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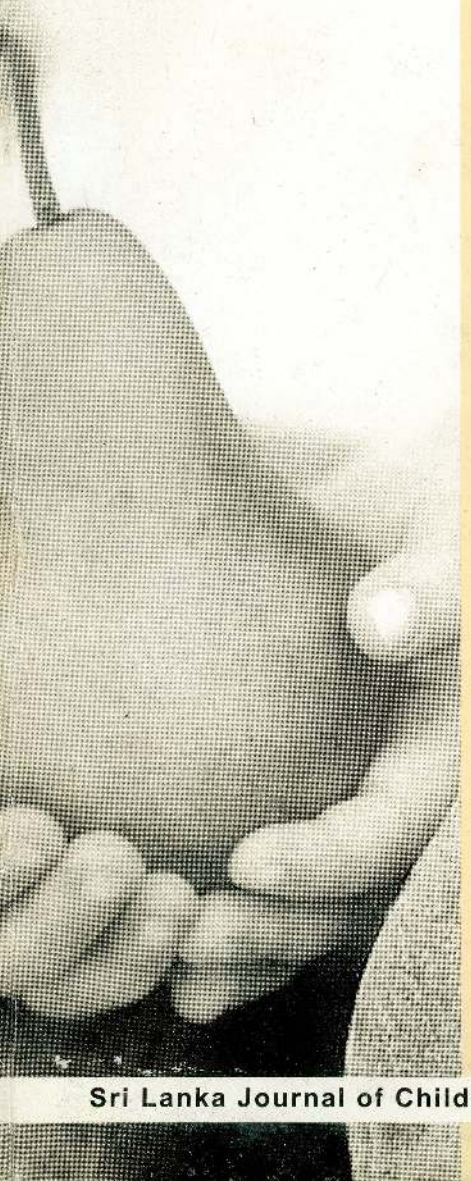

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Sri Lanka Journal of Child Health is the continuation of the Ceylon Journal of Child Health

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Editorial

Small is beautiful, but, NANO is incredible

Sri Lanka Journal of Child Health, 2004; 34:72-74

Over many centuries, medicine has progressed through cornerstones of innovations and revolutionary ideas. Long years ago assessment of illnesses was based on the macroscopic appearance of the patient or the organs. Then came the era of micromedicine which heralded unprecedented growth and advancement. However, despite spectacular progress, the state of the current medical scenario has been limited both by a certain lack of understanding and by the tools used. In many ways, medicine has remained as an art, rather than a science[1].

The technology required to truly understand and repair the human body is molecular technology. After all, the human body is an extremely complex system of interacting molecules or in other words, a molecular machine[1] Only over the last 50 years or so, did medical science venture into a path leading to examination and treatment of disease pathology at a molecular level.. However, from a molecular point of view, despite many impressive advances in the years gone by, medicine has remained rather simple and unsophisticated. Molecular Medicine will necessarily have to "catch up" with the current level of molecular technology in which other fields have rapidly progressed.

Imagine bones woven with a fabric so versatile that one could fall out of a high-rise building but yet walk away unharmed or medical nanites which are capable of consuming atherosclerotic plaques in blood vessels or be able to repair cell damage caused by cancer and tiny machines in the blood stream acting as security guards attacking any foreign entity that enters the bloodstream[1]. What if we could search out and destroy the very first cancer cells that would otherwise have caused a tumour to develop or replace broken parts of cells replaced or could implant pumps the size of molecules to deliver life-saving drugs precisely where and when they are required ? May be, these sound like extracts from a narrative on science fiction. Perhaps not quite.., these are real possibilities in the future. Welcome to the world of nanotechnology and nanomedicine.

Small has always been thought to be beautiful and nano means one billionth of a metre or 10^{-9} metres. Nanotechnology, also called molecular manufacturing, is a branch of engineering that deals with the design and manufacture of extremely small electronic circuits and devices built at the molecular level[2]. Nanomedicine is the application of nanotechnology to monitor, repair, construct and control the human biological system. In simpler words, it means a virtually fool-proof system of prevention and treatment of human disease. A natural consequence of our achieving this level of technology will be the ability to analyse, maintain and repair the human body as completely and as effectively as we can deal with any other machine today. In 1997, a group of health scientists in the United States concluded that if a breakthrough to a molecular assembler occurred within the next 10-15 years, an entirely new field of nanomedicine would emerge by 2020. They postulated that the initial applications would be outside the human body, in diagnostics and pharmaceutical manufacturing but the most powerful uses would be within the body[1]. They discussed some applications like cell-herding machines to stimulate rapid healing, tissue reconstruction and cell repair machines to perform genetic surgery. Nanomedicine is likely to have extraordinary and far-reaching implication for the medical profession, for the definition of disease, for the diagnosis and treatment of many and varied diseases of the human body and ultimately, for the improvement and extension of natural human biological structure and function[3].

There are several challenges and problems that have to be overcome in nanotechnological procedures. One such difficulty is the assembly of the actual item in question. Atoms and molecules are not stationary and are constantly moving, jiggling, combining, reacting and ready to confound the would-be molecular architect. Strings of atoms or molecules have to be added to the existing structure to produce the desired effect. Doing this without disturbing the molecular structure of the original structure is no mean task. The position of each atom is specified in a three dimensional format and it becomes a 3-dimensional problem. As atoms and

molecules are handled one at a time, assembly work has to progress very fast and such speeds are likely to generate mistakes. Thus, together with the assembling process, mistakes have to be detected and corrected. Very large amounts of the product would ultimately be required for a given purpose and at present there are no suitable means of such huge mass production.

A nanomedical company with successful products would collect huge profits. However, they will incur an even higher cost of bringing a product to the market when compared to the present day bio-technology and pharmaceutical companies. It would also be necessary to harness the expertise in many other fields like computer technology, nanopropulsion technology, nanocircuitary etc., to produce the final product.

The problems with drug discoveries today are that it is partly science, partly art and partly luck. The average time to discover and obtain approval for a drug is about 15 years. Even with this, 3 out of 10 new drugs fail the final human testing procedures. This long process plus the protection afforded by patents, allow a relatively long product life cycle for the newer drugs. However, nanomedical products, though protected by patents, will enjoy a much shorter product life cycle. This is simply because things are not left to chance or luck in nanomedicine and every molecule is purpose designed. Once the technology is freely available, the differentiator between companies becomes a function of engineering skills.

There are other minutiae of nanomedicine such as issues on sole proprietorship in view of the collaboration of many different industries in the production of nanoproducts and legal positions in respect of classifying the product as a drug or a device.

One interesting nanomedical application is using deoxyribonucleic acid (DNA) as a construction medium. DNA is thought of as the building blocks of life and the chemical basis of heredity. It is normally not thought of as a building material. Chemists at New York University have developed a means of utilising strands of DNA to construct three dimensional geometric structures. Utilising specific base pairings as the glue, they have linked strands of DNA and introduced bends, kinks, twists etc., which serve as building blocks for even more complex structures. These structures are easily programmable, their arbitrary sequences prevent the body from recognising and utilising them for protein production and they can be modified by a large battery of enzymes. The best use of this expertise is in the development of drug delivery technology. Such systems are expected to be user-friendly, pleasant, painless, convenient, ultra-efficient and be able to virtually eliminate side effects by targeted drug delivery.

However, the most fascinating application of nanotechnology in medicine is in nanorobotics. Nanorobots are nanodevices that will be used for the purpose of maintaining and protecting the human body against pathogens[4]. They will have a diameter of about 0.5 to 3 microns and will be constructed out of parts with dimensions in the range of 1 to 100 nanometers. The main element used will be carbon in the form of diamond or fullerene nano-composites which are expected to provide strength and chemical inertness to these forms. Many other light elements such as oxygen and nitrogen can be used for special purposes. To avoid being attacked by the host's immune system, the best choice for the exterior coating is a passive diamond coating. Smoother and more flawless the coating, the less is the reaction from the body's immune system. These nanorobots could be used as programmable antibodies. As disease causing organisms mutate in their endless attempts to get around medical treatments, nanorobots could be reprogrammed to selectively seek out and destroy them[2].

