to be transmitted through air because the only way virus gets into the air is in large droplets of vomit or saliva. These droplets are heavy and thus cannot travel very far. People may be able to catch virus if infected person directly coughs or sneezes directly onto them, but it has been observed that Ebola infected person generally do not cough or sneeze[11]. Health care workers can get the virus through objects contaminated with virus like needles or medical equipment. Ebola virus can only spread to others after symptoms appear in affected individual. Symptoms can appear from 2-21 days after exposure and these include fever, headache, fatigue, vomiting, diarrhea, aches and muscular pains, unexplained bleeding or bruising from any site. In the severe form of disease (Ebola hemorrhagic fever), bleeding can occur from any site of the body. The case fatality rate in the latest epidemic has been found to be 70.8% and New England Journal of medicine in latest issue of October 2014 concluded "Without drastic improvements in control measures, the numbers of cases of and deaths from EVD are expected to continue increasing from hundreds to thousands per week in the coming months9. World has become a global village. Increased travel around the world and the fact that Pakistan has UN peace keeping troops in West African countries especially Liberia poses a potential risk of contacts of Ebola patients to come in the country. It is mandatory that strict infection control practices are followed to limit the transmission of virus. Key elements pertaining to handling such patients as outlined by Centre of Disease Control (CDC) prevention are as follows [12].

a. Patient should be placed in a single patient room containing private bathroom with the door closed.
b. The facilities should maintain log of all the persons entering the patient's room.
c. Full personal protective equipment should be worn which includes surgical cap, goggles, rubber boots, medical mask, double gloves, apron / overalls made up of impervious material and even respirator if available.
d. All patient care medical equipment should be preferably disposable. All non dedicated and non disposable medical equipment should be cleaned and disinfected according to manufacturer's instructions or hospital policies. Hypochlorite solution or liquid bleach is considered very effective disinfectant.
e. Phlebotomy procedures and laboratory tests should be limited to minimum necessary for essential diagnostic evaluation and patient care.
f. Use of needles and sharps should be minimal and should be disposed off in puncture proof, sealed containers.
g. Meticulous hand hygiene practices should be followed before and after contact with patient, contact with infectious material and before and after use of PPE.
h. Health care workers with percutaneous or mucocutaneous exposures to blood, body fluids, secretions, or excretions from a patient with suspected EVD should stop working and immediately wash the affected skin surfaces with soap and water.

We as Muslims believe in Allah's will and control, yet we have to remain vigilant and well prepared for any eventuality. The only way we can fight Ebola is to have sufficient knowledge about the disease and determination

to implement the strict infection control practices in our hospitals.

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REVIEW ARTICLE

Salvadora Persica-Medicinal Properties

Talea Hoor

ABSTRACT:
Herbal medicines have long been the center of interest for the researchers. Herbs have long been used for the treatment of various ailments including diarrhea, ulcers, arthritis etc. people have always preferred herbal medicine believing it to be less toxic and inexpensive. Salvadora persica (miswak) is one of such plants which are used over the years mostly in the field of dentistry because of its religious significance in Islam. The purpose of this review is to go through the various medicinal properties of this plant. A literature search regarding this article was done on Google scholar and Pubmed /Medline during the time period 1988-2014.Most of the articles were related to oral health but few other properties are also found.
Key words: Salvadora persica, Miswak, Medicinal properties

INTRODUCTION:

Plants have served human kind as sources of medicinal agents since its earliest beginning. Today, natural products represent more than 50% of the available medicinal agents in use.

One of such examples is the miswak (Figure 1). It is obtained from Salvadora persica plant which is widespread, notably in thorn shrubs, desert floodplains, river and stream bank vegetation, and grassy savannahs. The plant is commonly known as miswak. It prefers areas where groundwater is readily available, by riverbanks, on perimeters of waterholes, in seasonally wet sites, and along drainage lines in arid zones. Also found in valleys, on dunes and on termite mounds.[2]

Salvadora persica is an evergreen shrub or small tree 6-7 m; main trunk erect or trailing with profusely branched, wide crown of crooked, straggling and drooping branches; young branches green in colour; bark slightly rough, greyish-brown on main stem, paler elsewhere. The generic name was given in 1749 in honour of an apothecary of Barcelona, Juan Salvadory Bosca (1598-1681), by Dr. Laurent Garcin, botanist, traveller and plant collector. The true specimen of this species came, as the specific name indicates, from Persia.[3]

This review is aimed at revealing the secrets of this magical plant and reinforcing the beliefs of a Muslim on a scientific basis as well as enhancing the tradition of research in Pakistan.

METHODOLOGY:

Literature search for this review was done from 1988 - 2014 with key words and phrases salvadora persica, miswak and medicinal properties. The search engines used are Google scholar and Pubmed/Medline.

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Figure 1
Salvadorapersica (Miswak)

Historical and Religious Background:

The use of Miswak is a pre-Islamic custom. It was adopted and Islamized by prophet Muhammad (PBUH) around 543 A.D. Arabs have used this kind of tooth brushing some 7000 years ago. Japanese and Romans also use it as well as the ancient Egyptians and Jews. Islam emphasized basic oral hygiene by incorporating it as a religious process. It has been narrated by many authorities that the messenger of Allah (PBUH) has emphasized much on the practice of using Miswak so much so that according to Hazrat Abu Hraira (may Allah be pleased with him) that messenger of Allah said "were it not that I might distress my people, I would have ordered them to delay the evening prayers and use miswak at every time of prayer".

Islam has great emphasis on the health and hygiene, on the cleanliness of mind and body. It was also said that messenger of Allah stated, "Cleanliness is half of faith". Miswak not only cleanses the teeth in physical manner but also have an anti-bacterial activity, which destroys the germs as well.

Functional uses of the Plant:

Food: Fruits have a sweet, agreeable, aromatic, slightly pungent and peppery taste. They can be eaten raw, cooked, or dried and stored. Fruit with or without seeds is said to contain 1.7-1.86% sugars when ripe. Fermented drinks are also made from the fruit. The leaf is somewhat bitter and aromatic, with a taste likened to mustard. The leaves are also cooked as a sauce and eaten with couscous or as a green vegetable. Tender shoots, seeds and seed oil are also edible. Edible salts are obtained from ashes.

Fodder: Leaves and young shoots are browsed by all stock, but normally cattle do not occur in the driest part of the Salvadora persica distribution range and hence it tends to be valued more as a camel, sheep and goat forage. Leaves make good fodder as their water content is high (15-36%). The high salt content of the leaves is said to affect the taste of milk, but the leaves are said to increase lactation in cows.

Apiculture: Salvadora persica is reported as a good source of nectar.

Fuel: The wood is sometimes used for firewood and charcoal. However, it is not used for cooking meat, as it leaves a foul taste.

Timber: The wood is soft, white, and easy to work and is not liable to termite attack. Used for coffins and clubs. Gum or resin: Resin that drips from the tree is supposedly useful for making varnish.

Lipids: Seeds of Salvadora persica contain 30-40% of greenish-yellow, non-edible oil that has over 50% lauric and myristic acids. It has a high melting point and a disagreeable odour that disappears on purification. The most important aspect of the oil is the presence of a low percentage of C8 and C10 fatty acids that are of great economic significance. The oil is an alternative source of oil for soap and detergent industries.

Medicine: Toothbrushes made from roots and small branches of about 3-5 mm diameter have been used for over 1000 years, especially by Islamic populations in India, Arabia and Africa. Several agents occurring in the bark and wood have been suggested as aids in prevention of dental caries, such as antimicrobial agents that suppress bacterial growth and the formation of plaque. The tooth stick is also said to relieve toothache and gum disease. Roots also are used for cleaning teeth and for relieving toothache. Decoctions of leaves are used as a mouthwash, and masticated leaves for tooth and gum problems. A decoction of the root is used to treat gonorrhea, spleen trouble and general stomach-ache. Roots are also used for chest diseases or pounded and used as a poultice to heal boils. The bark is scratched and the latex used for treating sores. Seeds are used as a tonic, and seed oil is used on the skin for rheumatism. Other products: Crusted leaves placed in cow urine together with leaves of Pergulariatomentosa are used to clear hair from tanned hides, allowing the hair to be removed with a knife. Roots contain salvadourea, a urea derivative[4].

Shade or shelter: Planted as shelterbelts and windbreaks to protect farm habitation, gardens and orchards. Reclamation: Planted in sand dune reclamation and also useful for reclaiming saline soils[5].

Pharmacological Survey of Medicinal Properties: Studies have indicated that Salvadora persica has plaque inhibiting and anti-bacterial properties against various types of bacteria.

Al-Lafi and Ababner[6] tested the anti-bacterial activity of Salvadora persica against S. aureus and found out that it has drastic effects on the growth of the said bacteria and a variable effect on some other species as well. Al-Bagieh,[7] suggested that aqueous extracts of miswak could be used to reduce the growth of Candida albicans. Such inhibitions last for up to 36 hrs at concentration of 15% and above. In another study conducted by Almas[8] the anti-microbial activities of the chewing sticks obtained by Neem and Arak were compared and it was found out that both are effective against bacteria especially against S.mutans and S.fecalis at the tested concentrations. Gazi[9] and Hattab investigated the immediate and medium term effect of miswak on the composition of Saliva which shows that it increases calcium and chloride and significant decreases in phosphorus and pH. Calcium saturation of saliva inhibits demineralization and promotes re-mineralization of tooth enamel and high concentration of chloride inhibits calculus formation.Mansour[10] studied the analgesic effect of miswak decoction when injected to mice. They found it to be more effective against thermal stimuli than chemical ones.

Mohammad,[11] investigated the cytotoxic potential of Salvadora persica on gingival and other periodontal structures and it showed that freshly cut and freshly used miswak has no cytotoxic property but after 24 hours it showed some harmful components. Miswak has been used therapeutically as a part of various toothpastes all over the world like sarkan toothpaste (UK), miswak (Pakistan) etc.

It has also been tested, as a part of mouth wash which showed reduction in plaque formation, but no currently available preparation contains miswak. Use of miswak was also found to be related with plaque reduction by many users. Babay and Almas [12] conducted a study on effect of miswak extract on healthy human dentin, which showed that alcohol extract of miswak along with saline remove the smear layer on the dentin. In studies carried out by Almas [13, 14, 15] showed that Salvadora persica is effective against S. fecalis and S. mutans. Khalid Almas[16] and Al zeid[17] conducted a study which concluded that Salvadora persica has an immediate anti-bacterial effect and S. mutans were more susceptible than lactobacilli[18, 19]. Monforte[20] studied the activity of Salvadora Persica extract as an anti-convulsant and sedative. One study conducted by Al-mohaya[21] showed that miswak can decrease the density of growth of oral candida in case of renal transplant patient. Another study conducted by Sanogo[22]showed antiulcer activity of Salvadora persica. Ali[23] in a study showed that Salvadora persica was found to be active against plasmodium falciparum NF54 strain. The anti-plasmodial activity of different extracts of Salvadora persica against P.falciparum NF54 strain was

found to be 0.6microg/ml (stem) and 0.7microg/ml (leaves).Galati[24] found Salvadora persica decoction to be able to reduce levels of cholesterol and LDL plasma levels, whereas HDL and triglycerides were unchanged. Al Khateeb[25] studied that people using miswak have a low level for the need of periodontal treatment. A similar study conducted by Darout[26] showed better periodontal status of Sudanese population using miswak as compared to toothbrush users. Salvadora persica showed a decrease in mice exploratory activity evidenced by a study conducted by Sulaiman[27] Darmani[28] investigated the toxic effects of Salvadora persica for 30 days on the reproductive system of male and female mice Al-Otaibi[29] conducted a research, which showed that Salvadora persica extract interfered with leukotoxicity of A.comitans. It was also concluded that miswak use was at least as effective as toothbrush for reducing plaque and gingivitis and the anti-microbial effect is beneficial for the prevention and treatment of periodontal disease. In 2004 Khalessi[30] conducted a double blind, cross over trial, which compared the efficacy of a mouth wash containing extracts of S.persica with commercially available ones. Results showed that use of tested mouth wash resulted in gingival health and lower carriage rate of cariogenic bacteria but did not help in plaque removal. In 2005 a study was conducted whose aim was to assess the anti-microbial activity of commercially available non-alcohol mouth rinses and 50% miswak extracts against S. fecalis, S. mutans, C. albicans, S.aureus and S.epidermidis. The extract showed a low anti-microbial activity as compared to commercially available mouthwashes.[31]

In 2006 Darmani[32] conducted a study which examined the effects of extracts of two chewing sticks on proliferation of fibroblasts and viability of cariogenic bacteria. Results showed that aqueous extracts of miswak (Salvadora persica) and derum (juglansregia) enhance the growth of fibroblasts and inhibit the growth of cariogenic bacteria.AL-bagieh[33] investigated that benzylisothiocyanate isolated from Salvadora persica roots showed a virucidal activity against HIV-1 at a concentration of 133.3ug/ml.

