Year 2014 Volume 01 Issue 01 (April - June)

ISSN– 2349-3178 (Print)
ISSN– 2349-3186 (Online)

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INTERNATIONAL JOURNAL OF MEDICAL SCIENCE RESEARCH AND PRACTICE
Print ISSN: 2349-3178 Online ISSN: 2349-3186

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International Peer Reviewed Medical Journal Committed for Excellence

Bringing Together Research and Practice

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EDITORIAL

Received on 14 May 2014 Accepted on 18 May 2014 Published on 22 May 2014

Research, to be meaningful to the community, should be able to affect or mold the practice of medicine, favorably. It is in this context that the *International Journal of Medical Science Research and Practice* (freely available at *http://www.ijmsrp.com/)* is being launched and I feel proud to be writing the inaugural editorial. The aim of the journal is to bring together the researcher and the practitioner on the same platform, so as to build up the providers, expertise, and capacity for evidence-informed practice. IJMSRP is a quarterly, open access, peer reviewed journal with wide scope of subjects, i.e. basic medical science subjects (anatomy, physiology, biochemistry), para-clinical subjects (pathology, microbiology, pharmacology, forensic medicine, community medicine); and clinical sciences (medicine, surgery, obstetrics gynecology, orthopedics, pediatrics, ophthalmology, otolaryngology, psychiatry, dermatology, medical ethics, and medical education) etc. Professionals of all levels should benefit from the wide range of high quality, accessible articles published in this journal.

What constitutes research and what kind of research deserves to be published is a never-ending debate. To me, every research is pertinent and merits publication as long as it is ethical, relevant (to be able to have an impact on practice of the specialty) and topical (applicable to current needs). The basic idea of a research is to clear doubts. The generalizability of the results would, however, depend upon the robustness of the methodology adopted to answer the research question. As there can be different paths to reach a destination, there can be several methodologies to answer a research question. Mount Everest has been conquered through various routes, and yet a perfect route is yet to be discovered—the 'perfect route' here referring to one where the mountaineer doesn't face death, illness or any other hindrances in achieving the goal. Such a route may, perhaps, never be discovered yet the mighty peak will continue to be the attraction of the climbers, to satisfy their passion of adventure. Same is true for research; all methods have one/another flaw and thus there is no method 'too perfect' to answer a research question. Knowing that fully well, we seek answers, even though they may not be the ultimate unchallengeable truth to the research question, relevant to the practice of medicine. It is a boon in disguise that no research is perfect. Had it been, there would be no new hypotheses, no new postulates, and no new theories to work upon.

Another question is “whether every research has to be novel”? Papers are often rejected for the lack of novelty. The editors look for a novelty not only in the research question, but equally so in the methods undertaken to solve this question. This may need some debate. Repetition of older experiments is also essential, not only to validate the earlier findings, but also to find out whether the results would change with change in setting of the study or experiment, or over a period of time. At the same time, a novel twist in the selection of participants, inclusion criteria, tools, case-definitions, outcome measures, study devotion, follow-up and statistical methods can serve to bring a new dimension to research. This needs to be amply highlighted when a paper is being sent for publication, so as to quench the editor's inevitable thirst for novelty. No research question is ever too stale despite it being repeated. There can always be newer settings, different tools, diverse population groups, and novel outcome measures with the same research question. What's more important is the honesty and confidence with which the research is conducted.

For me, another desirable function of a research is that it should be able to generate more queries than it is able to answer. This is essential for a cascading and never-ending quest for knowledge. Once Mount Everest was

conquered, it was not that the mountaineers stopped scaling the peak; rather, it was pursued with more vigor, it was planned with more knowledge and it revealed more of the mountain than had been known before. Several new questions were generated during each ascent and the focus then shifted to answering these, taking into consideration new parameters for the success of a journey like the shortest route, the safest route, the most feasible route, the least use of technological assistance, a differently-abled person as the traveler, preventing mortality and morbidity related to high altitude climbing, etc. A research question therefore remains alive by leaving in its wake more questions. That is the beauty of research. The natural hierarchical progression of translational research starts with the generation of research question, execution of technical research and its transformation into operational research before being finally absorbed as a policy into the (health) system.

Fellow editors and researchers, the choice is yours. You can hunt for the perfect research, the one that efficiently gives a precise and correct answer, or you can look for the research where you are left newer questions to contend with. As for me, I believe that every research is perfect as long as it provides new dimensions, presents understandable strong evidences and admits limitations. You can look for the perfect research according to the parameters you set, but odds are, it's right in front of your eyes.

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Please cite this paper as: Gupta P. Bringing together Research and Practice. Inter J Medical Sci Res Prac 2014; 1 (1): 1-2.

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE RESEARCH AND PRACTICE
Print ISSN: 2349-3178 Online ISSN: 2349-3186

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Meropenem: Current perspective

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REVIEW ARTICLE

ABSTRACT

Meropenem is an ultra broad spectrum parenteral carbapenem with excellent safety profile and minimal drug interactions. It is effective in a variety of tissue infections. But to prevent emerging drug resistance, its use should be restricted to complicated/serious infections not amenable to other antimicrobials.

Key Words

Carbapenem, meropenem, drug resistant enterobacteriaceae (DRE).

Received on 11 May 2014 Accepted on 15 May 2014 Published on 22 May 2014

INTRODUCTION

Meropenem, a member of the carbapenem family, is an ultra broad-spectrum β-lactam antimicrobial that has been in use clinically since 1994. It covers broad range of Gram-negative, Gram-positive and anerobic bacteria. It continues to be an important option for empirical treatment of serious bacterial infections and also considered as a last resort against ESBL (extended spectrum β lactamase) producing bacilli in intensive care settings.

Pharmacology - Like other carbapenems, meropenem is stable against chromosomal and extended-spectrum β-lactamases. But unlike imipenem, it does not require concomitant administration of cilastatin to inhibit human dehydropeptidase.[1,2]

Meropenem is not absorbed orally. It is administered intravenously as an infusion (over 15-30 minutes) or bolus injection (over 3-5 minutes). It can be given intramuscularly also. It rapidly achieves therapeutic level in various tissues (colon, gall bladder, fascia, muscle, omentum, skin, lungs, heart, kidney, and gynaecological organs) and body fluids (CSF, skin blister fluids and peritoneal fluid). [1,2,3]

It is widely distributed in humans, with a volume of distribution (V D) at steady rate on the order of 15-20 L. Only 2% drug is bound to plasma protein. Its elimination $t_{1/2}$ in an adult with normal renal function is approximately one hour and in children less than 2 years of age, it is around one and half hour. It is rapidly excreted by the kidney (by both glomerular filtration and tubular secretion) with 80 % of excretion occurring within 3 hours and increasing to 95% within 8 hours of administration. In urine, 60-80% of drug is excreted as such with only 15-25 % as an inactive open β-lactam metabolite (ICI 213,689). Around 2% of drug is excreted in faeces. [1,2]

Mechanism of action - Meropenem is a bactericidal agent. By binding to the serine residue of transpeptidase (Penicillin binding protein) and rendering it inactive, meropenem interferes with bacterial cell wall synthesis. Marked affinity for multiple different PBPs, and resistance to all serine beta-lactamases explain the potent bactericidal action of meropenem against a broad spectrum of aerobic and anaerobic bacteria.[4,5]

Antibacterial Spectrum - Meropenem is active against wide range of Gram-negative (including ESBL producing) , Gram positive and anaerobic bacteria. Its in-vitro susceptibility pattern include [2,5] -

Gram-negative group - Escherichia coli , Haemophilus influenzae , Klebsiella pneumoniae , Neisseria meningitidis , Pseudomonas aeruginosa , Proteus mirabilis, Proteus vulgaris, Enterobacter, Citrobacter, and Acinatobacter. Stenotrophomonas maltophilia are inherently resistant to the carbapenems including meropenem.

Gram-positive group - Enterococcus faecalis, Penicillin susceptible staphylococcus aureus, Penicillin susceptible staphylococcus epidemidis, Streptococcus viridians (penicillin-susceptible isolates only) and

Corynebacterium diphtheriae. It is not active against E. Faecium, and MRSA.

Anaerobes- Bacteroides fragilis, Fusobacteria, Propionibacteria, Peptostreptococcus and Clostridium group.