One nanorobotic discovery that is likely to have a tremendous impact in medicine is the mechanical artificial red cell or the respirocyte[5]. It is a spherical nanomedical device , one micron in diameter, made up of a flawless diamond or sapphire shell and constructed atom by atom. The device is simply an artificial oxygen carrier and utilises an active means of conveying gas molecules into and out of pressurised microvessels. Conventional red cell substitutes have a very short survival time, are not specifically designed to regulate CO_2 or to participate in acid-base buffering and several of them produce undesirable vasoconstriction. The radical innovation associated with the respirocyte overcomes many such problems of the conventional red cell substitutes.

Nanomedicine has the potential to virtually eliminate all common diseases of the 20th century and allow extension of human capabilities[5]. The attractive possibilities of this technology in paediatrics, which is plagued by a plethora of infective and genetic diseases, is perhaps endless. May be., just maybe, the most important long term benefit of nanotechnology to human society as a whole could be the dawning of a new era of peace. After all, we could just hope that, people who are independently well-fed, well educated, happy and most of all, disgustingly healthy, would have little motivation to make war[5].

As long ago as 1959, acclaimed physicist and Nobel laureate, Richard Feynman suggested that nature could be manipulated at a nanometre scale, atom by atom[6]. Today, although this discipline is still in its infancy, it has the potential to change medical science dramatically in the 21st century. We are rapidly approaching that era when such manipulations would produce spectacular advances in the diagnosis and treatment of human disease.

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B J C Perera
Joint Editor

Leading Article

Cochlear implants in children

Devanand Jha[1]

Sri Lanka Journal of Child Health, 2005; **34**: 75-78

Introduction

A cochlear implant is a small complex electronic device that can help to provide a sense of sound to a person who is profoundly deaf or severely hard of hearing. An implant does not restore or create normal hearing. Instead, under appropriate conditions, it can give a deaf person a useful auditory understanding of the environment and help the recipient to understand speech. Cochlear implants are now firmly established in the management of the profoundly hearing impaired children. Ever since the FDA approved the Nucleus 22 channel cochlear implant in 1990 for children between 2-17 years of age, thousands of children have received the cochlear implant. According to the FDA 2002 data, approximately 59,000 people worldwide have received implants, among them 13,000 adults and 10,000 children from the USA. The key to successful implant programme lies in careful patient selection, skilful surgery and experienced rehabilitation.

All cochlear implants have two components. The internal component is implanted and the external component is worn outside. The external component consists of a microphone, an external transmitter and a signal processor or speech processor. The microphone picks up sound from the environment. The speech processor selects and arranges sounds picked up by the microphone. The internal component consists of electrodes that are implanted into the cochlea, and a receiver that is embedded in the temporal bone behind the ear. The receiver stimulator receives signals from the speech processor and converts them into electrical impulses. The electrodes collect the impulses from the stimulator and send them to the brain. The incoming sound is analyzed by the signal processor and computed into fundamental acoustical information that represents key elements of human speech. The analysis results in coding of the appropriate electrode, current amplitude and stimulus rate. The processed signal is sent transdermally via radio frequency transmission to the internal receiver. The message is decoded such that separate bipolar pairs of electrodes are activated to stimulate segments of the auditory nerve.[1]

Candidate selection : The selection criteria for cochlear implants in children are as follows[2] :

1. Twelve months of age or older (FDA recommendation 2002). However, in specific circumstances, even before one year of age the child can be implanted as when meningitis is the cause of hearing loss. Meningitis causes ossification in cochlea as time passes rendering electrode insertion more difficult.
2. Profound bilateral sensorineural hearing loss.
3. No appreciable benefit from hearing aids.
4. No medical contraindications.
5. High motivation and appropriate expectations.
6. Enrollment in a programme that emphasizes development of auditory skills.

Preoperative evaluation:

Once a child is referred for cochlear implantation, a multidisciplinary evaluation should begin. The cochlear implant team should include a surgeon, an audiologist, a speech- language pathologist and teacher for the deaf. The preimplant begins with an audiologic evaluation. Unaided and aided hearing thresholds are obtained with the use of conventional amplification. Potential implant candidates must have bilateral, profound sensorineural hearing loss with a pure tone and unaided threshold equal to or greater than 95dB. In children less than 6 years of age, auditory brainstem testing

[1]*Consultant ENT Surgeon, Apollo Hospital Colombo*

is performed frequently to confirm the hearing loss. Every effort is made to establish the actiology of deafness. With few exceptions, experience with cochlear implant demonstrates that auditory neural elements that can be stimulated seem to be present, regardless whether the cause of deafness is congenital or acquired[3].

Prior to implantation, particular attention is paid to the tympanic membrane and the middle ear. An otologically stable condition should be present prior to implantation. If the child has recurrent otitis media, the condition should be treated first. Grommets can be inserted but they should be removed 4-6 weeks prior to implantation.

Radiologic assessment

High resolution thin section CT scanning of the cochlea and temporal bone is performed to assess the feasibility of implanting. It assists the decision on which ear to implant and ensures that the inner ear morphology is normal. Congenital cochlear abnormalities do not necessarily preclude implantation, but need to be identified pre operatively in order to assist in surgical planning. Absolute contraindications to implantation include cochlear aplasia or absence of the auditory nerve[4]. When the internal auditory canal is less than 2 mm in size , magnetic resonance imaging should be performed to confirm the presence of the cochlear nerve.

Psychologic and social considerations

The parents and family members should become an integral part of the implant team. The parents need to understand that a tremendous amount of post operative rehabilitation is carried out at home. At the current time, psychologic and social considerations for a successful candidate include[5] :

1. No evidence of severe organic brain damage.
2. No evidence of psychosis.
3. No evidence of mental retardation.
4. No behavioural or personality traits that would make completion of the programme unlikely.
5. No unrealistic expectations about the goals of the implant.
6. A pattern of parent/child interaction which indicates that the family will be able to follow the post implant rehabilitative programme effectively.

Surgical procedure

In children flap design is crucial because of delicate tissues and small dimensions. A post auricular incision is made and flaps elevated. A palvas flap is elevated based anteriorly. Cortical mastoidectomy is done and posterior tympanotomy is done to open into the middle ear and expose the round window niche. The bed of the receiver is drilled out posterior to the cortical mastoidectomy and tie down holes are drilled to keep the implant in place. A cochleostomy is done through the posterior tympanotomy window and the electrodes are inserted in the cochlea. The receiver is anchored with prolene and the wound closed in layers. Once the wound has healed and flap edema has resolved, approximately 4-6 weeks later, fitting and mapping of the signal processor begins.

Rehabilitation

Approximately 4-6 weeks after surgery, the child is seen for the initial mapping and tune–up session. During this session the child is fitted with the external equipment and the parents and child are given instructions in the maintenance of the unit. Threshold and comfort levels are obtained for each of the active electrodes. The threshold is defined as the minimum amount of current that is required for the child to indicate that the sound is perceived[6].

Every child is unique with respect to mapping. The parents' active participation during the sessions helps them to realize the benefits and limitations of the implant and gives them practice in working with the child. Depending on the device and the child's age and needs, the rehabilitation process may require daily sessions for 1-2 weeks until the map is set. The time commitment on part of the parents must be understood before the child undergoes implantation.

Results

Several factors including age at the time of deafness, age at the time of implantation, duration of deafness, status of the remaining nerve fibres, educational setting, type of implant, and the length of time with the implant, all play a role in the success of the implant.

Children with congenital deafness and children with prelingually acquired meningitic deafness

achieve similar auditory performance as long as the cochlear nerve is intact[7]. Children with a memory of previous auditory experience and a short period of deafness have a distinct advantage over children who are prelingually hearing impaired. Postlingual deaf subjects showed dramatic improvements on all perceptual tests after only 6 months of implant use because of advantage of previous hearing[8]. Prelingual hearing impaired children show large improvement in speech perception skills, but over a longer, protracted course. Perceptual performance increases on average with each succeeding year after implantation. The most important factor contributing to individual differences among implant users is the amount of experience that users have with the device[9].