Leaves of Salvadora persica have carminative, antiseptic and anti-fungal action[34]. Leaves are also used in the asthma, cough and rheumatism, scurvy, piles, leprosy, hepatic disorders[35, 36] Leaves are bitter and possess antiscorbutic, deobstruent, liver tonic, diuretic, analgesic, anthelmintic, astringent properties, hypoglycaemic, antimicrobial, anti-bacterial, anti-plasmodial because of the presence of fluoride in stems are used as traditional toothbrush or chewing stick or used as oral hygiene tool. Stem extracts shows anti-microbial[37], anti-caries[38], antispasmodial[39], anticonvulsant and sedative effects. Stem bark is used as an ascarifuge and for gastric troubles. Seeds are purgative and tonic. Seed oil is applied on the skin in rheumatism[39]. Flowers are used for de-worming, leprosy, gonorrheae. Root barks and leaves in piles and hepatic disorders[40]. Roots also possess anti-oxidant activity, anti-inflammatory activity. Roots and twigs also possess anti-microbial activity[41] Chlorine, trimethylamine and sulphur compounds in aqueous extract of roots of miswak tree shows anti-mycotic effect[42]. Antimicrobial activity of both glucosinolates: glucotropeol in and sinigrin were investigated against tooth decay microorganisms and bacterial species[43]. Aerial parts show anti-microbial, Anti-spasmodic, anti-arrhythmic anti-cholinergic activity[44, 45]. Decoction of miswak tree gives anti-ulcer activity

CONCLUSION:

It is quite evident from this review that Salvadora persica is a plant with tremendous medical benefits attached and further research is required to evaluate its full potential in different fields of medicine.

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ORIGINAL ARTICLE

Visual Outcome After Intravitreal Bevacizumab (Avastin) in the Treatment of Diabetic Macular Oedema

Saquib Naeem[1], Muhammad Waseem[2]

ABSTRACT:

Objective: To evaluate the visual outcome after intravitreal injection of bevacizumab (Avastin) in patients with diabetic macular edema.

Materials and Methods: A prospective study was conducted in PNS Shifa Hospital from 15 March 2010 to 15 Dec 2011 in patients with diabetic macular edema who were treated with at least one intravitreal injection of bevacizumab 1.25 mg in 0.05 ml. Patients underwent Snellen's visual acuity testing and detailed ophthalmic examination before the procedure and monthly follow-up visits for three months.

Results: There were 104 eyes of 71 consecutive patients with a mean age of 61.8 years (SD 16.1). The patients received a mean of 1.39 (SD1.35) injections of bevacizumab per eye. No adverse events were observed. The mean central macular thickness at baseline was 835 micron which improved to a mean of 360 micron at 3rd month ($P < 0.001$). The mean baseline acuity was log MAR = 0.52(SD 0.19) and at one month log MAR =0.22 (SD 0.20); the difference was significant ($P = 0.001$). At last follow-up of 3 months, the mean visual acuity was log MAR = 0.20 (SD 0.19), which was significantly better than baseline ($P < 0.001$). Visual acuity improved in 89 eyes.

Conclusion: Intravitreal bevacizumab resulted in a significant decrease in macular edema and improvement in visual acuity. The number of patients in this study was limited and the follow-up was too short to make any specific treatment recommendations, but the favorable short-term results suggest the need for further study.

Keywords: Avastin; Bevacizumab; Diabetic macular edema; Intravitreal injections; Vascular endothelial growth factor.

INTRODUCTION:

The commonest cause of visual impairment in diabetic patients is macular oedema. The pathogenesis of diabetic macular oedema (DME) is not yet clear. The important pathophysiology of DME is the loss of retinal capillary pericytes, resulting in increased vascular permeability.[1,2,3,4] The Early Treatment Diabetic Retinopathy Study (ETDRS) showed that the risk of moderate visual loss due to macular oedema was 32% at 3-years. Focal macular laser photocoagulation was effective in a large prospective multicenter randomized clinical trial of ETDR. [5] Efficient laser treatment could not be performed in many while some treated eyes were found to be resistant to photocoagulation due to diffuse macular oedema. Thus the failure of laser photocoagulation had warranted the need for other treatment modalities, such as intravitreal triamcinolone acetonide (IVTA) injection[6,7] or pars plana vitrectomy[8,9] .The primary cause of diabetic retinopathy is retinal hypoxia , which increases production of vascular endothelial growth factor (VEGF). VEGF is a potent inducer of vascular permeability that causes leakage from retinal vessels and contributes to DME [10]. Bevacizumab (Avastin), is a full length, humanized monoclonal antibody against VEGF, that inhibits all the active forms of VEGF, and approved by the Food and Drug Administration for the treatment of metastatic colorectal cancer.[11,12] It has shown beneficial effects in many ocular diseases.[13,14,15] There are only two studies showing the beneficial effect of intravitreal bevacizumab as a primary treatment for persistent DME.[16,17]

Present study was conducted to evaluate the visual outcome after intravitreal injection of bevacizumab (Avastin) in patients with diabetic macular edema (DME).

PATIENTS AND METHODS:

This is a prospective clinical trial in which diabetic patients coming for ophthalmic check up were seen in Eye OPD of PNS Shifa from 15 March 2010 to 15 December 2012. Consecutive patients with DME were included and treated based on a standardized protocol over a period of 21 months with monthly follow-up visits. Detailed routine eye examination was carried out. Best corrected visual acuity was noted. Optical coherence tomography imaging (SD-OCT, Spectralis, Heidelberg Engineering) and Digital fundus fluorescein angiography (FFA, Canon) were done before the procedure and at monthly intervals during the follow-up period for three months. All findings were documented on a specially designed performa. Patient with DME, having clear media, not having prior laser photocoagulation and willing for intravitreal bevacizumab therapy were included for the study. Patients having glaucoma, uveitis, vitreous hemorrhage, proliferative vitreo-retinopathy, retinal detachment uncontrolled systemic hypertension, severe renal dysfunction, nephrotic syndrome, and dysproteinemias or receiving vasoactive drugs were excluded.

A total of 104 eyes of 71 patients were included in this study that underwent intravitreal bevacizumab injection as the primary treatment for DME. All patients had macular oedema with hyperfluorescent leakage on fundus fluorescein angiography. Before intravitreal bevacizumab injection, no eye had received any laser treatment for

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DME. All patients were fully informed about the treatment and informed consent was obtained from each patient. The study followed the tenets of Declaration of Helsinki. Baseline parameters were documented including best-corrected visual acuity (BCVA), intraocular pressure, FFA findings and OCT. BCVA for each eye was checked using Snellen chart at 6 meters. The average VA was computed by converting the value to the LogMAR equivalent, and taking the average of the LogMAR values as described by Holladay. [18] Statistical calculations were performed using LogMAR values for VA. All patients received minimum of one intravitreal bevacizumab (Avastin® Genentech) injection at a dose of 1.25 mg (0.05 ml) and later if required at monthly intervals. All intravitreal injections were performed under local/ topical anaesthesia with all aseptic precautions in the operating room. The lid was prepared with povidone-iodine 5% and also applied directly to the eye. Bevacizumab was filled and packed under sterile conditions by the Aga Khan University Hospital institutional pharmacy, Karachi, using insulin syringes. It was injected into the anterior vitreous, 3.5 mm posterior to the limbus in pseudophakic eyes and 4.0 mm posterior to the limbus in phakic eyes. A cotton-tipped applicator was applied at the injection site immediately after the removal of the needle to prevent reflux. Topical moxifloxacin drops(Megamox,Sante) were applied four times daily for 1 week.

The eyes were examined after 1 week and every 4 weeks. Response to the treatment was monitored by VA assessment, FFA, and OCT. Potential drug or injection-related complications were recorded, if present. Patients received re-injections when there was a recurrence. Recurrence was defined when there was a decrease in BCVA associated with an increase of intraretinal fluid due to macular oedema as observed on FFA and/or OCT. The t test was used for statistical analysis of changes in visual acuity and central retinal thickness (CRT). A P-value of less than 0.05 was considered to be statistically significant.

RESULTS:

There were 48 males and 23 females.The mean age of the patients was 61.87±16.15 years (range, 24-90 years). Patients having clinically significant macular oedema were enrolled and completed 12 weeks of follow-up. 5 (7.04%) cases received a second intravitreal injection of bevacizumab, and 6 (8.4%) needed more than three injections. The mean VAs, and IOPs of the patients before and after intravitreal bevacizumab injection are presented in Table 1. Baseline mean visual acuity was 0.52 LogMAR (20/63), ranging from 1.0 LogMAR (20/200) to 0.10LogMAR (20/26) and baseline mean 1-mm CRT was 545 (range 835-360) µm, as measured by OCT. There was statistically significant difference in VA after bevacizumab injection when compared with pretreatment values (P<0.001). After a mean follow-up period of 3 months, VA improved in 89 of 104 eyes (85.6%) with a mean of 2.4±1.6, and 2.8±2.0 Snellen lines at 1 and 3-months, respectively. VA remained unchanged in 15(14.4%) eyes, and decreased in 4 (3.8%) eyes and showed increased fluorescein leakage on FFA (Table 1).

Table: 1

Mean Log MAR Value for the Visual Acuities and IOPs of Patients Before and After Intravitreal Bevacizumab Injection

	Log MAR value	IOPs (mmHg)
Pre Inj	0.52±0.19	15.0±2.1
1 month	0.22±0.20	15.8±2.2
3 months	0.20±0.21	15.1±2.4

IOP=intraocular pressure; Pre Inj=pre-injection.

93(89.4%) eyes showed a reduction in macular oedema on OCT after intravitreal bevacizumab injection. Oedema decreased from a baseline highest mean value of 835 micron to a lowest mean value of 360 at the last examination. Mean reduction of macular oedema at 1 and 3-month were statistically significant when compared with preinjection values (P<0.001). Average IOP values at 1, 2 and 3-month, were not statistically significant when compared with pre injection values.

Safety

After 06 months of follow-up, no severe ocular or systemic adverse events like endophthalmitis, retinal detachment, traumatic cataract, uveitis, thromboembolic event, systemic hypertension or kidney failure were reported. No progression of avascular areas was observed in fluorescein angiography. No patient developed neovascularisation of the optic disc, of the iris or elsewhere in the retina. Mild anterior chamber cellular reaction was observed in 12 eyes (11.53%), but the inflammation resolved within a week with topical corticosteroid. No other injection- or drug-related complications were observed.

DISCUSSION:

DME may persist in some eyes despite laser treatment or intravitreal injection of triamcinolone acetonide (IVTA injection), but is not without risks.[19,20] and complications can be due to the injection procedure or due to the steroid suspension. The efficacy of IVTA appears to be transient and repeated injections may be required. In diabetic patients, blood-retina barrier is broken with the production

of VEGF causing increased vascular permeability resulting in retinal oedema. Thus Anti-VEGF therapy may be a promising treatment option for DME.

Intravitreal injection of pegaptanib was reported by Cunningham[21, 22, 23] to have better VA outcomes with reduction in central retinal thickness and less additional therapy with laser photocoagulation.

Intravitreal bevacizumab safety has been confirmed by previous studies, has been shown to be effective in the treatment of oedema due to various etiologies.[24,25,26,27,28]

Results of our study have shown that intravitreal bevacizumab appears to be effective in the primary treatment of DME. In our study, 85.5% eyes showed an improvement in VA with a decrease in fluorescein leakage on FFA. The results of our study confirm previous reports showing the beneficial effect of intravitreal bevacizumab in the treatment of DME. An increase in VA of at least three lines was observed in 81 of 104 eyes at a 6-week follow-up, and in 89 of 104 eyes completing 12 weeks of follow-up. Mean reduction in central macular thickness was 17.2% at 6 weeks, 25.65% at 12 weeks after the injection. In this study, VA increased with a mean of 2.4, 2.7, and 2.8 Snellen lines at 1 and 3-month, respectively. Similar results were seen by study conducted by Haritoglou [16]

This high success in our study may be explained by performing intravitreal bevacizumab injection as the primary treatment of DME or a short duration of DME in our patients. Consistent with a decrease in CRT as seen by OCT, fluorescein angiography revealed a reduction in the area of leakage. No patient showed evidence of severe drug-related systemic or ocular adverse events during multiple treatments for as long as 6 months. Even if the study was too small to provide solid data on safety, several comparable studies showed similar results. [13,14,15,16,17]Although nearly all patients showed an immediate response to intravitreal bevacizumab treatment with a reduction in retinal thickness and an increase in visual acuity, macular oedema had not resolved completely in 10 patients even after four injections.