Emerging drug resistance –Recently Gram negative rods resistant to carbapenems have been reported. Mechanisms of resistance included modified penicillin-binding protein affinity, decreased uptake of β-lactams, production of carbapenem-hydrolyzing β-lactamases, and decreased outer membrane permeability.[4,6]

Comparison of meropenem with other carbapenems and piperacillin/tazobactam – Meropenem is 2 to 4 fold more potent than imipenem against Enterobacteriaceae, including strains producing ESBLs or AmpC. Doripenem is the most potent carbapenem against Pseudomonas. Ertapenem is not avtive against pseudomonas. Piperacillin/tazobactam is more potent than carbapenems against P.aeruginosa (90% of susceptible strains versus 84% for carbapenems).[7]

Ranking of meropenem against gram-negative isolates – The overall rank order of susceptibility is: meropenem (98%) > imipenem (97%) > cefepime (95%) > tobramycin (93%) > piperacillin/tazobactam = gentamicin (92%) > ceftazidime (91%) > ciprofloxacin (87%) > aztreonam

(86%) > ceftriaxone (74%). [8]

Dosage – It depends up on age group affected, severity of infection and susceptibility pattern of organism. [5,9]

Types of infection Age group	Complicated skin and skin structure infections	Complicated intra-abdominal infections	Severe infections (Meningitis, severe sepsis), Cystic fibrosis
Adults	500mg per 8 hour	1000mg per 8 hour	2000mg per 8 hour
Infants (>3months) and children	10mg/kg per 8 hour	20mg/kg per 8 hour	40mg/kg per 8 hour

Dosage adjustments

Renal failure - Plasma clearance of meropenem correlates with creatinine clearance, mandating dosage adjustments in renal impairment.

Recommended dosage in patient with impaired renal function. [2]

Creatinine clearance (ml/min)	Dose (dependent on type of infection)	Dosing interval
26 – 50	Recommended dose	Every 12 hours
10 – 25	½ of recommended dose	Every 12 hours
< 10	½ of recommended dose	Every 24 hours

Hepatic impairment – Dose adjustment is not required, as liver disease has no effect on the pK of meropenem.

Geriatric patients - . In elderly patients, age-related decline in renal function leads to delayed and decreased clearance of meropenem. So dosage adjustment is required when creatinine clearance is less than 50ml/min.

Hemodialysis – A certain amount of meropenem and its metabolite is lost through hemodialysis, requiring supplemental dose after the procedure.

Therapeutic use - To reduce the development of drug-resistant bacteria and to maintain the effectiveness of meropenem, it should only be used to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.

Meropenem is approved for use in complicated intra-abdominal infection, complicated skin and skin structure infection, bacterial meningitis, nosocomial pneumonia, community-acquired pneumonia septicaemia, febrile neutropenia, complicated urinary tract infection (UTI), obstetric and gynaecological infections, and in cystic fibrosis patients with pulmonary exacerbations. [10]

Adverse drug reactions - In a review of over 6000 patients treated with meropenem, the most common adverse events were diarrhoea (2.5%), rash (1.4%) and nausea/vomiting (1.2%). Overall incidence of adverse events was less than 3%. Initially meropenem was thought to provoke seizure in CNS disorder patients especially meningitis. But in recent studies no new cases of drug related seizure were reported. The most frequent meropenem-related laboratory adverse events were thrombocytosis (1.6%) and increased hepatic enzymes (1.5-4.3%). [11,12]

Penicillin allergy and Meropenem - In individuals sensitive to β lactam group, there is a risk of fatal anaphylaxis with meropenem. But Cunha et al in their study done in 110 penicillin allergic patients reported little or no potential cross reactivity between meropenem and penicillins even in patients with a definite history of anaphylactic reactions to penicillins.[13]

Drug interactions-

Aminoglycosides and meropenem- Uually an additive or synergistic effect is observed against Gram-negative species when meropenem is used in combination with an aminoglycoside.[14]

Vancomycin or Teicoplanin and meropenem – Synergism is observed against Staphylococcus aureus (MSSA), MRSA and Staphylococcus epidermidis. [14]

Rifampicin, cotrimoxazole or ciprofloxacin and meropenem – Synrgism or addition is observed against MSSA, MRSA, and Staphylococcus epidermidis. [14]

Valproic acid and meropenem– Like other carbapenems, meropenem rapidly decreases serum level of Valproic acid to subtherapeutic level. Concomitant administration of both drugs should be avoided, and if unavoidable serum level of Valproic acid should be monitored and therapeutic level should be maintained.[15]

Clavulanic acid and meropenem- The combination of

meropenem with clavulanate has high in vitro antimycobacterial activity against extensively drug-resistant Mycobacterium tuberculosis strains. This combination along with linezolid has been successfully used to treat an advanced extensively drug-resistant tuberculosis disease with complex second-line drug resistance in a case report. [16]

Probenecid and meropenem– Probencid increases $t_{1/2}$ of meroepenem by around 33% by competitively inhibiting tubular secretion of meropenem. [17]

CONCLUSION

Despite in clinical use for around two decades, meropenem has excellent activity against wide range of bacteria especially ESBL producing gram negative bacilli. But recently few strains of gram negative bacilli have developed resistance to it, so it should be reserved for serious bacterial infections. Its use as initial empirical therapy should be implemented only after consideration of local surveillance data and patient characteristics, and once the susceptibility results are available, therapy should be narrowed.

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Please cite this paper as: Goyal VK, Rajput S S. Meropenem: Current perspective. Inter J Medical Sci Res Prac 2014; 1 (1): 3-5.

ACKNOWLEDGEMENTS

Nil

PEER REVIEW

Double Blinded externally peer reviewed.

CONFLICTS OF INTEREST

Nil

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE RESEARCH AND PRACTICE
Print ISSN: 2349-3178 Online ISSN: 2349-3186

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Proton Pump Inhibitors in Gastroesophageal Reflux in Preterms: A Review

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REVIEW ARTICLE

ABSTRACT

Objectives

Gastroesophageal reflux is primarily physiological in newborns, especially in prematures less than 34 weeks of gestation. Recently there has been a surge in the use of anti reflux medications especially proton pump inhibitors to treat significant reflux in newborns the rewards of which are questionable and hence their use needs to be addressed

Material and Methods

A PubMed search was done using the key words "gastroesophageal reflux"[all fields] and "preterm"[all fields] and/or "term" [all fields] and/or "newborn"[all fields]. The articles included were randomized trials, prospective studies, retrospective studies, review articles and observational studies.

Conclusion

As per current evidence, the risk to reward ratio of proton pump inhibitors does not favour it to be routinely recommended for treatment of gastroesophageal reflux in preterm newborns.

Key Words

Gastroesphageal reflux, Preterm, Newborn, Proton pump inhibitors

Received on 15 May 2014 Accepted on 18 May 2014 Published on 22 May 2014

INTRODUCTION

Gastroesophageal reflux is common in preterm infants with a reported incidence of 22% in babies below 34 weeks of gestation.[1] Gastroesophageal reflux occurs on an average of 3-5 times per hour but to what extent is it a clinical problem remains a question, as many babies may just be happy spitters. [2]

A number of factors may contribute to this scenario: relatively abundant milk intake, supine posture which promotes the passage of liquid gastric contents into oesophagus, immature oesophageal motility and poor oesophageal clearance.[3] Though primarily physiological due to above factors, significant gastroesophageal reflux in preterm infants may lead to failure to thrive[4] and prolonged hospital stay.[5]

Though the management of gastroesophageal reflux in newborns remains controversial, there has been a recent surge in empirical use of antireflux medications both during hospital stay and after discharge.[6] Pharmacological therapy such as H2 blockers have been associated with higher incidence of necrotizing enterocolitis[7], other infections (sepsis, pneumonia and UTI), and fatal outcome in VLBW.[8] Corvaglia et al in their study has demonstrated that of all the gastroesophageal reflux episodes in newborns, 76% were due to non acid reflux as compared to 24% due to acid reflux.[9] However, most pharmacological therapies act on acid reflux and thereby the risk to reward ratio may not be beneficial.

This review aims to bring together evidence on potential benefits and adverse effects of proton pump inhibitors, a common class of antireflux medication, in gastroesophageal reflux in preterms.

MATERIAL AND METHOD

The data and material collected by A PubMed search done using the key words "gastroesophageal reflux"[all fields] and "preterm"[all fields] and/or "term" [all fields] and/or "newborn"[all fields]. The articles included were randomized trials, prospective studies, retrospective studies, review articles and observational studies.

DISCUSSION

Proton pump inhibitors act as blockers of gastric proton pump which catalyses the final phase of acid secretary process, hindering both basal and stimulated acid secretion by parietal cells.