In children with prelingual hearing loss who received implants, Gantz et al reported that 4 years following implantation 80% of children achieved open-set, sound-only, word understanding. Speech perception skills continue to develop and do not reach a plateau[8].

Age at the time of implantation is important. It is likely that the auditory and the central nervous system have a critical period of learning, and these systems must be stimulated before a certain age in order to achieve speech perception[8]. The age at which auditory information provided by cochlear implants becomes less useful to deaf individuals is unknown. Speech production results in a limited number of children with prelingual hearing loss, suggesting that children with early onset deafness (prior to 4 years of age) demonstrate more improvement of speech production skills than those who receive an implant after 10 years of age[10]. However, results have shown that prelingually deaf children up to the age of 13 years of age can obtain substantial speech perception from multichannel implants[8]. Because older children, on the whole, tend to perform more poorly, they should be assessed in a much more intensive manner to ensure proper selection of the appropriate candidate.

Living with an implant

There are a few things that children with implants should not do. They should avoid contact sports such as boxing where they might be hit on the head. Swimming is rarely a problem because the external part of the implant can be taken off while swimming.

Experience in Sri Lanka

Six patients have undergone cochlear implant surgery in Sri Lanka in the age range of 1 year to 56 years. Two of them are postlingual and the other four are prelingual patients. They are undergoing habilitation and rehabilitation and are doing well.

Conclusions

Currently children as young as 10 months of age with profound deafness are candidates for implantation. Auditory performance with cochlear implants varies among individuals, but data indicate that performance is better in children who have shorter duration of deafness, who have acquired speech and language before the hearing loss, and who have received the implant before the age of 6 (if prelingual). Auditory performance does not seem to be affected by the aetiology of the hearing loss. Access to optimal education and rehabilitation services is vitally important for children to maximize the benefits available from cochlear implantation. Cochlear implants continue to improve and current generation of intracochlear, multichannel implants with spectrally based speech processors provide a substantial improvement over devices of the previous generation. Advances that have been made in improving speech perception in cochlear implant users should continue to improve with changes in electrode design and signal processing strategies. In future it may be possible to implant the whole external and internal part behind the ear under the skin.

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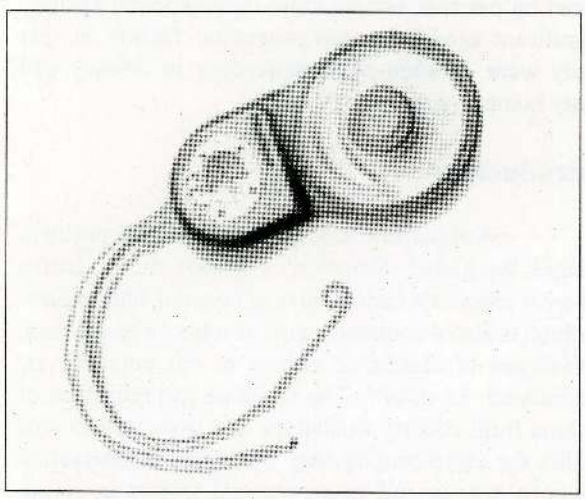
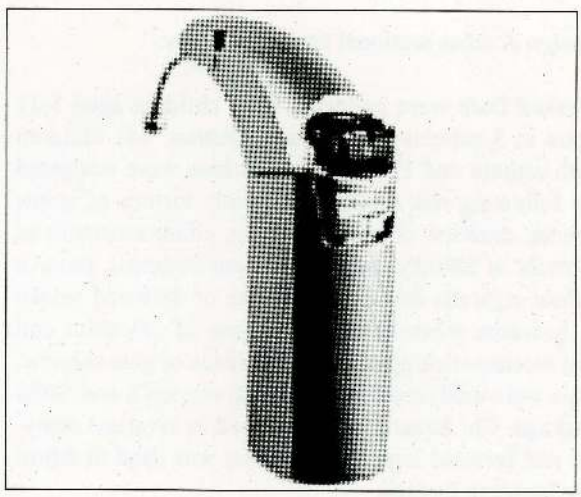


Nucleus contour device (implantable part) .



Nucleus Espirit 3G Speech processor

Editorial Comments

Cochlear implantaton services are now available in Sri Lanka.

Genetic and environmental risk for asthma in children aged 5-11 years

K A W Karunasekera[1], K P J Perera[2], M T P R Perera[3], J Abeynarayana[3]

Sri Lanka Journal of Child Health, 2005; **34**: 79-83

Abstract

Objective To assess genetic and environmental risk factors of asthma among children aged 5-11 years.

Design A cross sectional analytical study.

Method Data were collected from children aged 5-11 years in 3 schools in Gampaha District. 441 children with asthma and 1510 without asthma were evaluated for following risk factors viz. family history of atopy, gender, duration of breast feeding, commencement of formula in infancy, dusty home environment, passive indoor cigarette smoking, presence of firewood smoke in bedroom when cooking, burning of mosquito coil and incense stick/powder and presence of pets at home. Data were analyzed using Epi info version 6 and SPSS package. Chi Squared test was used in bivariate analysis and forward logistic regression was used to adjust confounding factors.

Results Risk of asthma in child (on bivariate analysis) was increased when father has a history of asthma (odds ratio (OR) 6.4 (95% confidence interval (CI) 3.2 -13.2), mother has a history of asthma (OR 4.4, CI 2.6 -7.5), sibling has asthma (OR 4.3, CI 2.0 -9.7), father has a history of allergic rhinitis (OR 2.0, CI 1.5-2.8), mother has a history of allergic rhinitis (OR 2.5, CI 1.9-3.4) and sibling has allergic rhinitis (OR 3.4, CI 2.1-5.4). Asthma risk was significantly increased with following environmental factors: non continuation of breast feeding beyond first 6 months in infancy (OR 1.5, CI 1.2-1.9), presence of firewood smoke in bedroom when cooking (OR 1.4, CI 1.1-1.9), use of mosquito coil (OR 1.5, CI 1.2 -1.9) and dusty home environment (OR 1.8, CI 1.4-2.3). After adjusting for confounding factors, paternal history of asthma, maternal history of asthma, allergic rhinitis in mother and sibling, non continuation of breastfeeding beyond first 6 months of life and dusty environment remained significant with increased risk of asthma ($p<0.01$).

Conclusions This study reinforces that asthma has a multifactorial aetiology. Childhood asthma is influenced by paternal asthma more than maternal asthma. Significant modifiable environmental factors in this study were duration of breastfeeding in infancy and dusty home environment.

Introduction

Asthma in childhood is a common problem around the globe[1]. Situation is similar in Sri Lanka where it remains a major cause of hospital admissions[2]. Asthma is also a common cause of school absenteeism. Prevalence of childhood asthma in our country varies between 15-25%[3,4]. The variation in prevalence of asthma from country to country and from area to area within the same country may be related to interaction between genetic and environmental factors in causation of asthma. Furthermore, significance of a given risk factor too, may vary among different communities. In addition, medical personnel and parents have certain myths regarding risk factors and these may affect the life style and control of asthma in the child. This study was carried out to evaluate the risk factors of asthma in a group of children aged 5 – 11 years.

Method

Data reported in study were collected as a part of the asthma prevalence study published in March 2003 issue of Sri Lanka Journal of Child Health[4]. Study population comprised 1951 school children, aged 5-11 years, in 3 schools of Gampaha District. Questionnaires were sent home with children, answered by their parents/guardians, returned to schools and collected by the researchers. Response rate was 93%. Questionnaires were filled by mothers in 66% of children, fathers in 30% and guardians in the rest.

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(Reviewed by international panel member 26 July 2004 and revised version accepted on 11 October 2004)

Questionnaire was aimed at identifying asthma in children using the clinical criterion adopted by the International Study of Asthma and Allergic Conditions (ISAAC)[1] (i.e. Has your child had wheezing or whistling noise in chest in past 12 months? When it had occurred in 2 episodes of illness or more we diagnosed it as asthma). We used the common terminology used by parents to describe the word "wheezing" and we tested the questionnaire amongst asthmatic children who attended the university paediatric clinic of North Colombo Teaching Hospital before commencement of the study.