CONCLUSION:

The use of intravitreal bevacizumab has shown to reduce the extravasation from blood vessels, and inhibition of neovascularization. It have beneficial effect in the treatment of macular oedema. Large randomised controlled clinical trials are needed to evaluate the long-term efficacy of intravitreal bevacizumab as a primary treatment in patients with diabetic macular oedema.

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ORIGINAL ARTICLE

Knowledge, Attitude and Perceived Barriers Toward Research Among Undergraduate Medical Students

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ABSTRACT:

Objective: To evaluate the knowledge, attitude and perceived barriers toward research among undergraduate medical students.

Materials and Methods: A cross sectional institution based study was conducted from April to June, 2014 on 3rd year MBBS students at Bahria University Medical and Dental College, Karachi, after approval by ERC-BUMDC. Data was collected by administering specially designed questionnaire, filled on one to one basis, after taking verbal consent. Analysis was done by using SPSS version 18.

Results: Out of total 104 students of 3rdyear MBBS at Bahria University Medical and Dental College, 96 students participated in the study. Response rate was 93%. The score on knowledge regarding basic concepts of research was found to be on the lower side (3.1+1.4 out of 10 questions).Overall, the students showed positive attitude toward research as majority of students agreed on positive statements toward research. Students highlighted many perceived barriers such as lack of time (92%), 'lack of rewarding and motivational system (86%) followed by inadequate funding and monetary system (79%) for undergraduate research.

Conclusion: This study showed low knowledge score coupled with a positive attitude toward research among undergraduate medical students. This could be related to various perceived barriers for undergraduate research identified by students. These barriers need to be addressed to ensure an improvement in the undergraduate medical research.

Key words: Knowledge, attitude, perceived barriers, research, undergraduate, medical students.

INTRODUCTION:

Research training has been recognized as an important component of medical education as the rapid expansion and progress in biomedical research is expected to transform medical care[1]. Researchers play key role in translating progress in basic science into clinical practice by defining physiological and pathological implications at the molecular level, guiding basic sciences research into clinically relevant directions and evaluating new therapies based on basic scientific discoveries.[2,3,4]. With incorporation of evidence based medicine in current health care arena, it is becoming substantial for health care providers to possess sound understanding of scientific principles and methods[5]. Experiencing research during undergraduate medical studies is associated with continuing professional growth and help in further career decisions. Involvement of medical students in research activities promises better understanding of research specific knowledge, teamwork, time management and critical appraisal. Studies have shown that early involvement in research promotes a tendency to continue the same in later stages of the medical profession[6]. Research experience as medical student does not lead to a career in academic medicine, However the experience can help improve student's skills in searching and critically appraising the medical literature and independent learning.[7,8, 9.]

Encouraging research and fostering the development of analytical skills among medical students is now a high priority[10,11.]

In USA, National Institute of Health (NIH) and the Doris Duke Clinical Research Fellowship (CRF) program are responsible for engaging students in medical research and sponsoring[13].

It is essential to inculcate critical thinking, reasoning skills and developing positive attitudes towards scientific research among medical students. Despite of the recognized importance of research at undergraduate level, studies have been conducted in the past to assess knowledge and attitude toward research among undergraduate medical students[14,15].

The objective of this study was thus to assess knowledge, attitude and perceived barriers toward research among undergraduate medical students at Bahria University Medical and Dental college.

Materials and Methods:

This cross sectional institution based study was conducted after approval by ERC-BUMDC at Bahria University Medical and Dental College, Karachi from April to June, 2014. The participants were 3rdyear MBBS students. The data was collected by using specially designed questionnaire, adapted from similar studies conducted previously.14,15,16 and pretested on a sample of 25 participants for validity and reliability. Modifications were then made to fulfill the objectives of our study. After the informed consent, respondents were given explanation about the purpose of the study. Questionnaire was filled on one to one basis by the investigator by taking oral interview and confidentiality was ensured. A questionnaire was used as the study tool. The details are:

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Questionnaire Development:

The questionnaire consisted of two sections:

Section One:

Section one contained the detailed demographic information of the students.

Demographic information:

Name, age in years, gender, academic year in medical college, residential address

Section Two:

Section two consisted of the following three components:

a. Assessment of knowledge toward research: Ten items (MCQ, one correct type, with four options a to d(a-d)

Correct response received a score of one, while wrong answer received a score of zero.

b. Assessment of attitude toward research: 12 items with a Likert scale ranging from strongly agree (1) to strongly disagree (5).

c. Assessment of perceived barriers toward research perceived by medical students: 10 items with Yes or No responses

Statistical Analysis:

Data was entered in Microsoft Excel and analysis was done by using SPSS version 20.

RESULTS:

Out of total 104 students of 3rdyear MBBS at Bahria University Medical and Dental College, 96 students participated in the study. Response rate was 93%. The detailed demographic characteristics of participants are shown in (Table 1).

Table: 1

Demographic characteristics of Participants
N=96

Variable	(%)
Mean Age:	21.5 years
Gender: Male Female	 33 (36%) 59 (64%)
Educational Level	Undergraduate
Academic Year	3rd Year M.B.B.S
Resident: Karachi Others	73 (79.3%) 19 (20.65%)

Table 2 depicts the number of correct responses of medical students of MCQs related to research. An average knowledge score of 3.1+ 1.4 toward research was obtained among 3rdyear MBBS students. Knowledge regarding basic concepts of research was found to be poor as only 40 students (42%) correctly defined the scientific hypothesis. The same was true for basic statistical concepts like statistical test (n= 15, 16%), relation between sample and representativeness (n=22, 23%), type of scale (n=10, 11%), and type of research study (n=20 21%).Knowledge regarding standard error and variable was (n=40,42% and n=33, 35 %) respectively. The respondents also showed a poor general awareness of concepts related to scientific paper (n=15, 16% and n= 23, 24%), and Medline (n=15, 16%) (Table2).

Table 2

Assessment of knowledge toward research among undergraduate medical students

Items	Correct responses (N=96)	N (%)
1. How would you define the scientific hypothesis? * An answer or solution to a question which has a capacity of verification or empirical demonstration.	40	42%
2. Statistical test used to compare observed data with data we would expect to obtain according to a specific hypothesis is called *Chi-square	15	16%
3. Representativeness is a key characteristic of : * Sample	22	23%
4. A scale from 1 to 5 (like grades on an examination is called: * Ordinal.	10	11%
5. The aspect of study which deals with distribution of disease is: *Descriptive studies	20	21%
6. What is the standard deviation of a sampling distribution called? *Standard error	40	42%
7. A variable whose value can be expressed numerically is called: *Quantitative variable	33	35%
8. The part of a scientific paper is: * Acknowledgment to persons who assisted you during the research	15	16%
9. MEDLINE is: *Medical database	15	16%
10. All listed rules apply to the process of writing an introduction section of a scientific paper Except: *Make it longer rather than shorter	23	24%
Average knowledge score: Mean± S.D3.1±1.4		

Table 3 shows the responses of medical students towards the attitude items on likert scale. For convenience, the results of agree and strongly agree, and disagree and strongly disagree were combined. Overall, the students showed positive attitude toward research as majority of students agreed on positive statements toward research of the respondents, 98% viewed research as the basis of progress in medical profession, 94 % believed that valid discoveries are impossible without scientifically sound research, 91% agreed that research is relevant to medical education and medical students can plan and conduct research. 89% of medical students thought that research promotes critical thinking while 84% agreed that research facilitates better understanding of health problems. However conducting research was found stressful by 89% of students. Although 67.7% of students agreed on

mandatory research projects during undergraduate medical studies, 89% did not agree that research should be an important criteria for acceptance to residency programs. Moreover. 99% of students did not agree on research being a long term career goal (Table 3).

Table 3

Assessment of attitude toward research among undergraduate medical students

Sr.# Items	Responses, N (N %) Agree	Neutral	Not agree
1. Research is the basis of progress in medical profession	94(98%)	2(2%)	0
2. Research facilitates better understanding of health problems	80(84%)	14(15%)	2(2%)
3. Research promotes critical thinking	85(89%)	5(6%)	6(7%)
4. Knowledge of research methodology is essential for obtaining accurate and objective data	60 (63%)	20(21%)	16(17%)
5. Conducting research is stressful	85(89%)	4(5%)	7(8%)
6. Research training should be a compulsory part of medical Curriculum	70(73%)	10(10.4%)	16(16.6%)
7. Research projects should be mandatory during undergraduate medical study	65(67.7%)	5(5.2%)	26(%)
8. Research experience should be an important criterion for acceptance in residency	10(11%)	6(7%)	80(84%)
9. Valid discoveries are impossible without Scientifically sound research	90(94%)	6(7%)	0%
10. Research is long term career goal	1(1%)	5(6%)	90(94%)
11. Research is relevant to medical education	87(91%)	3(4%)	6(7%)
12. Medical students can plan and conduct research	87(91%)	4(5%)	5(6%)

Students identified a number of perceived barriers toward scientific research. 92% students mentioned lack of time due to overburdened with educational activities, including exams. This was followed by management system for reward and motivation .86% and 79% medical students found inadequate funding and monetary as the third important barrier for conducting research (Table 4).

Table 4

Assessment of Perceived Barriers toward Research among Undergraduate Medical Students

Sr.# Items	YES Responses, N (%)	NO Responses N (%) N= (96)
1. You have adequate time apart from educational activities to pursue research at your institute	7 (8%)	89 (92%)
2. There is adequate training in research methodology at your institute.	77 (81%)	19 (19%)
3. Research supervisors are easily available at your institute	90 (94%)	6(6%)
4. Medical journals and other electronically relevant data base to research are easily accessible at your institute	88 (92%)	8(8%)
5. There is adequate facility in your institute to perform experimental studies e.g laboratory	60 (63%)	36(37%)
6. There is motivation or reward for doing research in your institute	13 (14%)	83(86%)
7. Your institute pays you back the allowances you spend in data collection (e.g visiting different institutes)	14 (15%)	82(85%)
8. Efficient faculty staff/mentors is available to deliver necessary knowledge and skills	77 (81%)	19(19%)
9. Institute gives you the opportunity to conduct your own research	87 (91%)	9(9%)
10. Adequate funding system is available for research at your institute	20 (21%)	76(79%)

DISCUSSION:

With increasing emphasis being placed upon evidence-based medicine and the application of scientific research into clinical practice, it is becoming increasingly important for medical professionals to possess sound understanding of scientific principles and methods, and to be skillful at acquisition and critical appraisal of new information.[17,18] The development of research capacity is imperative at the individual and institutional levels to attain a sustainable improvement in health research.[19]

Present study evaluated the knowledge, attitude and perceived barriers toward research among 3rd year MBBS students at Bahria University Medical and Dental College. The score regarding basic concepts toward research was found to be low that is 3.1+1.4 out of 10 questions. This was similar to the average score of knowledge reported by Hren (3.2 + 1.7 out of 8 questions) and Amin (3.6 +1.7 out of 10 questions) in undergraduate medical students.[20,21] A study from Pakistan by Khan showed mean score on a percentage scale of 49% for knowledge about research among undergraduate medical students14.However, the knowledge score reported by Vodopevic etal was 2.2 +1.2 out of 8 questions, as the participants were first year medical students [15]. In the present study, overall attitude of undergraduate medical students toward research was found to be positive as majority of students agreed on positive statements toward research.

The attitude toward research among undergraduate medical students reported by Hren and Amin were also positive. However, the study conducted by Siemens' etal in Canada showed negative attitude toward research among undergraduate medical students. The negative attitudes of medical students toward research have been found to serve as an obstacle to learning associated with poor performance in research. Lack of student conferences and research workshops are among the common reasons for such negative attitudes[22]. Khan etal reported mean attitude score of 53.7% on a percentage scale among undergraduate medical students[14].

The principal barriers toward research among undergraduate medical students identified in our study were shortage of time (92%), lack of reward or motivational system (86%) or lack of funding or monetary system (79%). While Hren found lack of time, incentives, research training and mentoring as major barriers toward research among undergraduate medical student[20]. Whereas Siemen also augmented lack of time as a significant barrier for pursuing research during medical school as only 31% of all respondents felt there was adequate allotted time for research endeavors. Furthermore, only 15% of respondents felt that there was sufficient training in research methodology in medical school, and only 25% agreed that there was adequate training in the critical appraisal of scientific literature. Another perceived barrier to participation in research was the difficulty in attaining a research supervisor; only 44% of respondents agreed that it was relatively easy to find a research mentor.[22] The barriers to participating in research among undergraduate medical students in study conducted by Alghamdi included lack of professional supervisors (84.7%), lack of training courses (88.8%), lack of time (72.3%) and lack of funding (54.1%).[23] The barriers mentioned by the medical students at the three Arab Universities by Amin etal were lack of time(62%), 'lack of rewarding and motivational system' (60%),deficiency of appropriate knowledge and necessary skills (55%) and inadequate mentoring to encourage and guide students in the field of scientific research (54.4%)[21]. Kasulkar also described the same barriers for undergraduate research in her study[24].