Since the therapeutic failure of H_2 blockers, use of proton pump inhibitors has significantly increased over the last ten years.[10] Apart from esomaprazole, none of the proton pump inhibitors are approved for use in infants (<one years of age). Esomaperazole has recently gained the indication for the short term treatment of erosive oesophagitis in infants from one to twelve months. Data with regards to proton pump inhibitors use in newborns is scant let alone in premature babies. Omari et al administered omeperazole in preterms at a dose of 0.7mg/kg/dose noted a significant decrease in acid gastroesophageal reflux frequency and of overall degree of oesophageal acid exposure, however there was no clinical benefit in the studies population.[11] Another study by Orenstein et al assessed the efficacy of lansoperazole versus placebo on a large cohort of term and preterm newborns (symptomatic infants) showing no significant advantage in symptoms due to gastroesophageal reflux such as crying, regurgitation, refusal to feed, back arching, wheezing etc.[12] On the other hand a higher incidence of lower respiratory tract infection was observed in the study group. Recently, another study by Omari et al to assess the effectiveness of esomeprazole in both term and preterm newborns showed acid bolus reflux episodes were reduced on therapy (median 30 vs 8, $P < .001$), as was the reflux index (mean % time esophageal pH < 4, 15.7% vs 7.1%, $P < .001$).[13]The number of gastroesophageal reflux symptoms recorded over 24 hours was also lower on therapy (median 22 vs 12, $P < .05$). However, as the sample size was small (26 infants) and the study was not placebo controlled the results need to be studied further.[13] Kierkus et al in a recent study using pantoprazole at a dose 1.2mg/kg have reported improved acid gastroesophageal reflux and median clearance time in an open label study after five consecutive daily dosage and was generally well tolerated for 6 weeks, though more than half of cohort showed anemia, hypoxia and constipation was observed. Since, preterms were not separately studied in the study, the results cannot be extrapolated to this group.[14]

Proton pump inhibitors can cause delay in gastric emptying,[15] inhibit neutrophil migration[16] and decrease gastric mucosal activity.[17] It should be noted that gastric pH physiologically decreases with increase in gestation.[18] Accordingly a higher incidence of intragastric bacterial infection has been reported in association with proton pump inhibitors therapy.[19] Hence, administering proton pump inhibitors to preterms who already have a lower pH may make them more susceptible for infections such as NEC. More et al in a recent systematic review showed that inhibitors of gastric acid secretion are associated with significantly increased risk of NEC (odds ratio [OR]: 1.78, 95% confidence interval [CI]: 1.4, 2.27, $p < 0.00001$).[20]

As most of the studies with respect to gastroesophageal reflux have not studied preterms separately from term newborns and since of the evidence available, majority deals with both H2 blockers and proton pump inhibitors (both in effects and side effects), further studies are needed before proton pump inhibitors can be recommended in this age group for the treatment of gastroesophageal reflux.

CONCLUSION

As per current evidence, the risk to reward ratio of proton pump inhibitors does not favour it to be routinely recommended for treatment of gastroesophageal reflux in preterm newborns. Further trials need to be undertaken to ascertain their role in gastroesophageal reflux in preterm population with regards to mortality, chronic lung disease, infections (especially NEC) and duration of hospital stay.

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Please cite this paper as: Verma N, Pancholi R, Verma R. Proton Pump Inhibitors in Gastroesophageal reflux in Preterms: A Review. Inter J Medical Sci Res Prac 2014; 1 (1): 6-8.

ACKNOWLEDGEMENTS

Nil

PEER REVIEW

Double Blinded externally peer reviewed.

CONFLICTS OF INTEREST

Nil

FUNDING

Nil

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE RESEARCH AND PRACTICE
Print ISSN: 2349-3178 Online ISSN: 2349-3186

UNIT OF AXIS JOURNALS

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Evaluation of Lung Function by Spirometry in 12-14 yrs Adolescents in schools of Raipur city Chhattisgarh

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ORIGINAL RESEARCH

ABSTRACT

Aim

The study was carried out in normal school children in Raipur city to determine pulmonary functions in the age group 12-14 years.

Background

Spirometry is an important tool for assessment of lung function by evaluating forced vital capacity (FVC), forced expiratory volume in first second (FEV1), the ratio of FEV1 to FVC, peak expiratory flow rate (PEFR). Indian norms for spirometric test values are different from Western and other norms. Even within the country the test values differ between different regional and ethnic groups.

Material Methods

This is a cross sectional analytical observational study. 267 subjects were evaluated through pulmonary function test by Spirometry. Results were expressed as Mean ± SEM (Standard error of mean). Pearson's correlation coefficient(r) is calculated between dependent and independent variables. Prediction equations were developed using the multiple linear regression procedure.

Results

In our study spirometric parameters for boys were higher than girls. All Spirometric values were found to increase in relation to increase in height in both girls and boys except for the FEV1 %. All Spirometric values were found to increase in relation to increase in Age (12 to 14 years) in both girls and boys except for the FEV1 %.

Conclusion

This study shows, all the independent variables (age, weight, height and BSA) have linear positive correlation with lung function parameters, both for boys and girls. Height is the most important and reliable single independent variable. Regression equations for spirometry variables for region have been developed.

Key Words

Forced Vital Capacity (FVC), Forced Expiratory Volume in First Second (FEV1), Peak Expiratory Flow Rate (PEFR)

Received on 06 May 2014 Accepted on 15 May 2014 Published on 22 May 2014

INTRODUCTION

Studies shows Indian norms for spirometric test values [1,2,3,4] are different from Western and other norms since the lung functions are affected by known variables such as age, stature, gender, ethnic group, and environmental conditions therefore correct interpretation of pulmonary function data requires use of locally developed prediction equations. The reference values of pulmonary function tests and regression equations are available for Caucasian, Negroid, Aboriginal and Chinese children[5,6].

No study till date was reported from Chhattisgarh region, hence we carried out a study to find out basic norms of pulmonary function tests in the healthy school children of Raipur city Chhattisgarh in the age group of 12 to 14 years and to find its correlation with regards to age, sex, height and weight and to develop regression equations for spirometry.

MATERIAL AND METHOD

This Cross sectional analytical observational study was conducted in the Schools of Raipur city during year July 2012 to July 2013. The study was approved by the Institutional Ethics Committee. Objectives & method of study was fully explained & informed consent was taken from subjects parents prior to start of the study. The subjects were evaluated through pulmonary function test by Spirometry method using schiller spirovit sp-1 Switzerland spirometer. A total of 267 subjects aged between 12-14 years were included in the study. Age in years, gender, weight, standing height, Body surface area (BSA) were recorded using standard method at the time of the testing.

Sample size Calculated by using WHO sample size determination in health studies. The estimated sample size was 267 with 95% Confidence level and 0.50 anticipated population proportions with 0.06 of absolute precision. Subjects having past history of chronic disease viz. pulmonary T.B. or having respiratory tract infection at the time of study, structural deformity of thoracic cage, Students < 12 yrs & >14 yrs were excluded from study.

Statistical Analysis

Results were expressed as Mean ± SEM (Standard error of mean). Pearson's correlation coefficient(r) is calculated between dependent and independent variables. Two tailed p-values were used throughout and p-values < 0.05 were judged statistically significant. Statistical analysis was carried out using statistical package for the social sciences (SPSS) 19.0 and Graph Pad Prism 6 software's. Analysis was carried out separately in boys and girls.

In the present study, the dependent variables were FVC, FEV1, and PEFR. Prediction equations were developed using the multiple linear regression procedure. Linear and nonlinear models were developed and the former was selected based on criteria of simplicity and ease of clinical application, high predictive capability (R^2) and yield of smallest residuals. The independent variables were height, age and weight & BSA. Regression equation was derived for spirometric variable FVC, FEV1 & PEFR for girls and boys separately.

RESULT

Total numbers of subjects in our study were 267. Boys were 109(40.82%) and Girls were 158(59.18%). In 12 years age group total subjects were 73 (27.34%), in 13 years 102 (38.2%) and in 14 years 92 (34.46%).

Table 1 shows in study group mean age was 13.07 years with SEM 0.048 and 95% CI was 12.98 - 13.17. Mean weight was 41.49 kg with SEM 0.41 and 95% CI 40.68 – 42.30. Mean Height was 149.64 cm SEM 0.55 and 95% CI was 148.55 – 150.73. Mean BSA was 1.31 with SE 0.008 and 95% CI was 1.29 – 1.33. Mean Age ±SEM for Boys were 13.14±0.07 and for Girls were 13.03±0.06 with Z-value of 1.17 and P value of 0.24. Mean Weight ±SEM for Boys were 42.93±0.67 and for Girls were 40.50±0.51 with Z-value of 2.91 and P value of 0.004. Mean Height ±SEM for Boys were 152.09±0.85 and for Girls were 147.95±0.69 with Z-value of 3.76 and P value of <0.001. Mean BSA ±SEM for Boys were 1.34±0.013 and for Girls were 1.29± 0.01 with Z-value of 3.31 and P value of <0.001.