Following questions were asked to identify risk factors for asthma: history of having asthma, allergic rhinitis and eczema in father, mother and siblings, gender of child, duration of breastfeeding and commencement of formula in infancy, passive indoor cigarette smoking, presence of firewood smoke in bedroom when cooking, frequent burning of mosquito coil and incense stick/powder (5 days or more per week), living in a dusty home environment, presence of pets (dogs and cats) at home and presence of ceiling in house. Dusty home environment was assessed subjectively. Number of parents with a history of eczema was small and hence eczema was not analyzed as a risk factor in study. Data were analyzed using Epi info version 6 and SPSS package. Chi Squared test was used to determine significance of each risk factor in bivariate analysis. Forward logistic regression was used to adjust confounding factors. Results in bivariate analysis are given as odds ratio (OR) so as to obtain uniformity in results since logistic regression model expresses its results as odds ratio. Ethics Committee of the Faculty of Medicine, University of Kelaniya granted ethical clearance for study.

Results

In study sample, 40% gave a positive family history of atopy (66% of asthmatic and 32% of non-asthmatic children). Results on bivariate analysis of genetic risk factors for asthma are given in Table 1. Accordingly parents having asthma and allergic rhinitis, sibling having asthma and allergic rhinitis were found to be associated with increased risk for asthma. Risk for asthma in males was not significantly different from that in females ($p>0.05$). Results on bivariate analysis of environmental risk factors are given in Table 2. Non continuation of breast feeding beyond first 6 months of life, presence of firewood smoke in bedroom when cooking, burning of mosquito coil and dusty home environment were found to be associated with increased risk for asthma in child. Results on logistic regression analysis after adjusting for confounding factors are given in Table 3. Parental history of asthma, history of allergic rhinitis in mother and sibling, non continuation of breastfeeding beyond first 6 months of life and dusty home environment remained significant.

Table 1
Genetic risk factors of asthma/allergic rhinitis – bivariate analysis

Variable	Number of cases		Number of controls		OR (95% CI)	p value
Asthma	*Yes*	*No*	*Yes*	*No*		
Father	25	416	14	1496	6.4 (3.2-13.2)	<0.001
Mother	35	406	29	1481	4.4 (2.6-7.5)	<0.001
Sibling	16	425	13	1497	4.3 (2.0-9.7)	<0.001
Allergic rhinitis						
Father	78	363	144	1366	2.0 (1.5-2.8)	<0.001
Mother	100	341	157	1353	2.5 (1.9-3.4)	<0.001
Sibling	41	400	44	1466	3.4 (2.1-5.4)	<0.001

Table 2

Environmental risk factors of asthma – bivariate analysis

Variable	Number of of cases	Number of controls	OR (95%CI)	P value
Breast feeding in infancy				
6 months or less	121	316	1.5 (1.2-1.9)	<0.01
more than 6 months	295	1153		
Formula feeding in infancy				
Yes	368	1201	1.4(1.0-1.9)	>0.05
No	*57*	*257*		
Passive indoor smoking				
Yes	122	384	1.1(0.9-1.4)	>0.05
No	288	1010		
Firewood smoke in bed room				
Yes	78	202	1.4(1.1-1.9)	<0.05
No	346	1265		
Frequent use of mosquito coil				
Yes	181	487	1.5(1.2-1.9)	<0.001
No	219	892		
Frequent use of incense stick/powder				
Yes	242	839	1.0(0.8-1.2)	>0.05
No	181	622		
Dust at home				
Yes	213	593	1.8(1.4-2.3)	<0.001
No	116	570		
Pets at home				
Yes	209	766	0.9(0.7-1.2)	>0.05
No	213	698		
Presence of ceiling in the house				
Yes	148	492	1.1(0.8-1.3)	>0.05
No	289	1008		

Table 3

Significant risk factors of asthma –Logistic regression analysis

Variable	Adjusted OR(95%CI)	P value
Asthma		
Father	4.2 (1.7-10.1)	<0.01
Mother	3.8 (2.1-6.7)	<0.001
Allergic rhinitis		
Mother	1.8 (1.2-2.5)	<0.01
Sibling	2.5 (1.4-4.4)	<0.01
Breast fed in infancy for 6 months or less	1.5 (1.1-2.1)	<0.01
Dusty home environment	1.5 (1.1-1.9)	<0.01

Discussion

Very few studies have been done in this country on genetic and environmental risk factors in childhood asthma. This population-based study shows that 40% of children have a positive family history of atopy. It is therefore necessary to differentiate between hereditary risk factors of asthma in chlldren. In this study, as in others, parental asthma is a risk factor for a child having asthma[5,6,7]. The finding that paternal asthma has more influence on asthma in child is consistent with that of previously reported study here[7]. However this is in contrast to the finding of Rusconi et al. where mother having asthma has a greater impact on asthma in child[6].

The finding that allergic rhinitis in mother and sibling increased the risk of child having asthma re-confirms the hypothesis that rhinitis is an independent risk factor for asthma[7,8,9]. In contrast to findings of the previous study done in Sri Lanka, this study shows that paternal allergic rhinitis was not associated with increased risk for asthma in child. This finding could be influenced by the fact that two third of questionnaires were filled by mothers in the study and allergies of the mother and in siblings are probably over represented and allergies of fathers may include more of the recent and severe type. A simple hereditary model cannot explain the proved independent relationship between asthma in child and allergic rhinitis in sibling. Concordance rate for asthma of monozygotic twins reared apart is quite similar to those of twins reared together, suggesting substantial genetic component for development of asthma[10]. But twin studies are unable to identify pattern of transmission. Although family history of atopy is a stronger risk factor for asthma in child, 34% of asthmatic children in this study did not have a positive family history, implying that environmental factors are also important in causation of asthma in the child.

Role of breastfeeding on subsequent development of asthma has been a controversial subject for many years. Some studies have proved that breast feeding protects children from getting asthma, while others disprove this[6,7,11,12,13,14]. This study, as well as the previous Sri Lankan based study, showed that breastfeeding more than 6 months in infancy has a protective effect on development of asthma in child. Most studies on breastfeeding and asthma, including present one, are observational epidemiological studies. In some of them, exposure and outcome data are collected retrospectively. Hence, selective recall would have induced parents of children with wheezing to over or underreport conditions that they believed to be associated with wheezing. It is a popular myth amongst our mothers that breastfeeding may be harmful if mother has asthma and this could also have influenced the results in this study. Therefore a prospective birth cohort would be required to evaluate duration of breastfeeding on subsequent development of asthma.

As observed by us and others, exposure to dust at home is known to be associated with an increased risk of asthma[7,15].We found that certain other previously known risk factors for asthma such as passive cigarette smoking and pets[8,15] were not associated with increased risk of asthma. One reported review shows that passive smoking is likely to increase the severity and frequency of asthma[16]. Thus finding of our study could be explained if environmental cigarette smoke is considered as a factor, which would precipitate an attack, rather than a cause for underlying asthmatic tendency.

Our study was a population based one and included a sufficiently large group of subjects to ensure

adequate statistical power. However, the retrospective design could have resulted in a biased recall on both diagnosis and risk factors. We used the clinical criterion adopted by ISAAC to diagnose asthma to get a uniformity of the diagnosis with world literature. We may have included in the control subjects a number of children who had asthma in the early years of their lives and who did not have wheezing in the previous 12 months at the time of data collection. In order to reduce selective recall bias with regard to the risk factors, we requested parents to select one of three responses under risk factor in the questionnaire; i.e. yes, no or cannot remember. The category that answered as "do not remember" was not included in the statistical analysis.

In conclusion, our study shows the effect of atopy in the family on development of asthma in the child. We also identified that breastfeeding longer than 6 months in infancy has a protective effect on development of asthma in children. Hence, recommendation of breastfeeding at least until one year by WHO should be reinforced.