It is obvious however that some barriers like time constraints are universal and hence research activities are not a priority for undergraduate students, tend to be sidelined. The solution for this would be to attempt to seamlessly integrate research into the undergraduate medical curriculum. Formal research training during the undergraduate period correlates positively with active involvement with research in future professional settings.[25]

CONCLUSION:

In this study student's positive attitude score towards research was overwhelming, but coupled with a low knowledge score among undergraduate medical students requires learning activities that can enhance knowledge. This could be related to various perceived barriers for undergraduate research. These identified barriers need to be addressed to ensure an improvement in the undergraduate medical research experience.

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ORIGINAL ARTICLE

Pattern of Horizontal Squint Presentation in Pediatric Eye Department at Civil Hospital Karachi

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ABSTRACT

Objective: To estimate the magnitude and types of horizontal strabismus in children presenting in pediatric ophthalmic and orthoptic clinics.

Materials and Methods: A prospective analytical study was conducted on strabismic children presentingin theoutpatient departmentof pediatric ophthalmology and orthoptic clinics at Civil Hospital Karachi from 2008 to 2012. Details of patient was recorded in orthoptic performathat includedbiodata,history of presenting illness, wearing ofglasses, patching treatment , previous squint surgery and family history of strabismus.Orthoptic examination as visual acuity assessment with age appropriate tests was performed. Cover test, prism cover test, cycloplegicrefraction, hand mountedSlit lamp biomicroscopyand dilated fundus examination was also performed on each patient.

Results:A total of 1170 children presented in the pediatrics eye department. 1074 out of 1170 (91.79%) children were diagnosed to have horizontal strabismus. Majority 429(40%) of them were up to four years of age. 698(65%) children had horizontal esotropic strabismus while 376 (35%) had horizontal exotropic strabismus. 276 (25.69 %) esotropics had concomitant constant esotropia while 244(22.7%) exotropics had constant early onset exotropia.Statistical analysis was done by using SPSS version16

Conclusion: The magnitude of horizontal squint was found to be high in children.Esotropia with concomitant constant type was the most common type of strabismus followed byexotropia of constant early onset type.

Key Words: Strabismus, Horizontal squint, Esotropia , Exotropia

INTRODUCTION:

It is normal for a newborn's eye to wander or cross occasionally during the first few months of life. By the time a baby is 4 to 6 months old, the eyes usually straighten out. If one or both eyes continue to wander in, out, up, down or even intermittently then the condition is called strabismus. If detected and diagnosed early, strabismus is curable through a variety of safe and effective treatment options. Moreover it is important for kids to be treated early because waiting too long or overlooking treatment completely can lead to permanent vision loss.The medical name for squint is strabismus It is misalignment or wandering of one or both eyes either inward (called esotropia), outward (exotropia), up (hypertropia), or down (hypotropia). The condition can be constant or parents may only notice it occasionally; for instance, when their child is tired or looking at something very close up. Strabismus can be present at birth or develop in childhood. In most cases, the cause is unknown, although kids with a family history of strabismus are at an increased risk for it.Most kids are diagnosed between 1 and 4 years of age. Rarely, a child might develop strabismus for the first time after 6 years of age. If this happens, it's important to contact your doctor immediately, who will then refer your child to a pediatric ophthalmologist and possibly a neurologist to rule out any underlying conditions that may be causing the problem.[1]

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Healthy eyes move together to send similar images along the optic nerve to the brain for fusion into a single 3-dimensional picture at the brain-vision junction, or visual cortex. Toward this end, six muscles attached to the outside of each eye contract and relax to move the eyes in perfect synchronization, permitting fusion, or binocular vision, across a large area of the visual field. Strabismic eyes, on the other hand, do not move infusion, A muscle may pull too weakly or too strongly against its opposing muscle, creating an imbalance that causes one eye to drift from parallel alignment with its mate; more than one pair of muscles may be imbalanced. Since each eye fixates on an object at a different point in space, the images received by the brain are dissimilar. The brain is unable to fuse the dissimilar images, resulting in double vision, which can be very disturbing. Without treatment, strabismus can cause permanent vision problems. For example, if the child is not using one eye because it is misaligned, he or she can develop poor vision in that eye (called lazy eye or amblyopia). In order for the eyes to move fully, together and in a co-ordinated way, there has to be correct functioning at three levels in the visual system:

- The six extraocular muscles: these are the four rectus muscles and the two obliques. When the eyes are looking straight ahead, they are said to be in the primary position. The extraocular muscles enable them to be moved into one of the six so-called cardinal positions of gaze (ie directed to one side or the other, either looking out and up, straight out or out and down) or into one of the two midline vertical positions (looking directly up or directly down). Deviations from these positions of

gaze provide the basis for diagnosis of a squint.

• The three cranial nerves: all the movements of the eyes are enabled by the third cranial nerve other than lateral abduction (lateral rectus) which is generated by the sixth (abducent) cranial nerve and a downward, inward gaze (such as looking where to put your feet when going down a flight of steps - superior oblique) which is generated by the fourth (trochlear) cranial nerve. If strabismus is present when the patient looks with both eyes, the condition is called manifest strabismus or Heterotropia. This condition includes horizontal tropias exotropia and esotropia which are outward and inward horizontal deviations and hypertropia and hypotropia which are when one eye is set higher or lower than the other eye. Exotropia and esotropia are also known as divergent or convergent squint respectively.A deviation present only after binocular vision (viewing with both eyes open) has been interrupted by occlusion of one eye, is called latent strabismus or Heterophoria. This condition includes exophoria, esophoria, hyperphoria, and hypophoria.Strabismus is divided into paretic and non-paretic types. The paretic type is due to paralysis of one or several muscles that are responsible for natural eye movements. Non-paretic strabismus is not due to paralysis of these muscles.Paralytic strabismus has many causes including Oculomotor nerve palsy, Fourth nerve palsy, Congenital fourth nerve palsy, Sixth nerve palsy, Progressive external ophthalmoplegia, and Kearns-Sayre syndrome.Other causes of strabismus include Brown's syndrome, Duane syndrome, and monofixation syndrome.[2]

Pseudo-strabismus is a condition when a person's eye appears mis-aligned but with accurate examination no deviation is observed.

Strabismus can be caused when the cranial nerves III (oculomotor), IV (trochlear), or VI (abducens) have a lesion. A strabismus caused by a lesion in either of these nerves results in the lack of innervation to eye muscles and results in a change of eye position. A vulnerable to damage from brain swelling, as it runs between the clivus and brain stem.[3] The primary sign of strabismus is a visible misalignment of the eyes, with one eye turning in, out, up, down or at an oblique angle.Recent evidence indicates that a cause for infantile strabismus may lie with the input that is provided to the visual cortex. Esotropia (crossed eyes) needs to be treated early in life to prevent amblyopia.Less noticeable cases of small-angle strabismus are more likely to cause disruptive visual symptoms, especially if the strabismus is intermittent or alternating. In addition to headaches and eye strain, symptoms may include an inability to read comfortably, fatigue when reading and unstable or "jittery" vision. If small-angle strabismus is constant and unilateral, it can lead to significant amblyopia in the misaligned eye.

MATERIALS AND METHODS:

The study was conducted in Paediatric Ophthalmology and Orthoptic Units of Department of Ophthalmology, Civil Hospital, Dow University of Health Sciences (DUHS) Karachi from September 2008 to Jan 2012.All children that presented with visible manifest horizontal squint were included while those who had phorias, vertical and pseudo squint and not diagnosed as a manifest squint were excluded from the study. A detailed orthoptic proforma was filled out including the biodata,history of presenting illness, wearing of glasses, patching treatment, previous squint surgery and family history of strabismus.Orthoptic examination included

• Visual acuity assessment with age, appropriate tests. Lea gratings, Kay picture test, Lea symbols and ETDRS (logMAR) were used for different age groups.

• For younger age patients who did not cooperate with visual acuity test, density of amblyopia was assessed by CSM (central, steady and maintained) fixation of child uniocularly and binocularly.

• Squint assessment included cover/uncover/alternate cover tests with and without glasses for near and far, prism cover test for near, far and in gazes, krimsky test for younger children.

• Titmus test and Lang test were used to check stereopsis.

• Worth 4 dot test was performed in older children.

• Extra ocular movements were checked in all positions of gazes.

• Cycloplegic retinoscopy was performed in 10 years and under and non cycloplegic for older patients.Ophthalmic examination included, anterior segment examination using table mounted slit lamp or hand held slit lamp as per age of the child.

• Indirect ophthalmoscope was used for fundus examination of all patients.

Analysis was conducted by using the statistical package for social sciences (SPSS) version16 and results were expressed as mean and percentage.

RESULTS:

A total of 1170 children presented in the pediatrics eye department. 1074 out of 1170 (91.79%) children were diagnosed to have horizontal strabismus. Boys were 54 % and girls were 46 % (Figure 1). Majority 429(40%) of them were up to four years of age (Table 1). 698(65%) children had horizontal exotropic strabismus while 376 (35%) had horizontal exotropic strabismus (Table 2). 276 (25.69 %) exotropics had concomitant constant esotropia (figure 2) followed by infantile, accommodative, paralytic and sensory exotropia (Table 3). while 244 (22.7%) exotropics had constant early onset exotropia(figure 3) followed by intermittent, sensory and paralytic exotropia (Table 4)

Table1
Age Wise Distribution

AGE IN YEARS	PATIENTS	%
0-4	429	40
05-08	290	27
09-12	191	17.78
13-16	164	15.27
TOTAL	1074	100

Table 2
Types of Horizontal Strabismus

Groups	No. of patients	%
Esotropia	698	65
Exotropia	376	35
Total	1074	100

Table 3
Types of Esotropia (ET)

TYPES	PATIENTS	%
Concomitent Constant ET	276	25.69%
Infantile Esotropia ET	161	15%
Accomodative ET	144	13.4%
Paralytic ET	60	5.5%
Sensory ET	57	5.3%
Total	698	65%

Table 4
Types of Exotropia (XT)

TYPES	PATIENTS	%
Constant (early onset) XT	244	22.7%
Intermttent XT	93	8.65%
Sensory XT	25	2.32%
Paralytic XT	14	1.30%
Total	376	35%

Figure 1:
Gender Distribution

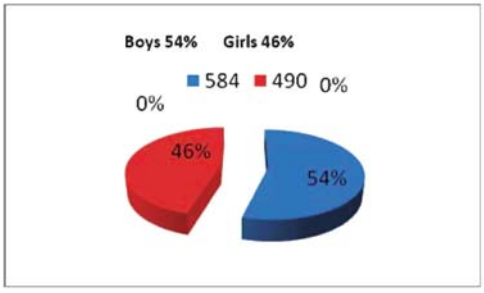

Figure 2
Concomitant Constant Esotropia

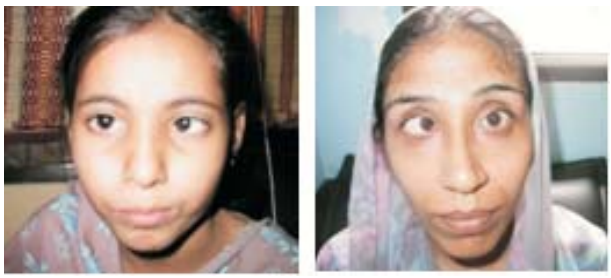

Figure 3
Constant exotropia

DISCUSSION:

Untreated strabismus leads to functional and psychological disturbances in the patient and his or her family, affecting the quality of vision and life. Children with strabismus suffer great psychosocial disadvantages and the same remains true even in adulthood.Thus appearance ofocular misalignment may interfere with social as well as psychological development with potentially serious effects for all patients with strabismus[4,5,6,7].

Squint and amblyopia are common conditions: about one in fifty children have squint[7] and up to 5% of the population have an amblyopic or lazy eye[8,9]. In view of their lifelong impact on visual function and physical appearance, with consequences for education, jobs and psychological wellbeing[10], good management offers substantial long-term benefits. Recent work favours early diagnosis and treatment, and there has been increasing effort to treat children as soon as possible. There is also renewed interest in the treatment of adults.

In our study total number of patients with horizontal strabismus was 1074.Eso-deviations698\1047(65%) were more frequent then exo-deviations 376/1074(35%).The esotropia werefound as a primary horizontal strabismus morbidity that included all types of esotropias.This is strongly supported by the study of Graham which documented that 60% patients had eso deviation and 20% have exo deviation. According to the study of Yekta the prevalence of exotropia and esotropia was 1.30 % and 0.59 %, respectively.