Table 1 shows In study group mean FVC was 2.4 L with SEM 0.025 and 95% CI was 2.35 – 2.45. Mean FEV1 was 2.67L with SEM 0.025 and 95% CI 2.62 – 2.72. Mean FEV1% was 94.37 % with SEM 0.213 and 95% CI was 93.95 – 94.79. Mean PEFR was 5.50 L/Min with SE 0.059 and 95% CI was 5.38 – 5.62. In study group mean ±SEM FVC for Boys was 2.53±0.039 L and for Girls was 2.31±0.031 with Z value of 4.23 and P value <0.001. Mean ±SEM FEV1 for Boys was 2.39±0.038 L and for Girls 2.18±0.030 with Z value of 4.19 and P value of <0.001. Mean ±SEM FEV1% for Boys was 94.53±0.351 % and for Girls 94.26± 0.266 % with Z value of 0.61 and P value of 0.54. Mean PEFR±SEM for Boys was 5.80±0.090 L/Sec and for Girls 5.29±0.073 with Z value of 4.36 and P value <0.001. In our study spirometric parameters for boys were higher than girls. Mean FVC, FEV1 & PEFR for boys was higher (2.53, 2.39, 5.80) than girls (2.31, 2.18, 5.29).

Table 2a & 2b shows Correlation of FVC, FEV1 & PEFR with different independent variable Age, Height, and Weight & BSA found significant for both boys & girls. The correlation coefficient (r) was more than 0.5 for all four variable with P value <0.001 which is highly significant. Correlation of FEV1% with different independent variable Age, Height, Weight & BSA was not significant for both boys & girls Except for the age in girl which was found significant with p<0.05.

Table 3 shows All Spirometric values were found to increase in relation to increase in height in both girls and boys except for the FEV1 %.

Table 4 shows Regression equation for prediction of lung function values (FVC, FEV1, PEFR from independent variable (height) for boys and girls were performed (Table IV) using Equation: Spirometric parameter = Constant + (β Coefficient for age x age in years) + (β Coefficient for weight x weight in Kg) + (β Coefficient for height x height in cm) + (β Coefficient for BSA x BSA in m2). In this study nomogram of FVC and FEV1 for boys and girls were constructed on the basis of regression equation (Table V), where height was considered as independent variable.

DISCUSSION

Forced vital capacity (FVC) represents by lung dimension, compliance and respiratory muscle power whereas PEFR is determined by alveolar caliber, alveolar elastic recoil and respiratory muscle efforts[7,8]. Lung volumes and flow rates measured by means of spirometry should be interpreted in relation to proper reference values. It is well known that ethnicity, sex, age, and height are the key factors affecting the spirometric parameters. India is a subcontinent with varying

geography and with a large multi-ethnic population; regional differences in lung functions in healthy Indians can thus be expected[9,10,11].

No study has been conducted in this region of India so the purpose of this study was to derive the prediction formula for estimation of the expected values of lung function of the healthy school children aged 12-14 years based on height, weight, age, BSA and sex residing in Raipur city Chhattisgarh and to calculate regression equations. The limitation of the study was multicentric study with participation of other cities of the region was not feasible because of limited resources.

In our study All Spirometric values were found to have linear positive correlation with height and age in both girls and boys except for the FEV1 %, whereas weight shows positive correlation with all lung function parameter. Lung function values in boys were found to be significantly higher as compared to girls. Height was the most important and reliable single independent variable shown to have maximum coefficient of correlation. Other studies conducted by Rajkapoor et al and Chowgule et al showed similar relationship.

Present study found a statistically significant difference in lung function between both sex groups. Lungs functions were higher in boys as compared to that of girls ($P<0.05$). These results were comparable with the study done by Rajkapoor et al [10] in which they found that mean lung function test was higher in boys than in girls.

The values of lung function in present study are slightly more than the study conducted by TaheraH et al [16] probably because of regional variation but are comparable with the study conducted by SK Chhabra et al [12] & Chowgule et al[9].

The values obtained by Rosenthal et al[10] while studying the lung function in white girls were higher than those obtained in the present study except PEFR probably because of difference in anthropometric variables. Mean FVC and FEV 1 values for comparable heights in each age group were greater for boys than for girls as reported earlier. These results indicate that lung capacity differs by sex irrespective of body built.

We have presented prediction equations for various spirometry parameters for children Chhattisgarh region between the ages of 12 to 14 years. The FVC, FEV1, PEFR, showed moderate to strong correlations with age, height and weight in both boys and girls. The values of different lung functions, both obtained and predicted, in the present work were compared with other Indian and foreign studies shown in Table 5 [12-18].

Our values were found to be consistently lower than their age matched counterparts in children of American blacks, European and Australian origin [5]. Hence the same sets of references as used for Indian children are not applicable to these children. We applied additional stepwise multiple regression analysis to develop prediction equations separately for boys and girls incorporating age, height, weight, and BSA. We assume that these prediction equations could be fairly applied to the Raipur city Chhattisgarh population within this age range. Environments and technical factors, such as equipments and maneuvers could be the sources of variance.

CONCLUSION

Measurement of lung function is an important part of current management of various pulmonary diseases. We have presented reference data which help to interpret the observed lung function values in healthy school children of Chhattisgarh aged 12-14 years. We recommend further active research to establish individual population based regression equations to predict lung volumes and flow rates.

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Please cite this paper as: Singh V [1], Kurrey VK[2], Khandwal O[3], Phuljhele S[3]. Evaluation of Lung Function by Spirometry in 12-14 yrs Adolescents in schools of Raipur city Chhattisgarh . Inter J Medical Sci Res Prac 2014; 1 (1): 09-15.

ACKNOWLEDGEMENTS

Nil

PEER REVIEW

Double Blinded externally peer reviewed.

CONFLICTS OF INTEREST

Nil

FUNDING

Nil

Table 1 - Anthropometric parameters and Spirometry value

Anthropometric parameters of subjects in study group (n=267)				Anthropometric parameters of boys & girls in study group							
				Boys (n=109)			Girls (n=158)			Z-value	P*
Variable	Mean	SEM	95% CI	Mean	SEM	95% CI	Mean	SEM	95 % CI		
Age	13.07	0.048	12.98 - 13.17	13.14	0.07	13.0 – 13.28	13.03	0.06	12.9 – 13.16	1.17	0.24
Weight	41.49	0.41	40.68 – 42.30	42.93	0.67	41.70 – 44.25	40.50	0.51	39.51 – 41.49	2.91	0.004
Height	149.64	0.55	148.55 – 150.73	152.09	0.85	150.4-153.78	147.95	0.69	146.57-149.33	3.76	<0.001
FVC	2.40	0.025	2.35 – 2.45	2.53	0.039	2.45 – 2.61	2.31	0.031	2.25 – 2.34	4.23	<0.001
FEV1	2.67	0.025	2.62 – 2.72	2.39	0.038	2.32 – 2.47	2.18	0.030	2.15 – 2.21	4.19	<0.001
FEV1 %	94.37	0.213	93.95 – 94.79	94.53	0.351	93.83- 95.23	94.26	0.266	93.99-94.79	0.61	0.54
PEFR	5.50	0.059	5.38 – 5.62	5.80	0.090	5.62 – 5.98	5.29	0.073	5.15 – 5.43	4.36	<0.001

Table 2a – pulmonary function test (Mean ±SEM) in Relation to Age

variable	12 years						13 years						14 years					
	boys			girls			boys			girls			boys			girls		
	Mean	SEM	95% CI	Mean	SEM	95% CI	Mean	SEM	95% CI	Mean	SEM	95% CI	Mean	SEM	95% CI	Mean	SEM	95% CI
FVC	2.12	0.046	2.03 – 2.21	2.04	0.037	1.96 – 2.12	2.44	0.041	2.36 – 2.52	2.29	0.044	2.20 – 2.38	2.88	0.06	2.77 – 2.99	2.60	0.046	2.51 – 2.69
FEV1	2.01	0.048	1.92 – 2.10	1.90	0.038	1.82 – 1.98	2.31	0.039	2.23 – 2.31	2.16	0.043	2.07 – 2.25	2.71	0.06	2.60 – 2.82	2.47	0.046	2.38 – 2.56
FEV1%	94.74	0.584	93.53 - 95.95	93.31	0.508	92.29 – 94.33	94.86	0.563	93.73 – 95.99	94.45	0.497	93.46 – 95.45	94.01	0.63	92.73 - 95.29	94.93	0.344	94.24 – 95.62
PEFR	4.84	0.122	4.59 – 5.09	4.65	0.090	4.47 – 4.83	5.69	0.127	5.43 – 5.95	5.44	0.135	5.17 – 5.71	6.51	0.09	6.32 – 6.70	5.73	0.09	5.54 – 5.92

Table 2b - Correlation of FVC, FEV1 & PEFR with different independent variable

	FVC				FEV1				FEV1%				PEFR			
	Boys(n=109)		Girls(n=158)		Boys(n=109)		Girls(n=158)		Boys(n=109)		Girls(n=158)		Boys(n=109)		Girls(n=158)	
Variable	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**
Age	0.707	<0.001	0.589	<0.001	0.674	<0.001	0.599	<0.001	-0.085	0.377	0.194	0.014*	0.661	<0.001	0.468	<0.001
Height	0.868	<0.001	0.890	<0.001	0.827	<0.001	0.869	<0.001	-0.10	0.298	0.102	0.201	0.714	<0.001	0.641	<0.001
Weight	0.697	<0.001	0.747	<0.001	0.667	<0.001	0.724	<0.001	-0.063	0.513	0.065	0.416	0.523	<0.001	0.504	<0.001
BSA	0.779	<0.001	0.834	<0.001	0.744	<0.001	0.810	<0.001	-0.075	0.436	0.079	0.322	0.599	<0.001	0.576	<0.001