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Short stature in Indian children: Experience from a community level hospital

Pankaj Garg[1]

Sri Lanka Journal of Child Health, 2004; **34:** 84-88

(Key words: Short stature, community hospital)

Abstract

Objective To study prevalence and aetiological profile of short stature in children attending outpatients department (OPD) of a community level hospital.

Method 625 consecutive children (>2 and <16 years) attending OPD of a community level hospital, catering mostly to rural and lower socioeconomic strata of society, were screened for short stature using NCHS charts of mean and standard deviations. A diagnosis of familial short stature was made after allowing for mid-parental stature. Prepubescent children were classified as short stature using percentile charts (<5th centile being taken as short stature) for affluent Indian children. All children were followed up for 6-12 months to establish growth velocity. To allow for onset of puberty and stage, Tanners chart for early (+ 2SD) and late (- 2SD) maturers was considered.

Results 86 children were identified as having short stature on first visit. Commonest cause of short stature was protein energy malnutrition (PEM) & chronic diseases occurring in 46 (53.5%) cases. Other causes included normal variant short stature (24.4%), endocrine problems (4.7%) and miscellaneous (5.8%). 11.6% could not be classified due to loss to follow up and inability to refer to tertiary centres. Overall prevalence of short stature was 13.8%, significantly higher than prevalence reported from tertiary centres ($p<0.05$).

Conclusion Prevalence of short stature is higher than previously reported. A large number of children with short stature may go undiagnosed in rural and lower socioeconomic strata of developing countries. Prevalence and aetiological profile of children with short stature in present study is more representative of community than previous studies in India.

Introduction

Stature is one of the most important determinants of personality in either sex. Several factors such as sex, race, prenatal and postnatal stature and hormones like growth hormone, thyroid hormone, insulin and sex hormones play an important role in short stature. Most studies on children of short stature in India are from tertiary level centres[1,2,3]. In India, the vast population, absence of proper referral system at primary and secondary health care levels and absence of coordination between public and private sectors of health care may result in the diagnosis being missed in many children with short stature. Aetiological profile and prevalence of short stature at community level hospitals may differ from those reported from tertiary centres. Present study was planned to study prevalence and profile of children with short stature and focus on problems in managing them at a community level hospital.

Method

625 consecutive children, (>2 but <16 years of age), attending paediatric OPD of Shanti-Mangalick hospital (150-bedded trust hospital providing care at low cost), Agra, India were screened for short stature. Criteria for diagnosis of short stature were:

[1]*Consultant Paediatrician, Shanthi Mangalick Hospital, Agra, India*

(Received on 16 Nov 2004)

1. Height >3 SD below mean for chronological age using NCHS mean and standard deviations chart[4].
2. Growth rate <5th percentile for chronological age using Agarwal growth chart for prepubescent children[5,6].
3. Height >2 SD below mean for chronological age for mid parental height and correlated using recommended method of evaluation for ascertaining familial short stature[7].

A detailed history focusing on nutritional and chronic diseases and endocrinal disorders and a complete physical examination including anthropometrics data, mid-parental height, arm span and any dysmorphic features were recorded. Skeletal survey for bone age, complete blood count, urea, electrolytes, serum creatinine, serum phosphorous, alkaline-phosphatase, x-ray skull and hormonal assays were planned and suggested to parents. Children were followed up for 6-12 months to calculate growth velocity and identify constitutional short stature for children achieving normal growth velocity on Tanner's height velocity curves[8]. Worm infestations and giardiasis were ascertained as cause of short stature by identifying catch up growth after de-worming and appropriate treatment (Worm infestations was corroborative diagnosis in children with definite history of passing worms or demonstration of ova on stool examination).

Results

86 (13.8%) children were identified as having short stature. The population characteristics of these children are shown in table 1. 66 children were prepubescent while 20 were in various stages of puberty (6 SMR I, 5 SMR II, 4 SMR III, 5 SMR IV). 12 were late maturers, 6 were average and 2 were early maturers. The aetiological profile of the 86 children is shown in table 2. 10 (11.6%) children who were identified as short stature on first visit, could not be classified as they were lost to follow up or parents were not available to ascertain familial short stature.

Table 1
Population characteristics

Age groups (Years)	No. of Males (%)	No. of Females (%)	Total No. (%)
2-5	21(24.4)	16(18.6)	37(43.0)
5-7	11(12.8)	11(12.8)	22(25.6)
7-13	11(12.8)	11(12.8)	22(25.6)
> 13	03(03.5)	02(02.3)	05(05.8)

Table 2

Aetiological profile of short stature in present study

S. No	Aetiology (N=86)	Total No.(%)
1.	**Malnutrition (PEM) & chronic diseases**	46 (53.5)
	Severe pulmonary TB	08
	Severe Extra pulmonary TB	13
	Giardiasis & worm infestations	07
	Stunted & wasted (PEM)	10
	Rheumatic heart disease (CHF)	03
	Chronic renal failure (CRF)	02
	Celiac disease	05
2.	**Normal variant**	21 (24.4)
	Constitutional growth delay	06
	Familial short stature	15
3.	**Endocrine causes**	04(4.7)
	Growth hormone deficiency	02
	Diabetes mellitus	01
	Hypothyroidism	01
4.	**Miscellaneous**	5 (5.8)
	Downs syndrome	02
	Klippel-fiel syndrome	01
	Apert syndrome	01
	Russell silver syndrome	01
5.	**Cannot be classified** (Missed diagnosis/ Loss to follow up)	10 (11.6)

Discussion

Prevalence of short stature in the present study was 13.8%. Colaco et al. have reported a prevalence of 5.6% in children admitted in hospitals[2]. Khadgawat et al have reported 7% prevalence among 280 normal school children[3]. The difference in prevalence of short stature in present study is statistically different from that of Khadgawat and Colaco ($p<0.05\%$). However Colaco has also found a prevalence of 10% in children utilizing outpatient services[2]. Prevalence in present study was different from these findings too ($p<0.05$). The higher prevalence in present study is expected as the hospital caters mostly to the under-privileged sections of society. Also a higher prevalence in studies from OPDs is expected as most children with chronic diseases and short stature are managed in OPDs rather than being admitted in developing countries. One may argue that a higher percentage of short stature may be due to use of NCHS charts in present study but this assumption may not be true as Indian affluent children (under five) are at par with the developed world[5]. There is, however divergence between NCHS growth pattern and growth pattern of Indian children in late adolescence[10]. But number of children in late adolescence is very small in present study as to significantly alter the results. Aetiological profile of short stature was different in present study. Commonest cause of short stature was PEM & chronic diseases, occurring in 46 (53.5%) cases. This is much more than previously reported [1,2,3]. Most children in puberty were late maturers due to malnutrition which is contrary to situation in the developed world[10]. Malnutrition in children continues to cripple Indian society due to poverty, ignorance and illiteracy[11]. Agra (city of Taj Mahal) is a region of very high environmental exposure to mycobacterial diseases[11]. We thus had many children (24.4%) with severe pulmonary and extra-pulmonary tuberculosis accounting for failure to thrive and short stature. Other chronic diseases included giardiasis and worm infestations due to overcrowding and unhygienic conditions prevailing in the region. Coeliac disease was diagnosed on basis of raised tissue transglutaminase levels and documented catch up growth on gluten free diet. Upper gastrointestinal endoscopies could not be done due to financial restraints and unwillingness of parents for referral. Normal variant short stature accounted for 24.4% cases. Some cases of normal variant short stature may have been missed, as parents were not available to ascertain familial short stature during first visit and subsequently were lost to follow up. As expected, prevalence of endocrine causes was much less (4.7%) in present study than reported from tertiary care centres (up to 56.8%)[12]. Hormonal assays were not routinely done at this hospital but a private laboratory was linked for study purposes. Though prevalence from a hospital based study cannot be extrapolated for the community as a whole, aetiological profile and prevalence of short stature in present study is more representative of the community in a developing country. Several children were lost to follow up missing the diagnosis in many children of short stature. A large number of children with short stature may thus go undiagnosed in the rural and lower socioeconomic societies of the developing countries.