In current study constant esotropia(as the name implies,esotropia presents all the time, usually develop between the ages of 2 and 4 years) found as

276\1074(25%) Infantile esotropia found as 161\1074(15%) An (esotropia that is constant by 6 months of age,) this persentage compared with other study that shows the incidence of infantile esotropia estimates vary from 8% of childhood esotropia and 1 in 400 livebirths .

Some evidence suggests that early surgery is associated with a better binocular outcome.

In current study the magnitude of accommodative esotropia (An esotropia that is acquired, is either constant or intermittent.

144\1074 cases(13.4%) patients presented with accommodative esotropia.On other hand population based survey conducted by Louwagie described theincidence of accommodative esotropia(36.4%)higher than infantile esotropia (8%.)16.It could be due to our hospital based study and earlier presentation of infantile esotropia as compaired to accommodative esotropia. Out of all accommodative esotropia, partial accommodative esotropia(A group of esotropias that are helped, but not cured, with glasses for hypermetropia)were 37\1074 (3.4%) in comparison to the study of Louwagie17that showed partial accommodative esotropia incidence of 10%. The association between hypermetropia and the development of strabismus is well documented in studies[18,19,20]

The incidence of strabismus increases to 17.6%v/s 3-4% when a positive family history is elicited.[21] The risk of developing esotropia in patients with a positive family history is increased four-fold in the presence of hypermetropia.[22] Rosner showed that given superficial instruction, parents can detect 66-76% strabismus.[23]

In current study the sensory esotropia (A convergent strabismus resulting from visual deprivation or trauma in one eye that limits sensory fusion) found 57\1074 (5.3%), almost same with slightly higher percentage of paralytic esotropia (esotropia that occur due to paresis of any of extra ocular muscles) 60\1074 (5.5%) although the difference is not significant. This is justifiedby the study of Greenberg in which the incidence and types of childhood esotropia in a population of 385 children was sensory esotropia 6.5 %, paralytic esotropia 6.5 %.[24]

In our study exotropia was found to be the second most common formof horizontal strabismus that is less frequent than the esotropia.This is supported by international statistics where approximate ratio of esotropia ET to exotropia XT is 3:1. , However, the National Health Surveyof individuals 4?74 years of age found a higher prevalence of exotropia(2.1%) than esotropia (1.2%) in the U.S. population. This difference is probably related to the fact that the overall prevalence of strabismus in persons 55-75 years of age (in whom exotropia is more common) is 6.1%substantially greater than for very young children 1-3 years ofage (1.9%) or children and adults 4-54 years of age (3.3%).

In current study the constant or congenital or early onset exotropia (The term congenital exotropia is typically reserved for patients presenting in the first year of life with a large, constant angle.) was found as the major type of the exotropia 244\1074 (22.71%)

However Hunter[25] stated no published study provides a rationale for this restrictive definition. In his study he evaluated differences between infants, aged younger than 1 year, with constant exotropia versus intermittent exotropia at presentation He found that half of infantile exotropia patients may present with intermittent exotropia, with similar clinical outcomes regardless of presentation. A study conducted by Moore, who limited his subjects to healthy infants ,(congenital) exotropia was reported 0.003%. Another researcher has also limited their sample to healthy infants under age one and reported a 0.12% prevelance rate of congenital exotropia.[26],This is quite low then current study it could be because our study included all children presenting with constant or congenital exotropiaand was not restricted only to healthy subjects. Several authors believe that intermittent XT is more prevelent than constant exodeviations.[27,28,29] but our data doesnot correlate with these studies asin our study intermittent exotropia was 93\1074 (8.65%) lower than constant exotropia. This may be because constant exotropia creates more visible cosmetic disability than Intermittent XT therefore parents bring their childrento hospitals for treatment as early as possible. Sensory exotropia causes a blind or poorly seeing eye that may drift outward. In our study sensory exotropia was found to be present in 25\1074 subjects(2.32%) that is not high in comparison to other types of horizontal strabismus, same remain true also for paralytic exotropia that was 14\1074 (1.30%) only.

CONCLUSION:

The magnitude of horizontal squint was found to be high in children. Esotropia with concomitant constant type was the most common type of strabismus followed by exotropia of constant early onset type.

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ORIGINAL ARTICLE

Accuracy of High Resolution Computed Tomography in Pre-Operative Acquired Cholesteatoma

Faiz Ahmed Siddiqui[1], M Tamim Akhter[2], Zareen Naz[3]

ABSTRACT

Objective: To determine the accuracy of high resolution computed tomography (HRCT) for diagnosis of acquired cholesteatoma using histopathological finding as gold standard.

Materials and Methods: This cross section study of 61 patients, males and females with ages between 10- 35 years was carried out in the department of radiology, Dr Ziauddin Hospital Karachi, from November 2008 to April 2009. Patients clinically diagnosed as having cholesteotoma were referred for scanning. They were selected according to inclusion criteria. Patients were scanned using HRCT technique. Non dependent soft tissue density attenuation mass associated bony erosion in the middle ear/external ear was considered as radiological positive case of cholesteatoma while dependent soft tissue attenuation mass without bony erosion was considered radiologically negative case for Cholesteatoma. Keratinized stratified squamous epithelium with keratin debris and an underline sub-epithelial fibro connective tissue associated bone resorption in it were considered histopathologically positive case for cholesteatoma and without bony resorption were considered negative.

Results: Out of 61 patients of clinically diagnosed acquired cholesteatoma 37(60.7%) were males and 24(39.3%) were females. 34(55.5%) patients showed right sided and 27(44.2%) left side temporal bone involvement. Mean age of patients was 22.93 years (SD±8.29). Sensitivity of HRCT technique was 96.4 %, specificity of 80%, positive predictive value of 98.18% and negative predictive value of 67 %.

Conclusion: High resolution computed tomography (HRCT) technique is found to have accuracy for diagnosis of pre-operative acquired cholesteatoma using histopathological finding as gold standard.

Key Words: Temporal Bone, Acquired Cholesteatoma, Diagnosis, Accuracy, Computed Tomography.

INTRODUCTION:

Cholesteatoma is a cystic structure lined by keratinized type of stratified squamous epithelium resting on fibrous stroma of variable thickness in which crystals of cholesterol, desquamated tissue debris, keratin and bacteria are embedded[1]. The expanding cystic cavity that may involve the mastoid and ossicles, erodes surrounding bone. Cholesteatoma are histologically benign, though biologically invasive lesions that arise as mentioned from the migration of squamous epithelium of the ear. Cholesteatoma can form in the middle ear in three ways[2]. A perforation of the eardrum occurring because of a chronic infection or direct trauma can lead to a cholesteatoma. The skin over the outer surface of the eardrum can start to grow through the perforation and into the middle ear. Some patients are born with small remnants of skin which become entrapped within the middle ear (congenital cholesteatoma) or petrous apex (Petrous apex epidermoid).These are classified as acquired or congenital respectively[3]. A separate and unusual type is the canal cholesteatoma. Congenital cholesteatoma is usually diagnosed in children of pre-school age and may arise in the middle ear or within the tympanic membrane[4]. It present as a white or pearly mass medial to the anterior-superior quadrant of an intact tympanic membrane[5]. Acquired cholesteatoma is usually diagnosed in older children and adults with a previous history of middle ear disease[6]. Acquired cholesteatoma are subdivided in to primary acquired and secondary acquired cholesteatoma[7]. Several pathologic mechanisms have been proposed to explain the formation of acquired cholesteatoma, with no single process being accepted as the mechanism for the development of such cases. The common factor of all acquired cholesteatoma is that the keratinizing squamous epithelium has grown beyond its normal limits[8]. Cholesteatoma if left undiagnosed or untreated can cause serious complications. Erosion of the ossicles or bones behind the ear drum can lead to a conductive hearing loss. The bones over the facial nerve can be destroyed and a facial paralysis can result. The inner ear is composed of bony labyrinth which can also be partially destroyed. This can lead to sensori-neural hearing loss and dizziness. The infection can also spread into the veins carrying blood from the brain to the heart. The infection can also spread to the covering of the brain and cause meningitis[9]. In rare circumstances, brain abscess can result[10]. Cholesteatoma is usually diagnosed in adults with a previous history of middle ear disease at least 8-10 weeks duration. Interpretation of finding always depends on the experience of the physician. The false-negative rate with plain film is high[11]. Computed Tomography of the temporal bone with high spatial resolution is an established standard examination technique for cholesteatoma[12]. Diagnostic quality images on CT are obtained in two different planes coronal and transverse acquisition[13]. CT offers high resolution images with a section thickness of 2.0mm, which allow for good visualization of the bony anatomy, ossicular and inner anatomy. On CT good

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contrast is demonstrated for bone, soft tissue and air[14]. On CT acquired cholesteatoma presents as a non-dependant soft tissue attenuation mass associated with bony erosion of adjacent structures in the middle or external ear[15]. CT scanning is used to establish the surgical procedures needed in each patient of cholesteatoma[16]. CT imaging of Pre-operative radiological evaluation provide clinically pertinent information from the images obtained[17]. The aim of this study is to determine the value of non-invasive high resolution computed tomography (HRCT) technique in the diagnosis of acquired cholesteatoma. There is a paucity of local data on this topic, which prompted the need to conduct this study.

Materials and Methods:

Clinically diagnosed cases of acquired cholesteatoma that is patients presenting with ear discharge, pain and conductive deafness of 6 months to 1 year aged 10-35 years, either gender were included in this study. History of trauma to middle ear, post surgical patients and patients who were previously diagnosed to have congenital anomaly were excluded. Patients were examined using HRCT technique. Non dependent soft tissue density attenuation mass associated bony erosion in the middle / external ear was considered as radiologically positive case for cholesteatoma. Dependent soft tissue attenuation mass without bony erosion was considered radiologically negative case for Cholesteatoma. Keratinized stratified squamous epithelium with keratin debris and an underline sub-epithelial fibro connective tissue associated bone resorption in it were considered histopathologically positive case for cholesteatoma and without bony resorption were considered negative. The interpretation of the images was done by trained radiologist. The findings were entered on specially designed performa.

RESULTS:

Total 61 patients presenting with history of ear discharge, pain, and conductive deafness of 6 months to 1 year duration were referred for HRCT scan of the temporal bone. Clinically they were suspected cases of acquired cholesteatoma. There age ranged from 10-35 years with mean age of 22.93years + 8.29 S.D. Clinical findings in our series showed that middle ear cholesteatoma was more common in male patients 37 cases (60.7%), 24 patients (39.3%) were female. (Table1).

Table 1

Gender Distribution

	Frequency	Percent
Male	37	60.7
Female	24	39.3
Total	61	100.0

34 (55.7%) patients showed right sided temporal bone involvement, 27 (44.2%) left sided involvement. Acquired cholesteatoma are characterized on CT by the presence of a non dependent, homogenous soft tissue mass with a focal area of bone destruction. This soft tissue density had mass like features were homogenous, polypoidal, non-dependent and expansile. The mass sub totally occupied the middle ear antrum in 13 cases. Soft tissue densities had totally filled the whole middle ear cavity in 27 cases, involving middle and external ear in 15 cases. Sensitivity of HRCT technique of temporal bone for cholesteatoma was 96.4%, specificity 80%. Positive predictive value for cholesteatoma detection on HRCT was 98.18% and negative predictive value 67%. 2 patients were false negative, 1 had granulation tissue and 1 had polyp, they had associated cholesteatoma. 01 patient who was false positive had effusion. Four patients were true negative on radiology and histopathology. (Table 2).They had chronic suppurative otitis media without cholesteatoma mass.