P<0.05 significant Z value > 1.96 significant p value- Significance(2tailed) r-correlation coefficiant

Table 3-Lung function test (Mean ±SEM) in Relation to Height

Height(cm.)	No.(n=267)		Age		FVC		FEV1		FEV1%		PEFR	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
121-130	-	04	-	12 ±00	-	1.71 ±0.01	-	1.63 ±0.02	-	93.75 ±1.56	-	3.95 ±0.05
131-140	12	32	12.42 ±0.15	12.38 ±0.09	2.01 ±0.06	1.89 ±0.03	1.91 ±0.06	1.77 ±0.03	95.11 ±0.82	94.03 ±0.61	4.77 ±0.22	4.47 ±0.09
141-150	40	61	12.80 ±0.10	12.97 ±0.10	2.27 ±0.03	2.21 ±0.03	2.15 ±0.04	2.08 ±0.03	94.66 ±0.53	94.25 ±0.41	5.24 ±0.11	5.26 ±0.11
151-160	35	48	13.34 ±0.12	13.38 ±0.10	2.68 ±0.04	2.59 ±0.02	2.54 ±0.05	2.44 ±0.03	94.56 ±0.71	93.93 ±0.53	6.31 ±0.13	5.81 ±0.11
161-170	21	13	13.81± 0.009	13.92 ±0.08	3.02 ±0.07	3.00 ±0.05	2.84 ±0.06	2.88 ±0.05	93.52 ±0.85	96.23 ±0.67	6.54 ±0.11	5.99 ±0.15
171-180	01	-	14 ±00	-	3.11 ±00	-	2.91 ±00	-	93.57 ±00	-	6.90 ±00	-

Table 5- Comparisons from other studies

	Present study		Tahera H et al		PP Sharma et al		Rajkapoor et al		SK Chabra et al		Chowgule et al		Rosenthal et al	
	Boys (n=109)	Girls (n=158)	Boys	Girls	Boys	Girls	Boys	Girls	Boys (n=365)	Girls (n=305)	Boys	Girls	Boys	Girls
Age	13.14	13.03	10.68 ± 1.34	10.63 ± 1.33					11.53±3.37	11.74±3.23				
Weight	42.93	40.50	35.73 ± 8.83	35.0 ± 8.91					44.56±18.42	40.97±13.82				
Height	152.09	147.95	142.34 ± 9.67	141.72 ± 9.56					1.49±0.18	1.45±0.14				
FVC	2.53	2.31	2.01 ±0.46	1.91 ± 0.47	2.29 ±0.8	1.91 ± 0.8,	1.63 1.47	1.63 1.47	2.88 ± 1.09	2.42 ± 0.72	2.54 - 1.94	2.54 - 1.94	2.82 - 2.17	2.82 - 2.17
FEV1	2.39	2.18	1.76 ±0.38	1.688 ± 0.40	2.15 ±0.6	1.86 ± 0.80	1.49 1.37	1.49 1.37	2.43 ±0.94	2.14 ± 0.65	2.26 - 1.77	2.26 - 1.77	2.36 - 1.91	2.36 - 1.91
PEFR	5.80	5.29	4.74 ± 0.96	4.47 ± 1.15	4.54 ± 1.0	4.30 ±1.3	3.845	3.633	5.47 ±2.02	5.0 ± 1.46	5.40 - 4.33	5.40 - 4.33	497 - 4.27	497 - 4.27

Table 4-Regression equations for spirometry parameters

Spirometry Constant	constant		βcoefficient for Age		βcoefficient for Weight		βcoefficient for Height		βcoefficient for BSA		Standard Error of Estimate		R^2	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
FVC	-3.873	-3.124	0.117	0.031	0.112	0.090	0.061	0.052	-6.831	-4.867	0.193	0.166	0.788	0.820
FEV1	-3.463	-3.180	0.109	0.048	0.085	0.085	0.050	0.049	-5.095	-4.616	0.216	0.180	0.715	0.784
PEFR	-7.868	-4.667	0.400	0.136	0.466	-0.115	0.191	0.015	-3.272	8.235	0.621	0.706	0.584	0.424

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE RESEARCH AND PRACTICE
Print ISSN: 2349-3178 Online ISSN: 2349-3186

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Comparative study of various techniques to measure neonatal hypothermia

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ORIGINAL RESEARCH

ABSTRACT

Aim

To compare different available modes (forehead infrared thermometer ,axillary temperature by thermister probe and digital thermometer, with axillary temperature by gold standard mercury thermometer) of temperature measurement in neonatal hypothermia in order to come out with most accurate one among them.

Background

Hypothermia is very important in essential newborn care as it can lead to mild to severe life threatening complication, so detecting hypothermia takes important role in its management.

Material Methods

Study Design: Setting was Neonatal Intensive Care Unit (Level 3), Kamla Raja Hospital ,Gajra Raja Medical College, Gwalior, India. A Prospective study of one year (July 2010 - June 2011) duration done with 1690 admissions of neonatal intensive care unit (full fill inclusion criterion) by applying Fisher test on 2×2 contingency table to get sensitivity , specificity , positive predictive value , negative predictive value and accuracy of above 4 methods by STATA 9.1 (STATA corporation, college station , TX, USA).

Results

Digital thermometer is having highest sensitivity (99.1%), specificity (98.1%), positive predictive value (97.4%) and negative predictive value(99.3%).

Conclusion

Digital axillary thermometry is the best alternative to mercury thermometer for measuring neonatal temperature compared with axillary temperature by thermister probe and forehead temperature by infrared thermometer.

Key Words

Neonatal temperature recording, Digital thermometer, Forehead infrared thermometer, mercury thermometer, Thermister probe.

Received on 15 May 2014 Accepted on 20 May 2014 Published on 22 May 2014

INTRODUCTION

Measurement of body temperature is one of the oldest known diagnostic methods and still remains an important indicator of health and disease, both in everyday life and in medical care.[1] Measuring body temperature is routinely performed in health care services, and can use different measuring instruments. The use of body temperature measurement and monitoring, in the oldest references in the first or second century BC and in 1592 Galileo manufactured a thermometer.[2]

Temperature regulation of neonate is of vital importance for their survival and well-being. It is important to assess the neonate at birth and maintain temperature within normal range because the neonates are prone to develop hypothermia after birth due to change in environmental temperature and various factors. These factors include following;

Large surface area as compared to body weight. Their surface area of head is 25% vs 10% in adults

Poor insulation for conservation of heat due to thin layer of subcutaneous fat

Non-shivering thermo genesis which involves increased metabolism and oxygen consumption

Reduced amount of brown fat[3]

Hypothermia is common in infant born at hospital (prevalence range 32%-85%) and home (prevalence range 11%-92%) even in tropical environment. Hypothermia contributed to substantial proportion of neonatal mortality globally, mostly as a co morbidity of severe neonatal infection, preterm birth and asphyxia. Addressing hypothermia might play a substantial role in reaching Millennium Development Goal 4, a reduction of child mortality.[4]

Hypothermia is very important in essential new born care as it can lead to mild to severe life threatening complications so detecting hypothermia takes important role in its management. But with advent of newer methods of temperature measurement like infrared and digital thermometer ,there is a need to find out most accurate one among them .As lot of studies going on regarding validation of these newer techniques,[5,6] we aimed to take three common methods and compared with gold standard axillary temperature by low reading mercury thermometer .

MATERIAL AND METHOD

Ethical Approval: Study protocol was reviewed and approved by Ethical committee of the Medical College.

Study design: cross-sectional, analytic in tertiary care Medical College Hospital

Subjects: 1690 Neonates admitted in NICU over a period of one year

Exclusion criteria:

1.Neonates with major congenital anomalies (e.g. gastroschisis, omphalocele)

2.Neonates with severe birth asphyxia (Levene Score).

Consent: Informed consent of parent or guardian was taken prior to enrolling the neonate.

Materials used:

1.Low reading Medical mercury thermometer (up to 32 °C)

2.Thermister probe (product of Zeal ,<40°C)

3.Digital thermometer (product of Dr.Morepen ,up to 32 °C)

4.Infrared thermometer (HT-F03B Forehead temperature IR thermometer <100°C)

Methodology:

Temperature of each neonate was recorded by 4 different methods as described below

1.Low reading medical mercury thermometer: device cleaned with cotton swabs; shaken to get the mercury column at starting point. Axilla of neonate was dried with cotton and bulb of thermometer was kept at tip of axilla for 5 minutes, babies arm was held close to the body to keep thermometer in place and the reading was taken at eye level and recorded.