Acknowledgement

Author thanks Dr A K Singh, Medical Superintendent, and Shanti-Mangalick hospital for giving permission to carry out study.

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Retinopathy of prematurity

Pratik Sen

Sri Lanka Journal of Child Health, 2005; **34:** 89-91

History

Retinopathy of prematurity (ROP) was first noted in the 1940's when more and more oxygen was being administered to premature infants. This disease was called retrolental fibroplasia by Terry in 1941[1]. The term retinopathy of prematurity was coined by Heath in 1951[2].

Embryology

The vascular precursors of the retinal blood vessels enter the eye at 6 weeks of gestational age and slowly reach the nasal periphery at 36 weeks. The temporal periphery gets vascularized at 40 weeks. This process is susceptible to many external influences once the child is prematurely born.

Aetiology

Factors which can stop the normal vascularisation of a premature neonate are

1. Prematurity
2. Low birth weight
3. Post natal infections
4. Oxygen administration

Classification of ROP [3,4]

Three clinical parameters are considered when classifying ROP. They are

1) Stage of vascular proliferation
2) Location of the disease
3) Extent of involvement in clock hours

1) Stage of vascular proliferation

Stage 1- Demarcation line
Stage 2- Ridge
Stage 3- Ridge + fibrovascular proliferation
Stage 4- Partial retinal detachment
Stage 5- Total retinal detachment

2) Location of the disease

Zone 1- Circle around the disc with a radius of two disc diameters temporal to macula.
Zone 2- Between zone 1 and a circle concentric to zone 1.
Zone 3- An area of temporal crescent beyond zone 2.

3) Extent of involvement

This can be calculated by noting the extent of retinal involvement in clock hours involved.

Plus Disease

In addition to the above criteria for classification a separate disease entity named as "Plus Disease" is diagnosed in ROP with the following criteria:

1. Enlarged venules and tortuous arteries in the posterior pole.
2. Iris vascular engorgement.
3. Vitreous haze.

Screening protocol

All newborns with the following criteria should be screened for ROP.

[1]*Consultant Ophthalmologist, Apollo Hospitals Colombo*

1. Neonates born before 32 weeks of gestation.
2. Neonates who had a stormy postnatal period.
3. Neonates with a birth weight less than 1500 g.

First screening should be done in the neonate at 31 weeks of post conceptional age or at 4 weeks of chronological age after birth. At this screening the neonate may or may not found to be having ROP. If ROP is found it is classified into threshold, prethreshold or Rush disease by the following criteria (Figure 1).

Threshold ROP

1) Disease in Zone 1 or 2.
2) Stage with plus disease.
3) 5 continuous or 8 cumulative clock hours of involvement.

Prethreshold ROP

1) Stage 1 or 2 disease.
2) Disease in Zone 3.
3) Less than 5 clock hours of involvement.

Rush disease

1) Zone 1 or post zone 2 disease
2) Plus disease

These patients have very low birth weight, presents within three weeks of chronological age and very rapidly progress to active threshold ROP.

Modalities of treatment

Laser Treatment

This modality of treatment does not need anaesthesia and does not leave any morbidity. However it is difficult to do in small pupils and needs more patience.

Cryo treatment

This procedure is done under anesthesia and may need conjunctiva incision to reach posteriorly.

Cryo ROP study [5]

This multicentre study showed that early treatment can reduce an unfavourable outcome in 48.5% of cases with active ROP. It also showed that zone 1 disease is associated with a poor outcome in 78% of cases in spite of prompt laser or cryo treatment.

Surgery in ROP

This modality of treatment is reserved for stages 4 and 5. There are two types of surgeries that could be done. Of these Scleral buckling is done for stage 4 disease without macular involvement. The results of this procedure are fairly good. Vitrectomy is reserved for stage 5 and the results of this procedure are poor.

Post treatment follow up

The patient needs to be followed up weekly and if inadequate regression is seen may need further treatment. The signs of regression are:

1. Reduction in the tortuosity of blood vessels
2. Regression of new vessels on the ridge
3. Clearing of the vitreous haze
4. Reduction in iris vascular engorgement

Spontaneous regression of ROP

ROP can regress in 80% of cases even without treatment and it is usually the prethreshold stage which may spontaneously regress.

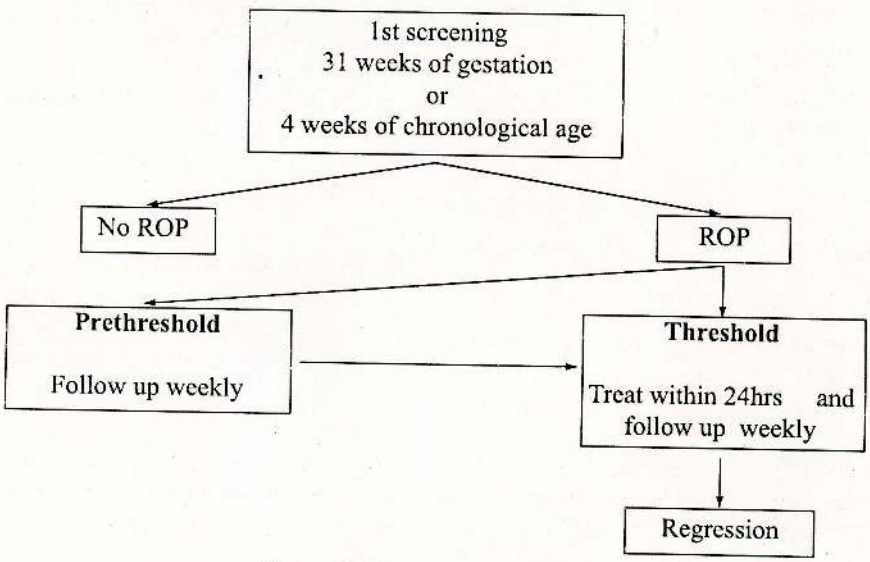

Figure 1 –Management protocol

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Snippets from the world wide web

Sri Lanka Journal of Child Health, 2005; **34:** 92-93

Waist Circumference May Predict Insulin Resistance Syndrome in Children

The investigators suggest that measuring children's waists should be routine clinical practice to identify children at risk.

http://mp.medscape.com/cgi-bin1/DM/y/ernm0EIZ1O0DzQ0GoLS0EG

Circumcision Prevents UTIs, but Risk-Benefit Ratio Is Debatable

Results of a meta-analysis confirm that male circumcision reduces the risk of urinary tract infections -- but more than 100 boys need to be circumcised to prevent one UTI.

http://mp.medscape.com/cgi-bin1/DM/y/ernm0EIZ1O0DzQ0GoPD0E4

Prophylaxis Cuts Jaundice Risk, Doesn't Affect Breastfeeding

Giving breast-fed infants a few ounces of a beta-glucuronidase inhibitor daily for the first week of life reduces their risk of developing jaundice, according to a new report in the August issue of Pediatrics.

http://mp.medscape.com/cgi-bin1/DM/y/ernm0EIZ1O0DzQ0GoP40En

Fluticasone Propionate-Salmeterol Safe in Children With Persistent Asthma

In children with persistent asthma, twice daily treatment with fluticasone propionate-salmeterol is well tolerated with a safety profile similar to fluticasone propionate alone, investigators report in the Annals of Allergy, Asthma and Immunology for July.

http://mp.medscape.com/cgi-bin1/DM/y/ernm0EIZ1O0DzQ0GoPv0Et

Psychiatric Polypharmacy in Children on the Rise

The practice of prescribing multiple psychotropic medications to children and adolescents has increased over the last decade, results of a literature review suggest.

http://mp.medscape.com/cgi-bin1/DM/y/ernm0EIZ1O0DzQ0GoPC0E3

Montelukast Similar to Fluticasone for Mild Childhood Asthma

Montelukast compares favorably with fluticasone in controlling mild asthma in children 6 to 14 years old, according to a report in the August issue of Pediatrics.