Table 2

Patient Distribution Histopathology

	Disease Positive (+VE)	Disease Negative (-VE	
HRCT+ve	TP a 54	FP b 1	
-ve	FN c 2	TN d 4	
	56	5	61

TP (True positive), FP (False positive)
FN (False negative), TN (True negative)

$$\text{Sensitivity} = \frac{a}{a+c} \times 100 = 96.4\%$$

$$\text{Specificity} = \frac{d}{b+d} \times 100 = 80\%$$

$$\text{PPV} = \frac{TP}{TP+FP} \times 100 = 98.78\%$$

$$\text{NPV} = \frac{TN}{FN+TN} \times 100 = 67\%$$

DISCUSSION:

The diagnosis of cholesteatoma is usually made on examination of ear by ENT specialist[18]. In case in which the diagnosis is in doubt, computerized tomography can be employed. Cholesteatoma can be accurately diagnosed by the HRCT scan in vast majority of cases. Mafee[19] has reported in his series of 48 patients with cholesteatoma that 46 of them were diagnosed correctly with the pre-operative CT scan. In our case 54 out of 61 patients were correctly diagnosed. Our sensitivity of 96.4% and specificity of 80% correlated with O`Reilly et.al[20] and positive predictive value of 98.18% and negative

predictive value of 67%. Acquired cholesteatoma is most commonly encountered in the middle ear cavity. It is a rear disease entity, accounting for 0.1 to 0.5% of new otolaryngology patients in external auditory canal[21]. A soft tissue seen in the external auditory canal with adjacent bone erosion on HRCT is typical finding of external auditory canal cholesteatoma. With use of high resolution CT scan, Heilburn[22] reported that 7 of their 13 patients with external auditory canal showed a soft tissue mass with adjacent bone erosion and intramural bone fragments. In our case 6 patients out of 61 were found to have external auditory canal cholesteatoma. Years of experience with HRCT have clearly demonstrated its superiority for the evaluation of temporal bone, particularly utilizing the thin section, high resolution techniques. HRCT provides a more precise definition of the anatomic extent of the disease of the middle ear and the relationship of these cholesteatoma masses to the contiguous structures. High resolution CT (HRCT) with bone window settings is considered the method of choice for examination of the middle ear structures. It provides excellent contrast between osseous structures, ear and soft tissues, together with a high spatial resolution. In most cases, HRCT can differentiate between inflammatory changes, cholesteatoma and tumor. The high spatial resolution of HRCT technique allows demonstration of subtle osseous details and provides good identification of erosion of the ossicles, delineation of the tegmen and bony labyrinth and enables reliable evaluation of the tympanic segment of facial nerve. Therefore, HRCT remains the primary examination tool for the evaluation of suspected cholesteatoma and, more importantly, its extension. After clinical examination, otoscopy and diagnosis of cholesteatoma, CT scan determines its extent by revealing a soft tissue mass and bone erosion, with 80% specificity[23]. In our case specificity was 80%. This study was conducted on a single-detector row CT with high spatial resolution. The technique for examination of temporal bone cholesteatoma is axial and coronal planes. We have also followed the same technique. (Figure1 and 2).

Figure 1
Coronal views temporal bone

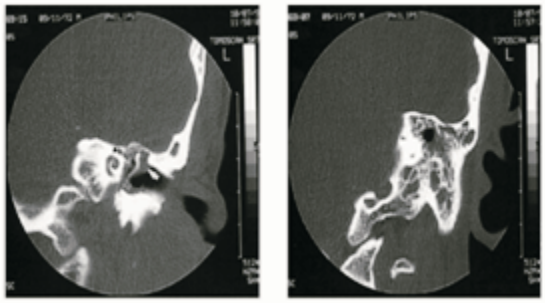
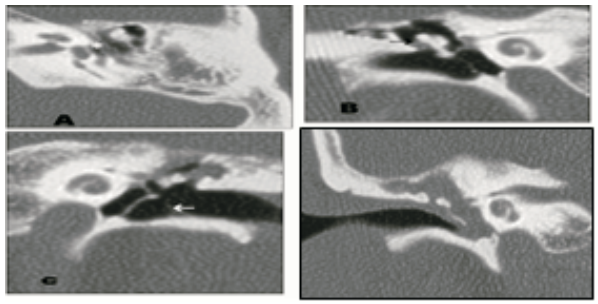


Figure 2
Cholesteatoma



However in future with the addition of multi-detector row CT there will be much more improvement in detection of cholesteatoma and its complications using HRCT technique[24]. Also the role of HRCT early in the course of disease can potentially reduce the risks of late complications associated with under diagnosed cholesteatoma. CT imaging has proven to be an accurate method of depicting the characteristic finding of middle and external ear cholesteatoma, including the extent and complications[25].

Thus close collaboration between radiologist and an otologist sufficiently flexible to tailor surgical management according to radiological finding is the ideal. Advantages of scanning will then include: (1) A visual aid to pre-operatives counseling of the patient, (2) Avoidance of unnecessary surgery owing to its high degree of sensitivity / specificity to middle ear disease.

(3) A prediction of the anatomy, ease of surgical access and extent of disease all of which guide surgical approach, (4) Anticipation of complications of chronic suppurative otitis media[26].

CONCLUSION:

High resolution computed tomography (HRCT) technique is found to have accuracy for diagnosis of pre-operative acquired cholesteatoma using histopathological finding as gold standard.

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MEDICAL EDUCATION

Adult Learning Principles and its Application

Nighat Huda

ABSTRACT:
Andragogy, a Greek word refers to adult learning. In late1960s Malcom Knowles work in adult education spread in North America. Knowles hypothesized a set of assumptions on the characteristics of adult learners. The assumptions are that: adults are independent and self-directed learners, bring rich experience to the educational setting, enter educational settings with readiness to learn, adults are problem-centered in their learning, and best motivated by internal factors. Further research on andragogy led to reform in all forms of adult education including health profession education and distance learning.

Key words: andragogy, pedagogy, assumptions, self-directed learning, problem-based learning.

INTRODUCTION:

Globally, the perception and understanding of 'andragogy' varies for different people. Andragogy, is a Greek word that refers to man learning while pedagogy (Greek word as well) to child-learning derived from.[1,2] In 1833, a German school teacher Alexander Kapp used the word 'andragogy' referring to education at the man's age.2 The later part of the twentieth century witnessed development in andragogy that has led to reform in all forms of adult education including health profession education and distance learning. In the late 1960s, in North America, Malcom Knowles, first began work in adult education.[2,3] Knowles work emphasized that teachers' priority should be students' interest while planning instructional activities with supportive learning resources as mature students' desire learning to be relevant to their future practice with guided interactions based on mutual respect[2,3,4]. This was in contrast to traditional role of teachers as 'knowledge providers' who provided knowledge according to their belief of importance.

Although Knowles did not claim to have research evidence, he hypothesized a set of assumptions on the characteristics of adult learners which included that: adults are independent and self-directed learners, adult learners bring rich experience to the educational setting, adults enter educational settings with readiness to learn, adults are problem-centered in their learning, and best motivated by internal factors.[3,4] These assumptions have become educators' guidelines for content development and adapt to best teaching learning and assessment practices.

First, adult learners assume responsibility of their own learning in a supportive and encouraging environment. As one matures, self-directed learning takes precedent over teacher dependent learning. Knowles describes self-directed learning (SDL) as a process in which individuals take control of their own learning that is, from setting goals, to seeking different resources, implementing a plan to achieve goals and evaluate the learning experiences without the help from others[3,4]. Mature learners will get more out of the experience if they work autonomously in contrast to younger learners who need more guidance through the learning process.

In seventies, the initiation of Problem-based learning (PBL) at McMaster University in its new medical program is considered a major development on increased relevance of medical curricula and student-centered learning. In small PBL groups, students' activate prior knowledge on carefully designed problems, derive learning goals and through independent study find answers and build new knowledge on existing knowledge. The facilitator role is that of an active listener who guides mostly through thought provoking questions. The PBL process allows students to use problem solving techniques, self-directed learning strategies, team participation skills, and disciplinary knowledge[6-10]. Traditionally, students have been 'spoon fed' with knowledge through lectures and notes. The challenge remains for teachers to create learning experiences that offer minimal teacher-directed instruction.

In addition to PBL, medical schools worldwide have adapted learning activities such as simulated learning, practicing skills in skills laboratory, e-learning, self-study or group assignments that involve minimal instructors' intervention[15]. Similarly, small group discussion rooms, learning resource center with digital library, internet facilities, skills laboratory, and multi-discipline laboratory take precedent over classical lecture halls, library or discipline based practical sessions in laboratory. In clinical training, patients' are extremely important learning resource. A follow up discussion on patient cases with active students' participation is more meaningful and beneficial to students in real practice settings. Clinical educators' responsibility should be to direct students toward further research on patient interaction, examination, investigations or treatment.[11,12,14] Adult learners have an urge to find out what they can perform with proficiency or what requires more practice and similarly with knowledge acquisition as well .Constructive feedback integrated into the learning process will help

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students to become responsible for improvement of their own learning[11,12,13].

One assumption is on the fact that adult learners have accumulated a wealth of life experiences with a wider knowledge base and if utilized can become an increasing resource for learning[2,4,8]. In other words, students are not 'blank slates' when they enter professional education and their previous experiences if attached with new ideas and skills will strengthen learning. Moreover, adult learners have an urge to share what they have learned and can provide examples that may benefit the class. Adults associate experience to self-identity and may see it as a rejection of them if experience is not utilized in a training experience.[2,5]

Prior to formal learning activities, a survey will help determine adult learners' knowledge limitations, and their education levels. Students' existing knowledge and past life experiences, will enable teachers to create stimulating and engaging learning.[8,9] For medical students, training in actual settings, case discussions, ward rounds are few examples where individual learners will be able to share the information, solve problems, reflect and apply clinical reasoning process[12]. Such experiences will help students toward deeper and permanent learning. Students mostly adapt to superficial learning or rote learning when they fail to build new knowledge on their previous experiences.

Thirdly, adult learners demonstrate an eagerness to learn and further expand knowledge and develop skills in the chosen profession or topic of interest. Adult learners are goal-oriented as they recognize the value of new knowledge for future career.[2,5,8] Moreover, adults are inclined towards application of new knowledge and skills that have immediate application in contrast to child learning who accept that the knowledge acquired may not be of immediate use. Therefore, teachers can motivate adult learners with relevant course, module and meaningful learning activity, or assessment[14]. Knowles assumed that learners needed to feel a necessity to learn and that identifying one's own learning needs was an essential part of self- directed learning.[4,5]

Fourthly, adults' prefer task or problem orientation to that of subject centerdness. Medical students will find the subject matter interesting if the emphasis is on the relevance that an adult learner will regularly encounter in real life context.[2,5,13] Medical educators' have integrated meaningful and engaging activities that excite students who can see the relationship with common health issues and practices.[12,15] For example, case studies, patients' in real settings presenting problems with diarrhea or dental cavities will motivate students to clarify concepts, learn with understanding to solve problems, practice necessary skills on patients with enthusiasm and develop team working and communication skills. Another likely example could be a community survey to find out health seeking behavior of a defined population and interventions that can improve quality of life. For motivating adult learners, it is important for educators to relate learning process with tasks in real practice situation, otherwise adults will not see any usefulness for acquiring the new knowledge or skills.[9,10,11,15]

The fifth assumption focuses on the key role of motivation plays in adult learners who are influenced by both extrinsic and intrinsic motivators. Knowles publications emphasize that motivation to learn is internal for adults. Intrinsic motivators such as the need for recognition, self-esteem, achievement, and improved quality of life have much greater influence on adults in contrast to extrinsic motivators that focus on high salary, promotion, increments or bonuses attract adults[2,8] Adults may not be motivated if forced to learn; however learning experiences built around the concept of intrinsic motivators will find adults response with enthusiasm to such learning activities. In traditional medical education, patients' exposure begins in third year and students find themselves confined to lecture halls and basic science practical sessions. In contrast, patient exposure has recently been introduced in first year to motivate students who can develop concepts and see the relationship to real life practice. Also, clinical experiences based on active learning where students repeatedly practice skills by themselves, and interact with patients that focus more on hands-on problem solving experiences benefit learners in actual practice settings[11,13]. The onus lies on curriculum planners to design a curriculum that is relevant to students' needs, evolve active students' participation, encourage independent learning that help students' to reflect and assess their performance.

Together, these assumptions suggest that a change of mindset of academic leaders, faculty, and students is critical to implement adult learning principles. The foremost step will be to have a willing leadership along with a like-minded team of faculty who implement faculty development activities, and develop learning resources to enhance self-directed learning activities.

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COMMENTARY

Chemically Induced Mice Cough Model

Riffat Farooqui

ABSTRACT:
Cough is the most common respiratory symptom that has been experienced by every human. Both the chemically and mechanically sensitive airway nerves take part in mediating the cough reflex and establishing synapses in the brainstem's caudal two-thirds of the nucleus tractus solitaries. The sensation of an "urge to cough" is ostensibly associated with activation of broncho- pulmonary C-fibers. These C-fiber nerves become directly activated, 'sensitized' or 'hyper-activated' by chemicals such as capsaicin, bradykinin, adenosine, prostaglandin type E-2 (PGE2), citric acid, hypertonic saline solution, Sulfur dioxide (SO2). Chemically induced cough facilitates the quantification of cough and the assessment of antitussive effects of specific therapeutic agents. Sulphur dioxide gas has been used to elicit cough in various experimental animals like cats, rats and mice.
Key Words: Cough, Cough model, Mice, Tussive, Sulfur dioxide gas.