2.Digital thermometer: After switching the device on, and drying the axilla of neonate and the tip of digital thermometer was placed at apex of axilla and neonate's arm was held close to the body to keep thermometer in place until there was a beep from instrument indicating it had finished taking temperature and the reading was noted down. Less than 32 °C was shown as Low, for the rest we had reading displayed.

3.Thermister probe: Once the baby was kept on cot of radiant warmer, axilla was dried and thermister probe was placed at the apex of it, until the flashing temperature reading over monitor becomes static and that temperature was noted down.

4.Forehead Infrared Thermometer: It is specially designed with Heiman Infrared probe for measuring forehead temperature, with dynamic offset for the ambient temperature and forehead temperature. To measure the temperature ,window of instrument was aligned in the direction of forehead at distance of 50-100mm,and measure button pushed to get reading on LED screen , which was noted down (as per manufacturer instruction).

Statistical analysis:

Data was compiled in to on 2×2 contingency table and fisher test was applied to get sensitivity , specificity , positive predictive value , negative predictive value and accuracy of above 4 methods by STATA 9.1 (STATA corporation, college station , TX, USA)[7].

RESULT

Out of 1690 neonates 700 neonates were found hypothermic by low reading clinical thermometer. Thermister probe was in agreement for 681 neonates (True positive 681) but there was mismatch in 19 hypothermic neonates whom Thermister probe found normothermic (False negative 19). Out of 990 normothermic neonates as per low reading clinical thermometer Thermister probe was in agreement for 944 neonates (True negative 944) , and there was mismatch in 46 normothermic babies (False positive 46) whom Thermister probe found hypothermic. (Table I)

Table I: Diagnostic accuracy of Axillary temperature by Thermister probe (Standard: Low reading Mercury Thermometer)

Method		Hypothermia	Normal	Total
Thermister probe	Positive	681 (True)	46 (False)	727
	Negative	19 (False)	944 (True)	963
	Total	700	990	1690

Out of 700 hypothermic neonates, measured by low reading clinical thermometer Digital thermometer was in agreement for 694 neonates (True positive 694) but there was mismatch in 6 hypothermic neonates whom Digital thermometer found normothermic (False negative 06). Out of 990 normothermic neonates as per low reading clinical thermometer Digital thermometer was in agreement for 972 neonates (True negative 972), and there was mismatch in 18 normothermic neonates (False positive 18) whom Digital thermometer found hypothermic. (Table II)

Table II: Diagnostic accuracy of Axillary temperature by Digital thermometer (Standard: Low reading Mercury Thermometer)

Method		Hypothermia	Normal	Total
Digital thermometer	Positive	694 (True)	18 (False)	712
	Negative	06 (False)	972 (True)	978
	Total	700	990	1690

Out of 700 hypothermic neonates, measured by low reading clinical thermometer, Infra red thermometer was in agreement for 687 neonates (True positive 687) but there was mismatch in 13 hypothermic neonates whom Infra red thermometer found normothermic (False negative 13). Out of 990 normothermic neonates as per low reading clinical thermometer Infra red thermometer was in agreement for 922 neonates (True negative 922), and there was mismatch in 68 normothermic babies (False positive 68) whom Infra red thermometer found hypothermic. (Table III)

Table III: Diagnostic accuracy of Forehead temperature by Infrared thermometer (Standard: Low reading Mercury Thermometer)

Method		Hypothermia	Normal	Total
Infrared thermometer	Positive	687 (True)	68 (False)	755
	Negative	13 (False)	922 (True)	935
	Total	700	990	1690

Overall, Digital thermometer is having highest sensitivity (99.1%), specificity (98.1%), positive predictive value (97.4%), negative predictive value (99.3%) and overall Accuracy 0.98 (Table IV).

Table IV: Comparison of Accuracy of various modes of temperature measurements (Standard: Low reading Mercury Thermometer)

	Thermister Probe	Digital Thermometer	Infrared Thermometer
Sensitivity	97.2%	99.1%	98.1%
Specificity	95.3%	98.1%	93%
Positive Predictive Value	93.6%	97.4%	90.9%
Negative Predictive Value	98.0%	99.3%	98.6%
Likely hood ratio (+)	20.9	54	14.2
Likely hood ratio (-)	0.02	0.008	0.01
Kappa	0.92	0.97	0.90
Overall Accuracy	0.96	0.98	0.95

DISCUSSION

Padilla et al observed Digital axillary thermometry in children is having sensitivity of 88.46%, specificity of 98.65%, positive predictive value of 95.83% and negative predictive value of 96.05%.[2] Uslu S et al compared the accuracy of digital axillary thermometer, rectal glass mercury thermometer, infrared tympanic thermometer and infrared forehead skin thermometer measurements with traditional axillary glass mercury thermometer for intermittent temperature measurement in sick newborns and found good correlation between digital axillary thermometry and axillary glass thermometry in sick newborns.[5] Sganga A et al compared newborn temperature measurements obtained by digital disposable, electronic and tympanic thermometers with glass mercury thermometers and observed good correlation between digital axillary thermometry and axillary glass thermometry in healthy newborns.[8] Oncel MY et also observed that digital axillary thermometry in newborns by mother and physician showed a significant correlation which suggest that axillary digital thermometry is as good for taking temperature in community setting in newborns.[9]

CONCLUSION

Overall in the present study Digital thermometer has best likely hood ratio, kappa value (0.97) and overall accuracy (0.98), followed by thermister probe and Infrared thermometer. Digital axillary thermometry is

the best alternative to mercury thermometer for measuring neonatal temperature compared with axillary temperature by thermister probe and forehead temperature by infrared thermometer. This is user and eco friendly without need of expertise, time saving and no inter observer difference. It can be recommended for both institutional and home use.

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Please cite this paper as: CD Veerbhadra, Ambey R, Gaur A, shingwekar AG. Comparative study of various techniques to measure neonatal hypothermia. Inter J Medical Sci Res Prac 2014; 1 (1): 16-19.

ACKNOWLEDGEMENTS

We acknowledge Dr GS Patel, Dean, GR Medical College for his motivation and guidance for the research work.

PEER REVIEW

Double Blinded externally peer reviewed.

CONFLICTS OF INTEREST

Nil

FUNDING

Nil

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE RESEARCH AND PRACTICE
Print ISSN: 2349-3178 Online ISSN: 2349-3186

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Anonychia congenita totalis with epilepsy and mental retardation

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CASE REPORT

ABSTRACT

Anonychia congenita is a rare disorder characterized by absence of several or all fingernails and/or toenails since birth. A 35-year-old man with mental retardation presented with a history of absence of all nails since birth. There was also a history of epileptic fits since early childhood.

Key Words

Anonychia, anonychia congenita, RSPO4 gene

Received on 18 April 2014 Accepted on 11 May 2014 Published on 22 May 2014

INTRODUCTION

Absence of nails from birth (congenital anonychia) is a rare congenital anomaly. It may occur as an isolated symptom or be a part of other developmental defects of digits or any structures,[1] which are sometimes hereditary.[2] Anonychia may not be complete and often there are rudimentary nails on some fingers and toes (hyponychia). Anonychia occur sporadically, it may have dominant or recessive inheritance pattern.[3] Very few cases have been reported till now. We herein, report a rare case of anonychia congenita totalis with epilepsy and mental retardation.

CASE REPORT

A 35-year-old product of non-consanguineous marriage presented with a history of complete absence of nails of all fingers and toes since birth. (Fig 1 & 2) There was no other associated bony abnormality of hands or feet. He was otherwise physically normal, except that he had mental retardation.

On further questioning from family members, he was found to be on treatment for epilepsy since early childhood. There was no history of any drug intake by his mother during pregnancy. His parents and other siblings were normal.

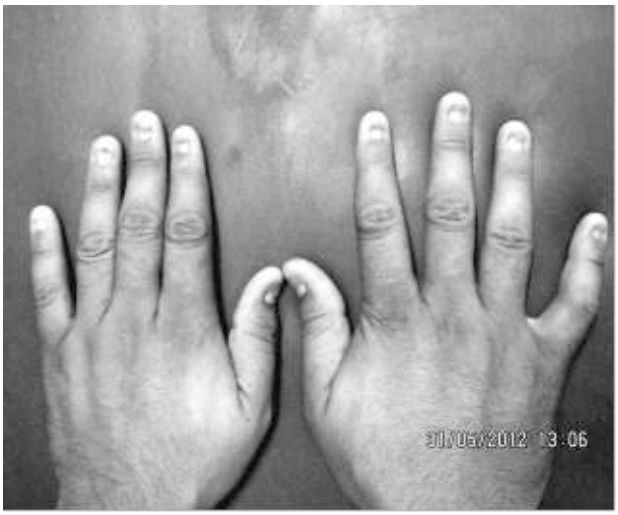

Figure 1: Hands showing absence of all nails

The skin around the absent nails was normal. Hair and teeth of the subject were also normal. Systemic examination was normal. Routine laboratory investigations including complete blood count, liver function tests, urine examination were normal. Radiological examination of hands and feet were unremarkable. Based upon the history and clinical features, a diagnosis of anonychia congenita totalis with epilepsy and mental retardation was made.