http://mp.medscape.com/cgi-bin1/DM/y/ernm0EIZ1O0DzQ0GoPw0Eu

Hydrocortisone for Neonatal Lung Disease Does Not Impair Brain Development

Corticosteroid treatment of neonatal chronic lung disease with hydrocortisone, rather than dexamethasone, does not result in impaired structural or functional brain development, according to a report in the July issue of Pediatrics.

http://mp.medscape.com/cgi-bin1/DM/y/eraY0EIZ1O0DzQ0GnSt0EM

Resistant HIV in Mother and Infants Reduced With Three-Drug Combination

A randomized trial suggested that adding lamivudine and zidovudine to nevirapine for vertical prophylaxis reduced the ate of drug-resistant HIV in mothers and infants.

http://mp.medscape.com/cgi-bin1/DM/y/eraY0EIZ1O0DzQ0GnQd0E3

Obesity, Diabetes-Linked Gene Found on Chromosome 6

French researchers have identified a gene associated with increased risk for obesity and type 2 diabetes in European children and adults.

http://mp.medscape.com/cgi-bin1/DM/y/eraY0EIZ1O0DzQ0GnN40ED

Buccal Midazolam May Be Better Than Rectal Diazepam for Acute Seizures in Children

In a randomized trial, buccal midazolam was more effective for children presenting to a hospital with acute seizures and was not associated with increased incidence of respiratory depression.

http://mp.medscape.com/cgi-bin1/DM/y/erMv0EIZ1O0DzQ0GmHo0EE

Methotrexate Helpful Against Uveitis in Children

Low-dose methotrexate appears to be a safe and effective treatment for chronic anterior and intermediate uveitis in children, UK researchers report in the July issue of the British Journal of Ophthalmology.

http://mp.medscape.com/cgi-bin1/DM/y/erMv0EIZ1O0DzQ0GmKu0EN

Immunoglobulin Speeds Recovery in Childhood Guillain-Barre

Intravenously administered immunoglobulin may hasten recovery in children with Guillain-Barre syndrome, but shows no other beneficial effects, German researchers report in the July issue of Pediatrics.

http://mp.medscape.com/cgi-bin1/DM/y/erMv0EIZ1O0DzQ0GmIj0EA

Miniature Ventricular Assist Device May Be Useful in Children

A rotary dynamic ventricular assist device has been developed specifically for use in children, even newborns, with heart failure.

http://mp.medscape.com/cgi-bin1/DM/y/erMv0EIZ1O0DzQ0GmK40EI

Small Bowel Injury Common With Child Abuse Involving Abdomen

Half of children with abdominal injuries due to abuse have damage to the small intestine, new research indicates. By contrast, with accidental abdominal injuries, the small bowel is affected in no more than a fifth of cases.

http://mp.medscape.com/cgi-bin1/DM/y/erMv0EIZ1O0DzQ0GmK50EJ

Coronary Dilation in Juvenile Arthritis Can Resemble Kawasaki Disease

Coronary artery dilation is a fairly common finding among patients with systemic-onset juvenile idiopathic arthritis, and may resemble that seen with Kawasaki disease, according to a report in the July issue of Pediatrics.

http://mp.medscape.com/cgi-bin1/DM/y/eq5F0EIZ1O0DzQ0GlBT0ER

B J C Perera
Joint Editor

Case Report

Kohomba oil induced encephalopathy : lessons in prescribing traditional medicines

S Sri Ranganathan[1], R Fernandopulle[1], BVDSP Abeywardena[2], HMKN Hathlahawatta[3], KR Gunatilaka[4]

Sri Lanka Journal of Child Health, 2005; **34**: 94-95

Introduction

Kohomba oil is a fatty acid rich extract of the Neem (Azadirachta indica or Margosa) seeds. It is used as a traditional medicine in many countries including India, Burma, Thailand, Malaysia, Indonesia and Sri Lanka as an external application[1]. Rarely, it is administered orally to infants in small amounts[1]. Several cases of Kohomba oil encephalopathy have been reported from Malaysia and Singapore[1,2]. Here we report a case of encephalopathy in a child following Kohomba oil ingestion.

Case report

A 7 year old girl had been prescribed Kohomba oil orally by an Ayurvedic practitioner for a skin lesion. 30 minutes after ingestion of two teaspoons of the oil she developed vomiting, followed by drowsiness. She was admitted to Kahawatte Base Hospital and three hours later she developed status epilepticus. She was given rectal diazepam and intramuscular paraldehyde but as the fits continued she was transferred to Ratnapura General Hospital for specialised management. At Ratnapura, she was given buccal midazolam and intravenous (IV) phenobarbitione.

Convulsions stopped around 4 hours from onset but within an hour she developed respiratory arrest and was intubated and ventilated. She was extubated after 36 hours but developed hypotension, bradycardia and apnoea and was re–intubated. She also received IV dobutamine, cefuroxime, netilmicin, metronidazole and aciclovir. On third day she was successfully extubated and medications were discontinued. As there was no recurrence of symptoms she was discharged on eighth day after admission.

She was a previously healthy child with no past or family history of convulsions. Parents were confident that she had not ingested any other unknown substances except Kohomba oil. She did not have any antecedent symptoms such as fever, headache or malaise. Apart from skin lesion (eczema and healing scabies), the general, systemic and funduscopy examinations were normal. On day two she showed polymorphonuclear leucocytosis (total count 2.73 x 10^9/l with neutrophils 91%), moderate metabolic acidosis (pH 7.16, pO_2 46.0, pCO_2 34.6, bicarbonate 12.3 meq/L, base deficit -15.4), elevated transmainases (>109 IU/L, reference range 0-40) and normal prothrombin time (test 13, control 12 seconds). Cerebrospinal fluid examination on day two was normal. Electroencephalogram on day 8 suggested an encephalopathic or encephalitic picture which reverted to normal on day 30.

Discussion

A clinical diagnosis of encephalopathy following Kohomba oil ingestion was made based on (i) time relationship between the ingestion and clinical manifestations, (ii) absence of alternative explanations and (iii) evidence of similar cases reported in the literature.

Cases of Kohomba oil encephalopathy reported from Malaysia and Singapore[1,2] too had a similar sequence of events and biochemical changes. The

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dose of Kohomba oil ingested by these patients varied from 5–30 ml and the latent period between ingestion and onset of symptoms varied from 30 minutes to 4 1/2 hours[2].

Encephalopathy following Kohomba oil ingestion could be either an adverse reaction to the therapeutic dose or a toxic effect due to over dosage. Therapeutic dose of Kohomba oil is required to differentiate these two possibilities and this information is not available in the literature.

Studies on animal models have demonstrated both toxicity to the nervous system and pronounced fatty infiltration of the liver and proximal renal tubules with mitochondrial damage and cerebral oedema, occurring within 3 hours of administration of Kohomba oil, compatible with Reye syndrome[2,3,4]. The authors suggest that Kohomba oil causes changes in fatty acid metabolism which in turn interferes with mitochondrial respiration[4]. Onset of hepatic toxicity is quick as the oil reaches hepatocytes within 30 minutes of ingestion[3]. Similar pathological findings were seen in a child who died of Kohomba oil ingestion[2].

The most likely diagnosis in our child is neem oil induced Reye syndrome, although the respiratory arrest could be either due to status epilepticus and its treatment or secondary to hepatic encephalopathy. Hypotension and consequent oliguria is most likely due to Kohomba oil, as studies in rats have shown that Kohomba leaf extracts caused bradycardia, cardiac arrhythmia and significant, dose related hypotension which are immediate, sharp and persistent[5].

Management of Kohomba oil encephalopathy is mainly supportive and control of convulsions. In most reported cases prognosis was good, although occasional fatalities and neurological deficits were reported[1]. Our child too recovered completely without sequelae in 72 hours.

Conclusion

Kohomba oil is a common ayurvedic medicine used in Sri Lanka. Health professionals should be aware of the adverse and toxic effects of Kohomba oil ingestion and its proper management. General public should also be educated that complementary and alternative medicines are not free of risk and to seek medical advice if they notice any new symptoms following their use.