INTRODUCTION:

Cough can be defined as a forced expulsive maneuver usually against a closed glottis and is associated with a characteristic sound.[1] It can be measured subjectively using symptom scores and specific quality-of-life measures, and objectively by measuring cough numbers and intensity, and by assessing the cough response to capsaicin, citric acid and other chemicals.[2] Cough often presents as the first and most persistent symptom of many respiratory diseases and some non-respiratory disorders, but can also be idiopathic, and is a common respiratory complaint for which medical attention is sought.[3] In the modern world of science animal models specially the laboratory animal models play a vital role in the drug discovery process. They are also employed for testing various new properties and effects of existing and old drugs. Enhanced coughing can be produced in a variety of animal models, including guinea pig, cat, dog and pig etc. Typically, airway inflammation has been produced by sensitization, exposure to cigarette smoke, sulphur dioxide or angiotensin-converting enzyme inhibitors in different animal models.[4]

Cough can be induced in experimental animals by the following[5]

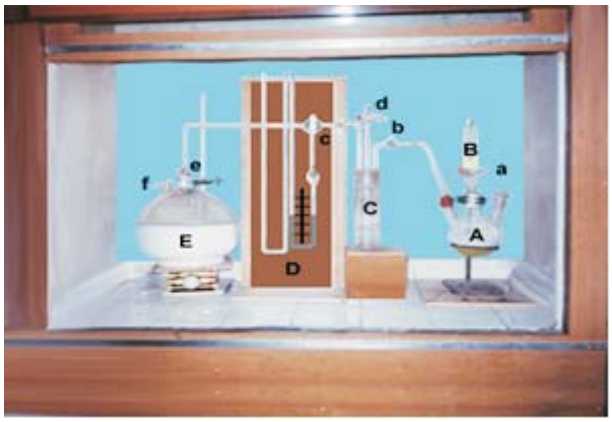
- Chemical stimulation of sensory nerve
- Mechanical stimulation of sensory nerve
- Electrical stimulation of sensory nerve

The chemical induced cough facilitates the quantification of cough and the assessment of antitussive effects of specific therapy.[6] Sulphur dioxide gas has been used to elicit cough in various experimental animals, e.g., in cats[7] , in rats[8], in mice[9] etc. In animal models, there is activation of interneuron pathways located between the medullary nucleus tractus solitarius and the nucleus ambiguus during coughing. Stimulation of the superior laryngeal nerve can evoke different laryngeal adductor muscle responses including coughing, swallowing, gagging, laryngeal spasms, bronchoconstriction, apnea, and retching. The type of the evoked reflex response depends on the considerations of the stimulus used, [10, 11] and is utilized in conducting various types of research projects.

In 2007 the author employed mice cough model developed by Miyagoshi & colleagues (1986) to test activity of an antitussive drug.[9]

Cough Model Developed By Miyagoshi & Colleagues: Apparatus and Solutions: A is 500 ml three-necked flask containing aqueous saturated sodium hydrogen sulfite solution. By opening the cock of a dropping funnel B, conc. sulfuric acid is introduced to generate sulfur dioxide gas. Sulfur dioxide gas is filled previously in A and C, a gas reservoir, and by opening cocks c and b, pressure in the gas C is elevated which is recorded by water manometer D. Then the cock b is closed and the cock d is opened slightly until the pressure in D (11 mm I.D.) reaches to 75 mm H2O, when the cock d is closed (Figure 1).

Figure 1
Apparatus used for antitussive activity



A: Three-necked round bottom flask, containing 39% NaHSO3 solution, B: dropping funnel having conc. H2SO4, C: Gas reservoir, D: water manometer, E: Desiccator.

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Method/ Technique:

Testing material was orally administered to mice. Initially the cough responses were observed at zero (0) minute by placing the animals in the desiccator E. The cock C, F and E were opened in order, and when the pressure in D became zero mm H2O, the cock E and F were closed immediately. A certain amount of sulfur dioxide was introduced in the desiccator E by these operations. After one minute of introducing sulfur dioxide gas, the mice were taken out of the desiccator and frequency of cough was observed for 5 minutes in an up-ended filter funnel with a stethoscope at the tip, in which the mouse was confined. In the same fashion the frequency of cough was observed at 30 and 60 minutes respectively. The effects of long-term exposure to sulfur dioxide can be studied only in experimental animals. At concentrations in excess of 28.6 mg/m3 (10 ppm), prolonged exposure has been shown to produce damage to the epithelium of the airways. This may be followed by epithelial hyperplasia, a dose-related increase in goblet cells and hypertrophy of the submucosal glands. These changes are similar to those seen in chronic bronchitis in humans. Prolonged exposure of rats to sulfur dioxide has also been used to produce a chronic cough model for testing antitussive agents.[12]

Search words of cough, cough model, mice, tussive and sulfur dioxide gas from 1986 to 2014 using google search engine revealed use of 5 chemicals with 5 different methods for inducing cough in animal models (Table.1)[13,14,15,16,17,18.]

Table 1

S.N	Chemical	Animal Used	Author	Year of Study
1	Adenosine and Capsaicin	Mice	Ryan P. Vaughan	2006
2	Citric acid and Capsaicin	Guinea pig	Sum Yee Leung	2007
3	Sulphur dioxide (SO2)	Mice	Gupta YK	2009
4	Acrolein, Acetic acid & Cyclohexanone	Mice	Daniel N. Willis	2011
5	Sulphur dioxide (SO2)	Mice	Rizwan ul Haq	2013
6	Sulphur dioxide (SO2)	Mice	Riffat Farooqui	2014

Most of these studies have utilized mice to make cough model. It is evident that sulphur dioxide (SO_2) was used alone by three researchers (including author) in 2009, 2013 and 2014 respectively for the investigation of antitussive materials whereas other chemicals were used by researchers in combinations. It is said that mice demonstrate an increased cough response to sulphur dioxide gas, this explains development of exacerbated cough following sulphur dioxide gas exposure in this laboratory animal. Mice cough model is thus a convenient method for research studies and estimation of antitussive effects of agents.

Sulphur dioxide gas induced murine cough model, developed by Miyagoshi and colleagues in 1986 is a simple, reliable and reproducible method that can be used to investigate antitussive efficacy of testing material. Enhancing the literature search in terms of time frame, number of search engines and comparing various available methods for inducing cough model to determine the most simple, reliable and reproducible method, are open avenues for future research.

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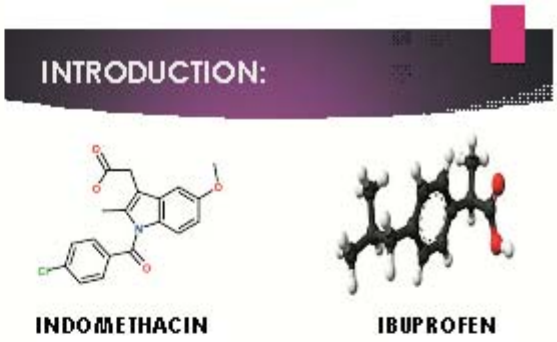
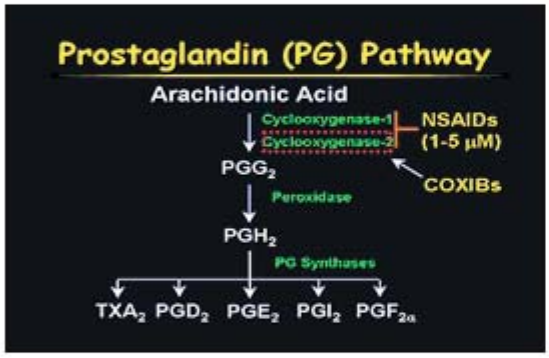
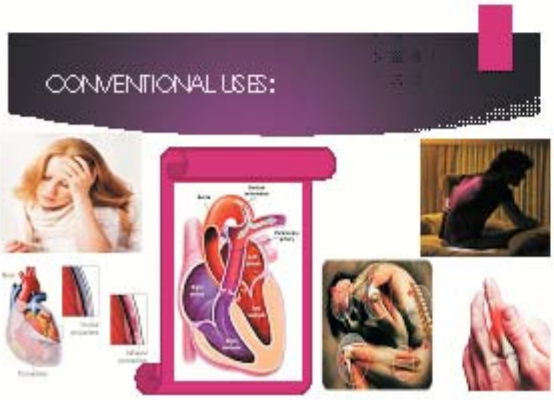
STUDENTS CORNER

Student`s Drug Updates Session-National Pharmacology Conference 2014, Pharmacological Trends 21st Century. Slides of winner # 1.

Safia Anwar







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Date of Access: May 24, 2014

PATENT DUCTUS ARTERIOSUS ?

- Congenital Heart disorder
- Small opening or pathway between the pulmonary and aortic

INDOMETHACIN VS IBUPROFEN

EFFECTS	INDOMETHACN	IBUPROFEN
Non COX Pathway	Yes	No
GI PERFORATIONS	Yes	No
NECROTIZING ENTEROCOLITIS	Yes	Slight
RENAL FAILURE	Yes	No

INDOMETHACIN VS IBUPROFEN: MOA

- Non selective COX Inhibitor (particularly COX-1)
- Inhibits other Non-COX pathways(inhibits cerebral, renal and mesenteric blood flow) which adds to its deleterious effects

- Reversible Non-selective COX inhibitor
- **No effect on Non-COX pathways** hence safer

CONCLUSION:

IBUPROFEN is a better drug in comparison to INDOMETHACIN for treating PDA and is also a more safer drug

CASE REPORT

Extensive Hypopharyngealcarcinoma Treated by Total Laryngo-Pharyngo-Esophagectomy with Gastric Pull-Up at PNS Shifa Hospital

Sana Muhammad Sadiq[1], Iqbal Hussain Udaipurwala[2],
Amer Sabih Hydri[3], Shahzad Hanif Mehr[4]

ABSTRACT:
Reconstruction of the defect created after total laryngo-pharyngo-esophagectomy has been one of the challenging task for the head and neck surgeons. There is a lot of debate among the different workers regarding the best method for such reconstruction. Many believe that gastric pull up is still one of the best option in such cases. We are presenting a case of 50 years old lady with extensive squamous cell carcinoma of the hypopharynx which was also involving the larynx and the cervical esophagus. Total laryngo-pharyngo-esophagectomy was done as a primary treatment. For reconstruction of the defect gastric pull up operation was done. Post-operative recovery was uneventful with no major complication. Adjuvant radiation therapy was also given post-operatively. During the follow up period of 6 months, patient was completely alright with almost normal oral feeding and no recurrence of the disease.

Key words: Hypopharyngeal carcinoma, Pharyngo-laryngectomy, Stomach pull-up, Esophagectomy.

INTRODUCTION:

Surgical treatment of advanced cancer of the hypopharynx remains a dismal disease that poses a therapeutic challenge to the treating physician, with an extremely high incidence of morbidity and distant metastasis. Hypopharynx extends from 4th to 6th cervical vertebrae and is interposed between the oropharynx and the upper end of esophagus with the larynx located anteriorly. It includes posterior pharyngeal wall, pyriform fossae and the post cricoid area. The incidence of hypopharyngeal cancer is approximately 1 in 80,000, with a poor prognosis having 5 year survival rate only up to 22%[1].

Carcinoma of the hypopharynx involves unavoidable impact on deglutition, respiration and phonation functions as the anatomical structure is located at the crossing point between airway and digestive tract[2]. The degree of impairment is directly proportional to the extent of resection. Ablative surgery for stage III and IV malignancy usually result in complex defects with loss of function and continuity in the upper digestive tract and soft tissue deficiency. The method used for reconstruction should establish the integrity of the digestive tract and cover the cervical defect with healthy and well vascularized tissue[3,4]. We are presenting a case of extensive carcinoma of the hypopharynx, also involving the larynx and cervical esophagus which was treated by total laryngo-pharyngo esophagectomy with reconstruction by gastric pull-up operation.

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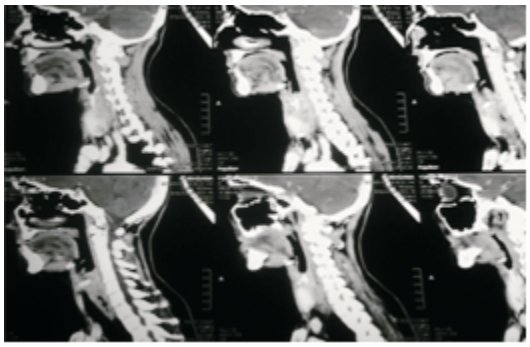
CASE REPORT:

A 50 year old lady, resident of urban area of Sindh, presented through outpatient clinic in P.N.S Shifa Hospital, Karachi, in March 2014 with the complaint of dysphagia for last six months. It was progressive in nature, initially for liquids and later on progressed for solid food as well. She also complained of pain in throat which radiated to ear as well. She was progressively losing weight which was assessed by family members by her loose clothes. According to the patient her mother also died with same complaints but she could not provide any documented evidence. She belonged to a lower socioeconomic group. On general physical examination she was found to be anemic.