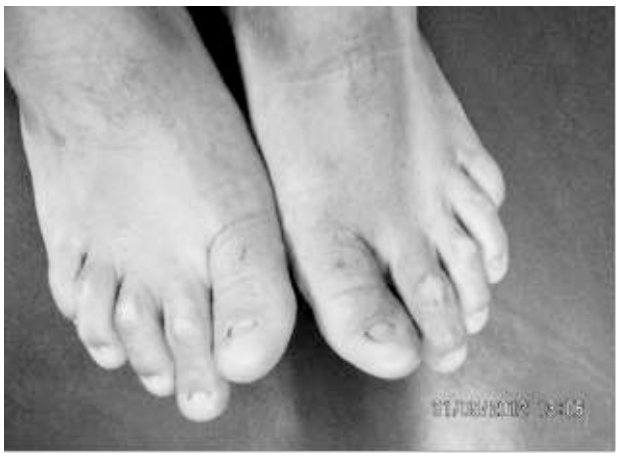

Figure 2: Feet showing absence of all nails

DISCUSSION

Anonychia congenita is an extremely rare disorder characterized by complete absence of fingernails and toenails.[1] It may occur singly or as a part of some syndromes like nail patella syndrome, hypohidrotic ectodermal dysplasia, tricho-odonto-dental syndrome, DOOR syndrome (deafness, onychodystrophy, osteodystrophy and mental retardation), AEC syndrome (ankyloblephron, ectodermal defects, cleft lip/palate), and various craniofacial malformation syndromes.[4] Simple anonychia means congenital absence of nails without any other coexisting major congenital anomaly.[5] Non-syndromal anonychia can present as partial or total anonychia. The partial form involves any thumb with autosomal dominant inheritance while the involvement of second third and fourth digits represents an autosomal recessive trait.[6]

Development of nails begins at 8-10 weeks of expected gestational age and is completed by fifth month.[4] Drugs consumed by the mother during first or second trimester are extremely significant for nail formation. Phenytoin or warfarin may cause hypoplasia of nails, while alcohol may lead to anonychia.[7] Although, mother of our patients had not taken any medicines.

Absence of nails probably represents a mesenchymal dysplasia occurring during the morphogenesis of the digits. The gene RSPO4 has been identified responsible for anonychia, which is a member of R-spondin family of secreted proteins. Due to frameshift and non-conservative missense mutation in the exon 2 of R-spondin 4 gene present on chromosome 20p13 which helps in activating the Wnt/beta-catenin signalling pathway, that affects the highly conserved first furin-like cysteine-rich domain which plays a crucial role in nail morphogenesis, resulting in absence of nails.[8] Interestingly there is no family history of anonychia in our case and this condition seems to be caused by sporadic mutation.

Several syndromic variants of this disorder have been reported in the literature.[3,5,6] Our case was unique as congenital anonychia was associated with epilepsy and mental retardation. Whether it an association or mere coincidence is a matter of debate?

CONCLUSION

As this condition does not interfere with daily activity of the affected individuals, he/she should be assured about the condition. The patients of congenital anonychia should be examined thoroughly because of possible association, some of which are mentioned above. This case is presented in view of its rarity of this condition.

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Please cite this paper as: Garg A, Garg S, Saraswat PK. Anonychia congenita totalis with epilepsy and mental retardation. Inter J Medical Sci Res Prac 2014; 1 (1): 20-22.

ACKNOWLEDGEMENTS

Nil

PEER REVIEW

Double Blinded externally peer reviewed.

CONFLICTS OF INTEREST

Nil

International Journal of Medical Science Research and Practice
pISSN: 2349-3178; eISSN: 2349-3186

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Print ISSN: 2349-3178 Online ISSN: 2349-3186

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Extensive patch type granulomas annulare: A rare case report

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CASE REPORT

ABSTRACT

A 16-year-old girl presented with multiple, asymptomatic, progressive, hyperpigmented patches of 6 months duration over trunk and thighs. Histopathology showed features of interstitial granuloma annulare. The clinical diagnosis was consistent with patch type granuloma annulare.

Key Words

Granuloma annulare, patch type granuloma annulare, interstitial pattern, palisading granuloma, necrobiosis

Received on 18 April 2014 Accepted on 12 May 2014 Published on 22 May 2014

INTRODUCTION

Granuloma annulare (GA) is a benign cutaneous disease that classically presents as localized clusters of small skin colored or erythematous papules that coalesce to form annular plaques. It was first described by Colcott Fox in 1895.[1] Lesions are typically asymptomatic with various color shades and can occur in all age groups. Other variants include generalized, perforating, subcutaneous, and patch type GA. Patch type GA, the rarest form manifests by erythematous or hyperpigmented patches, without scaling over the trunk and extremities.[2,3] It may take annular configuration, but shows the classic histopathologic findings of interstitial GA.[2] We hereby present a case of patch type granuloma annulare with histological features consistent with interstitial GA.

CASE REPORT

A 16-year-old girl presented with six months history of multiple, asymptomatic, slowly progressive, discrete as well as confluent, round to oval, non-scaly, non-indurated, non-tender, slowly progressive, hyperpigmented patches of various sizes over abdomen (Fig 1), lower back and both thighs. There was a difference in the shades of hyperpigmentation at the centre and periphery. She denied having any other medical illness and was not on any medications. Physical examination was otherwise normal.

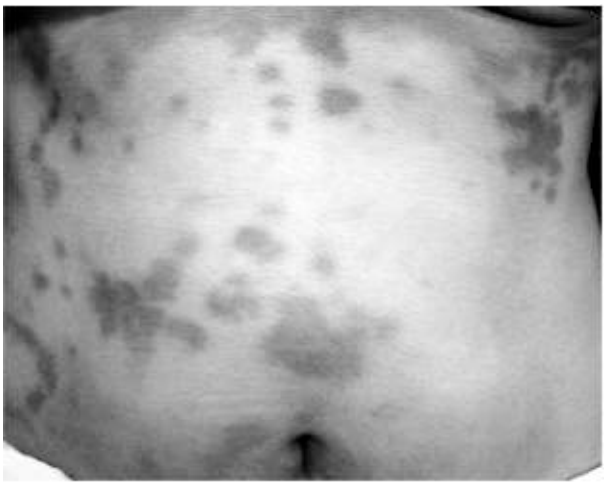

Figure 1: Multiple, discrete as well as confluent, round to oval, hyperpigmented patches over abdomen

Routine hematological and biochemical investigations were normal. A differential diagnosis of lichen planus pigmentosum, morphea and parapsoriasis was considered. Skin biopsy from the lesion over abdomen showed moderately dense superficial and deep peri-vascular and periappendageal lymphocytic infiltrate. The upper and the mid reticular dermis showed several foci of necrobiosis with a few histiocytes scattered interstitially without well-formed palisading granulomas. (Fig 2 and 3)

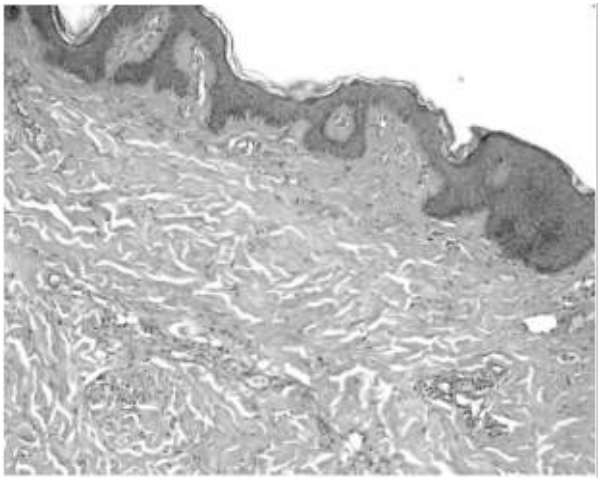

Figure 2: Superficial and deep peri-vascular and periappendageal lymphocytic infiltrate with foci of necrobiosis and few histiocytes in upper and mid reticular dermis without well-formed palisading granulomas (H&E,10x)

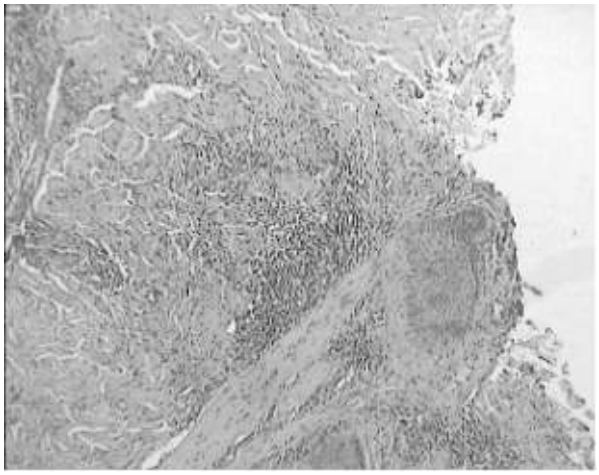

Figure 3: Basal hyperpigmentation and ill-formed palisading granulomas (H&E,40x)

Based on clinical and histopathological features, a final diagnosis of patch type granulomas annulare with histological features of interstitial pattern was made. Patient was treated with tacrolimus 0.1% ointment, twice daily for 4 weeks . There was no significant improvement in the lesions. The lesions did not regress after performing biopsy.