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Severe reaction following a combined vaccine

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Introduction

With the expanded programme of immunization (EPI) achieving near 100% coverage, the demand for non-EPI vaccines is rising. The combined vaccines have become popular among health care providers and the patients due to easier administration and a single injection covering many diseases. They have been shown to be safe and effective[1,2]. We report a child who developed a severe febrile illness following a combined DPT+HepB+Hib vaccine.

Case report

A one and a half year old girl who has been previously well was given OPV + combined DPT+HepB+Hib vaccine. She developed high fever within 8 hours.

During the next 2 days child continued to have fever spikes ranging from 38-39^{0}C but her general condition remained well. On the third day she developed an urticarial rash with angioedema and was treated with antihistamines and 2 doses of hydrocortisone. Following day child was found to have moderate jaundice. She continued to have wildly swinging temperatures which were difficult to control with paracetamol. Examination revealed bilateral ankle swelling and tender hepatomegaly.

Following results were obtained from investigations done during this stage. Bile was present in the urine. The total white cell count was 20 x 10^9/l with a differential count of 79% neutrophils and 19% lymphocytes. Platelet count was 523 x 10^9/l and the haemoglobin was 9.6 g/dl. Blood film was negative for malarial parasites. Serum bilirubin was 71 µmol/l. SGPT was 476 u/l and SGOT 126 u/l. In the peripheral blood film red cells were hypochromic and microcytic; white cells were predominantly neutrophil with no abnormal cells; platelets were normal in appearance. Blood urea was 2.3 mmol/l, serum sodium 139 mmol/l and serum potassium 4.2 mmol/l. Prothrombin time was 14 seconds (control 12 seconds). Ultrasound scan of the abdomen was unremarkable except for a non-specific mild hepatomegaly.

Child was started on intravenous cefotaxime and gentamicin after a lumbar puncture was done and samples of urine and blood obtained for culture. Cerebrospinal fluid did not show any abnormality. Urine and blood cultures were negative. Despite antibiotic therapy child remained febrile, irritable and ill and complained of painful limbs. The results of investigations at this stage were as follows:

Total white cell count was 30 x 10^9/l with a differential count of 70% neutrophils and 29% lymphocytes. ESR was 132 mm in first hour. The chest x-ray, electrocardiogram and echocardiogram were normal. Cold agglutinins, mycoplasma antibodies, antinuclear antibodies and rheumatoid factor were negative. There was no growth in blood and urine cultures. Hepatitis B surface antigen and Hepatitis A IgM were negative.

Although the results of investigations were inconclusive, antibiotics were continued for a period of 7 days. She made a slow recovery and became as-

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ymptomatic by the 12th day. The full blood count, ESR and liver function tests were repeated after 4 weeks and were normal.

Discussion

Mild febrile reactions that settle in 2-3 days and local reactions at the site of injection site following immunizations are common. Very rarely anaphylaxis, allergic reactions and serum sickness like diseases have been reported1. Thrombocytopenia[3], Guillain-Barre syndrome, Bell palsy, abnormal liver function tests and convulsions have been reported with Hepatitis B containing vaccines[4,5,6]. Severe prolonged febrile illness with hepatitis following the combined DPT+HepB+Hib has not been documented. Clinicians have to be aware of the possibility of this type of reaction following combined vaccines.

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Picture Story

A mother with complete absence of breast milk due to ectodermal dysplasia

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Complete absence of secretion of breast milk due to an anatomical, physiological or pathological cause is rare. Congenital hypoplasia of breasts, Sheehan syndrome due to anterior pituitary failure following post-partum haemorhage and bilateral mastectomy are some important rare causes. We report a mother with complete absence of breast milk due to hypohidrotic type of ectodermal dysplasia.

Case report

A nineteen year old unmarried mother from a remote village in Mahiyangana delivered her second baby, a boy weighing 2100g, at term following an uneventful pregnancy. Her first baby delivered at 26 weeks of gestation had died soon after birth. Examination of the newborn was normal; however the mother complained of complete absence of breast milk. Examination of mother revealed the following. (Figures 1 and 2).

Face showed frontal bossing, malar hypoplasia, flattened nasal bridge, recessed columella, thick everted lips, and hyperpigmented periorbital skin. Her entire body skin was dry without secretion of sweat and she complained of feeling feverish on warm days. Scalp hair was sparse, fine, unruly and hypopigmented while eyebrows and eyelashes were absent. She only had a couple of teeth which were widely spaced and peg shaped. Her breasts were hypoplastic with no evidence of secretion of milk. She was born to non-consanguineous parents and examination of her fourteen year old paternal aunt's daughter also revealed similar features.

The above findings suggested a diagnosis of hypohidrotic type of ectodermal dysplasia and as the mother did not have breast milk the newborn was started on an infant formula.

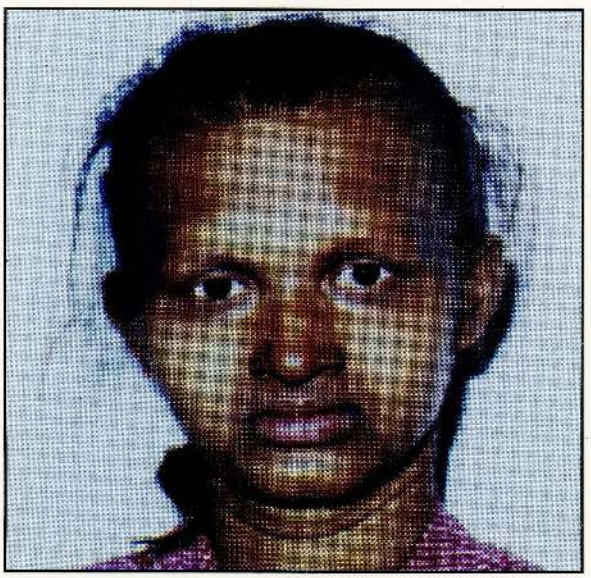

Figure 1

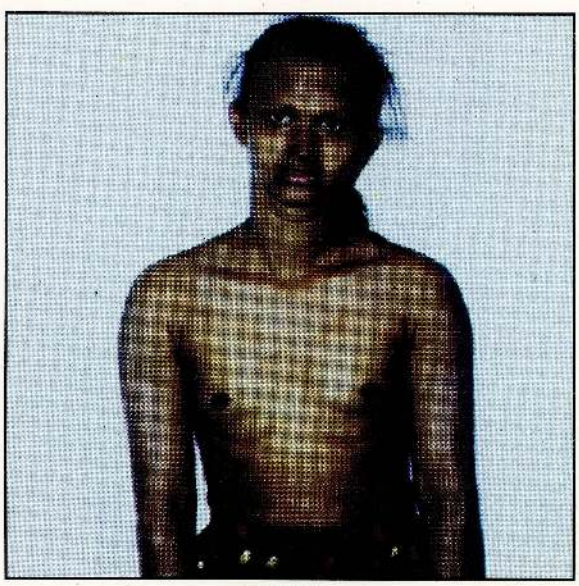

Figure 2

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Discussion

Ectodermal dysplasia is a rare group of inherited disorders characterised by aplasia or dysplasia of tissues of ectodermal origin, such as teeth, skin, and appendageal structures including hair, nails, sweat and sebaceous glands[1]. A detailed classification of these syndromes has been produced recently[2]. The most common, classic type is hypohidrotic ectodermal dysplasia (HED), also known as Christ Siemens Touraine syndrome, previously reported in children by BJC Perera in 1972[3]. It is characterised by a triad of hypohidrosis, hypotrichosis and hypodontia[1]. The clinical features of our patient suggest this diagnosis. It is inherited commonly as an X-linked recessive trait with the gene carried in the female and manifested in the male[4]. However an autosomal recessive type of inheritance is also reported in certain families[2]. Hypoplastic or absent mammary gland is a well described feature of carrier females with HED[2]. This case reiterates the fact that mammary gland is a modified sebaceous gland and identifying patients with ectodermal dysplasia in the antenatal period makes anticipation of the problem with breast feeding possible.

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Instructions to Authors

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