On indirect laryngoscopy, Chavellier Jackson sign was positive i.e. pooling of saliva in both the pyriform fossae. Upon neck examination laryngeal crepitus was absent (Trotter's sign) but the cervical lymph nodes were not palpable. On fiberoptic direct laryngoscopy, extensive growth was seen at the apex of left pyriform fossa extending medially to involve posterior pharyngeal wall and post-cricoid area. Lower limit was not possible to assess on FODL. Vocal cord mobility was impaired on both the sides. CT scan with contrast was done which showed extensive growth going downwards to involve the upper part of the esophagus as well (Figure 1). Pan-endoscopy under general anesthesia was done, biopsy taken for histopathology which showed poorly differentiated squamous cell carcinoma.

Figure 1

CT scan with contrast of the neck (Sagittal view) showing extensive growth involving the hypopharynx, larynx and cervical esophagus



Case was discussed in detail with the patient and her family members and after taking informed and written consent, she was planned for total laryngo-pharyngo-esophagectomy with gastric pull-up operation. Case was also discussed with the multidisciplinary team, nutritional status was built up by guidance of dietician and anemia was corrected by blood transfusion.

Two surgical teams, one of ENT surgeons and one of general surgeon were involved. Total laryngo-pharyngo-esophagectomy with stomach pull up was done (Figure 2a, 2b and 2c).

Figure 2a

Per-operative photograph of the neck after removal of the larynx, hypopharynx and the esophagus

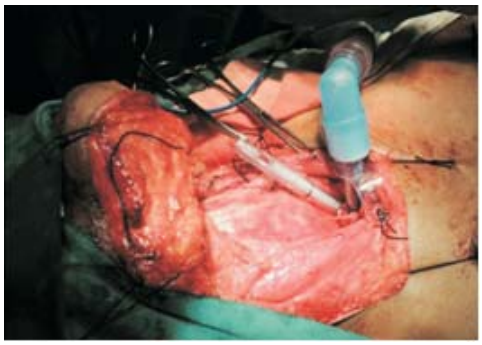


Figure 2b

Surgical specimen of the whole larynx, hypopharynx and esophagus after removal.

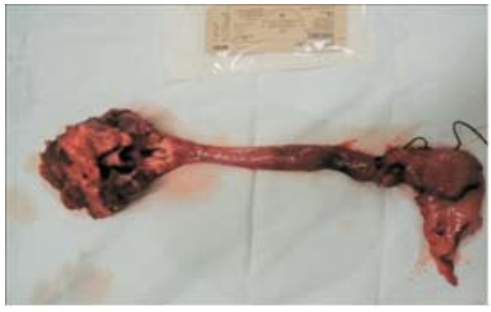
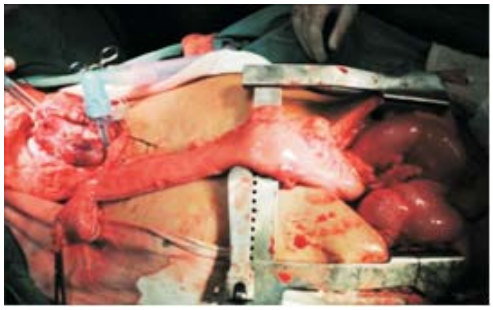


Figure 2c

Per-operative photograph of the patient showing the stomach ready for anastomosis in the neck



A gastro-jejunostomy tube was inserted at the time of harvest to allow for early postoperative feeding and simultaneous gastric decompression. Later on patient was sent for post-operative adjuvant radiation therapy. Post-operative follow-up was done regularly and till date patient is doing well. There was no recurrence of the disease during this period and patient is taking normal oral feeding.

DISCUSSION:

Tumors of the hypopharynx are usually diagnosed at an advanced stage and are associated with a poor prognosis5.Squamous cell carcinoma of the hypopharynx has a particular trait of invasiveness through the sub-mucosa to induce distant lesions known as skip lesions[6]. That is why total laryngo-pharyngectomy is widely utilized to treat such carcinoma with or without adjuvant radiation therapy[7]. Reconstruction of the hypopharynx after total pharyngectomy represents a challenge for the surgeon. Even though the hypopharynx is a tubular duct but actually it is a complex arrangement of constrictive forces regulated by the sensory input during the pharyngeal phase of deglutition. It is for this reason that total pharyngectomy damages this sensory-motor mechanism and impairs deglutition and protection to the lower respiratory tract.

Workers have proposed methods for classification of the defects after total laryngo-pharyngectomy and reconstructive strategies. If a flap is required to reconstruct the defect, its choice must be made taking into account the anatomical and functional characteristics of the tissue removed, the characteristics of the recipient and the donor site, the patient's general condition and the experience of the surgeon. Several reconstructive methods are available for pharyngeal and esophageal defects after pharyngo-esophagectomy operations. These include pectoralis major myo-cutaneous flap, gastric pull-up, jejunal free flap, radial forearm and antero-lateral thigh fascio-cutaneous flaps[8].

Free jejunal flap is considered as a very good flap for reconstruction of the defect after total pharyngectomy and cervical esophagectomy because it is naturally tubular,

visceral tissue is similar to hypopharynx and possesses intrinsic peristaltic movement[2]. The disadvantage of this flap is that two surgical teams are required and high risk of thrombosis of the vascular pedicle with subsequent flap necrosis. Pedicled pectoralis major myo-cutaneous flap should be considered as a second choice to repair such defects but the results in terms of recovery of swallowing are controversial. The radial forearm flap is also very popular for reconstruction of the hypopharyngeal defect but there is significant donor site morbidity including large scar and wrist joint stiffness. Gastro-omental free flap is another method for reconstruction of the hypopharynx. Reconstruction by transferred gastric mucosa and the capacity of the omentum to protect the anastomosis of the vessels represents good indications of using this flap in complex irradiated defects[9]. In spite of all these methods, some workers still believe that gastric pull-up is very effective and it should be regarded as the method of choice in hypopharyngeal reconstruction[10,11,12]. The use of stomach as a method of hypopharyngeal reconstruction was first described by Turner in the year 1936. Overall morbidity and mortality in using this procedure is very less, hospital stay is less and there is rapid return to successful oral feeding. Our experience with this procedure is also very encouraging. No peri or post operative complication occurred in this patient and patient is well in follow up of more than six months.

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LETTER TO EDITOR:

Dentin Hypersensitivity: Recent Trends in Management

Shama Asghar

Madam,

Dentinal hypersensitivity (DH) is one of the most commonly encountered clinical problem.[1] It is characterized by short, sharp pain arising from exposed dentine in response to stimuli, (thermal, evaporative, tactile, osmotic or chemical) which cannot be ascribed to any other dental defect or pathology. DH is a painful clinical condition with an incidence ranging from 4 to 74%. A slightly higher incidence of DH is reported in females and most affected patients are in the age group of 20-50 years. Canines and premolars of both the arches are the most affected teeth.[2]

Three major mechanisms of dentinal sensitivity have been proposed in the literature.[2,3] These are (1)Direct innervation theory (2) Odontoblast receptor (3)Hydrodynamic theory. Diagnosis of DH starts with thorough clinical history and examination.[4] The other causes of dental pain should be excluded before a definite diagnosis of DH is made. A simple clinical method of diagnosing DH includes a jet of air or using an exploratory probe on the exposed dentin, in a mesio-distal direction, examining all the teeth in the area in which the patient complains of pain.[5]

By removing the etiological factors, (faulty tooth brushing, poor oral hygiene, premature contacts, gingival recession because of periodontal therapy or physiological reasons, and exogenous/endogenous non-bacterial acids)the condition can be even prevented from occurring or recurring.[4] The patient should be taught the correct method of tooth brushing with the help of a model. A detailed dietary history should be taken. The quantity and frequency of the foods containing acids should be reduced. An occlusal splint can be fabricated to cover the affected areas, to prevent their contact with the acids.[3]

At home, desensitizing therapy include toothpastes, mouthwashes and chewing gums.[4] Majority of the toothpastes, mouthwashes and chewing gums contain potassium salts, sodium fluoride, strontium chloride and stannous fluoride. Potassium salts act by diffusion along the dentinal tubules, decreasing the excitability of the intradental nerve fibers by blocking the axonic action.[1]

In-office, desensitizing agents (glass ionomer cement, composites, varnishes, oxalates) decrease the dentinal permeability by precipitation of calcium fluoride crystals inside the dentinal tubules. These crystals are partially insoluble in saliva. Copal varnish can be applied to cover the exposed dentinal surface. But its effect is for short term and is not recommended for long term management of DH.[2]

Resin-based dental adhesive systems can provide a more durable and long lasting dentine desensitizing effect.[2] They can seal the dentinal tubules effectively by forming a hybrid layer.[5] Recently, some dentin bonding agents have been introduced in the market with the sole purpose of treating DH. Gluma desensitizer contains HEMA, gluteraldehyde and fluoride.[3] HEMA forms deep resinous tags and occludes the dentinal tubules;Gluteraldehyde causes coagulation of the proteins inside the dentinal tubules.[1] The use of bioglass in management of DH forms an apatite layer, which occludes the dentinal tubules. Nd-YAG laser application coagulate the proteins inside the dentinal tubules and block the movement of fluid.[4] Recently, milk protein casein (GC Tooth Mousse) has been used to develop a remineralizing agent.[5] There is a need to provide awareness to the community regarding this preventable and commonly encountered clinical problem.

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1. Abstract

It should have no more than 150 words for unstructured abstracts or 250 words for structured abstracts. The abstract should state the purpose of the study(objective), basic procedures (materials & methods with study design, subjects/animals, place & duraton of study, drug/chemical/equipment, procedure or protocol), main findings (results) and conclusion. It should emphasize new and important aspects of the study.Below the abstract provide, 3-10 key words that will assist indexers in cross-indexing the article and may be published with the abstract.

2. Introduction

State the purpose of the article and summarize the rationale for the study. Give only strictly pertinent references and do not include data or conclusions from the work being reported.

3. Materials & Methods

Describe your selection of the observational or experimental subjects (patients or laboratory animals, including controls) clearly. Identify the age, sex, and other important characteristics of the subjects. Identify the methods, apparatus (give the manufacturer's name and address in parentheses), and procedures in sufficient detail to allow other workers to reproduce the results.. Identify precisely all drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration. For randomized clinical trials provide information on all major study elements, including the protocol (study population, interventions or exposures, outcomes, and the rationale for statistical analysis), assignment of interventions (methods of randomization, concealment of allocation to treatment groups), and the method of masking (blinding).Authors submitting review manuscripts should include a section describing the methods used for locating, selecting, extracting, and synthesizing data. These methods should also be summarized in the abstract.All studies must be approved by the relevant Ethics Committee/InstitutionReview Board of the respective institutions.

4. Results

Present your results in logical sequence in the text, tables, and illustrations. Do not repeat in the text all the data in the tables or illustrations; emphasize or summarize only important observations. Describe appropriate indicators of measurement error or uncertainty such as confidence intervals, P values.Report complications of treatment & dropouts from a clinical trial. Specify any general-use computer programs employed for analysis.

5. Discussion & Conclusion

Emphasize the new and important aspects of the study and the conclusions that follow from them. Do not repeat in detail data or other material given in the Introduction or the Results section. Include in the Discussion section the implications of the findings and their limitations, including implications for future research. Relate the observations to other relevant studies.Link the conclusions with the goals of the study

6. Acknowledgments

List all contributors who do not meet the criteria for authorship, such as a person who provided purely technical

help, writing assistance, or a department chair who provided only general support. Financial and material support should also be acknowledged.

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All authors have to disclose and submit any financial /personnel relationship that might bias and inappropriately influence their work.

9. References

The Vancouver style should be followed. Examples are:

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List the first six authors followed by et al.
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II) More than six authors:

Parkin DM, Clayton D, Black RJ, Masuyer E, Friedl HP, Ivanov E, et al. Childhood leukaemia in Europe after Chernobyl: 5 year follow-up. Br J Cancer 1996;73:1006-12.

b) Organization as author

The Cardiac Society of Australia and New Zealand. Clinical exercise stress testing. Safety and performance guidelines. Med J Aust 1996; 164: 282-4.

c) No author given

Cancer in South Africa [editorial]. S Afr Med J 1994;84:15.

d) Chapter in a book

Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension: pathophysiology, diagnosis, and management. 2nd ed. New York: Raven Press; 1995. p. 465-78.

e) Newspaper

Hasan Mansoor. Excessive use of drugs creating resistance to antibiotics. The Dawn 2013, 24 June; sect. Metropolitan (col.1-4)

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