DISCUSSION

Five morphologic variants of GA have been described: localized, generalized, perforating, subcutaneous, and patch type.[2] Patch type granuloma annulare is a relatively recently described variant, which presents as erythematous to brown patches with or without scales, which may have annular configuration on the trunk or extremities.[2,3] Female predominance has been reported, as with other forms of GA.[3] High index of suspicion and clinico-pathologic correlation is required to make a diagnosis of patch type of GA. The clinical differential diagnosis of patch type GA includes morphea, erythema annulare centrifugum and parapsoriasis.[4]

Histologically GA can present in three patterns, necrobiotic granuloma, interstitial or incomplete form and granuloma of sarcoidal or tuberculoid type.[5] Interstitial pattern was the most common histological pattern in a study.[6] Interstitial pattern is most often found in patients with patch type GA, as was seen in our case.[7] Histologically interstitial GA shows 'busy dermis' with increased number of inflammatory cells in the dermis separated by connective tissue mucin. The infiltrate is composed of lymphocytes and histiocytes. Inflammatory cells are also noted around blood vessels and between collagen bundles without well formed area of necrobiosis.[8]

Differential diagnosis of interstitial type GA includes morphea, mycosis fungoides, xanthoma, interstitial granulomatous drug reaction and interstitial granulomatous dermatitis.[3,4] Histologically morphea can be confused with interstitial type GA but the subtle presence of histiocytes in an interstitial pattern usually allows a definitive diagnosis of GA.[1] Increased hyalinization of collagen is a feature of morphea, which is not seen in GA. Mycosis fungoides can have granulomatous infiltrate with a GA like pattern. This can easily be recognized by the presence of at least some intraepidermal lymphocytes.[9] Xanthoma can be differentiated from interstitial pattern of GA on the basis of foamy appearance of histiocytes which is completely lacking in GA and there is also a lack of perivascular lymphocytic infiltrate in xanthomas.[1] Interstitial granulomatous drug reaction shows predominantly eosinophils, lichenoid changes at dermo-epidermal junction while tissue necrobiosis is rarely noted. Interstitial granulomatous dermatitis shows predominance of neutrophils and neutrophil fragments. Histiocytes, lymphocytes and eosinophils are also present within palisades of histiocytes around basophilic collagen fibers. Changes may involve full thickness of dermis.[10]

CONCLUSION

The tendency of GA to remit spontaneously complicates accurate assessment of the efficacy of any treatment. Systemic therapies are not necessary because of asymptomatic nature of the disease. It is reported that patch type GA will respond to the same therapy as other types of GA.[3,4] Resolution of patch type GA after biopsy has also been reported.[11]

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Please cite this paper as: Garg A, Garg S, Gupta LK, Khare AK, Mittal A. Extensive patch type granulomas annulare: A rare case report. Inter J Medical Sci Res Prac 2014; 1 (1): 23-25.

ACKNOWLEDGEMENTS

Nil

PEER REVIEW

Double Blinded externally peer reviewed.

CONFLICTS OF INTEREST

Nil

FUNDING

Nil

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE RESEARCH AND PRACTICE
Print ISSN: 2349-3178 Online ISSN: 2349-3186

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Bilateral Portwine Stain in a child with Sturge Weber Syndrome

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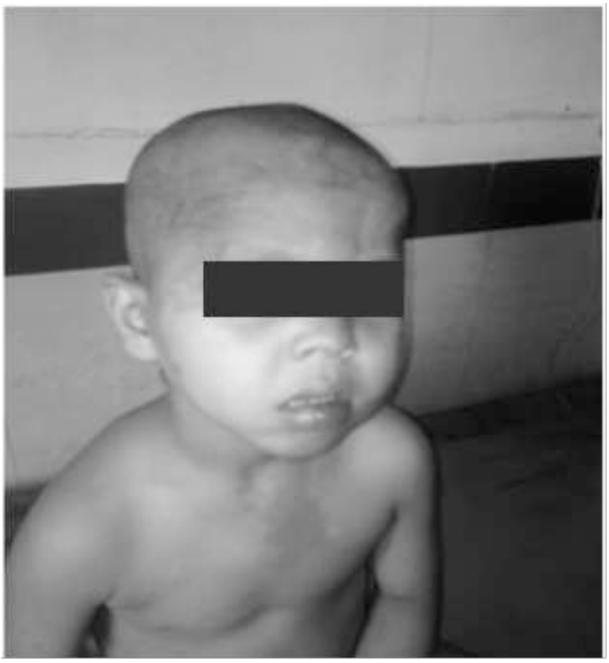
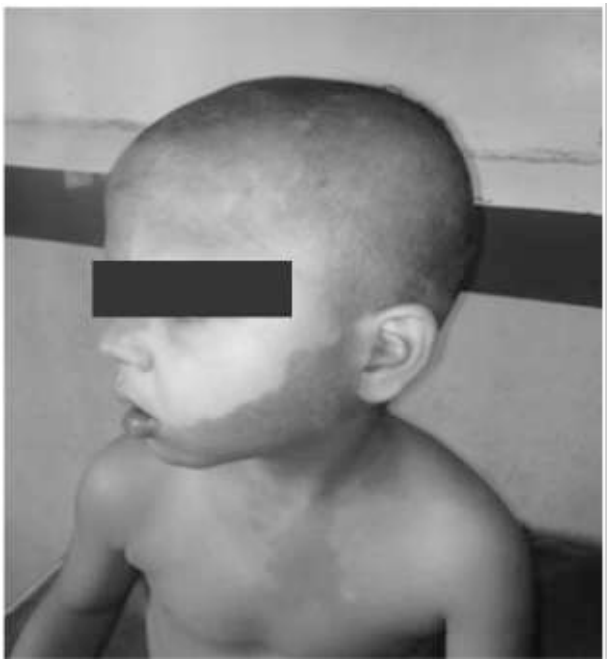
IMAGE

A 3 year old child presented with generalized seizures for one year. Child was the product of non consanguineous marriage with no family history of seizure and developmentally appropriate for age. On examination child was having very peculiar pattern of portwine stain on face. It involved the territory of Right ophthalmic division and Left mandibular division of trigeminal nerve. On right side it involved forehead, nose, upper eye lid and bulbar conjunctiva and on left side it involved left cheek, part of pinna, mandibular area, lip, oral mucosa and neck. Child was having nine ash leaf spots over trunk and extremities. Intraocular pressure was normal. On CT scan of head there was bilateral tram track calcification in cerebral cortex with atrophy. Child was started with valproic acid and seizure free for last three months.

Received on 01 May 2014 Accepted on 10 May 2014 Published on 15 May 2014



Portwine stain in the territory of right ophthalmic division of trigeminal nerve



Portwine stain in the territory of mandibular division of left trigeminal nerve

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Please cite this paper as: Ambey R, Singh A. Bilateral Portwine Stain in a child with Sturge Weber Syndrome. Inter J Medical Sci Res Prac 2014; 1 (1): 26.

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE RESEARCH AND PRACTICE
Print ISSN: 2349-3178 Online ISSN: 2349-3186

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ULCERATIVE COLITIS

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MEDICAL POEM

Received on 15 May 2014 Accepted on 20 May 2014 Published on 22 May 2014

- Begins in the rectum and backwards it goes
  No mercy to any part of colon it shows.

- Continuous it is, skip areas without
  Ulcerative colitis it is, without a doubt.

- Mucosa has ulcers, you should know
  Linearity & superficiality they show.

- Muscle contracted & narrow, problem does pose
  Provides it, the appearance of a garden hose.

- Sometimes it waxes and sometimes wanes
  Accordingly active or resolving status it gains.

- Crypt abscesses are always produced
  And goblet cells are markedly reduced.

- Congestion & mucosal regeneration noted have been
  Dysplasia to Neoplasia-spectrum entire is seen.

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Please cite this paper as: Narang S. Ulcerative colitis. Inter J Medical Sci Res Prac 2014; 1 (1): 27

International Journal of Medical Science Research and Practice
Print ISSN: 2349-3178; Online ISSN: 2349-3186

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