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Title: Genetic basis and phenotype of congenital nephrotic syndrome

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Abstract

Introduction: Congenital nephrotic syndrome (CNS), characterised by onset of severe edema at <3-months-old and progression to end stage renal disease by 5-yr-old, is a rare disease caused by homozygous mutations in genes encoding glomerular podocyte proteins. NPHS1 defects underlie the majority of cases in Caucasian patients.

Aims & Objectives: To understand the genetic basis of CNS in Indian patients in relation to disease severity and extrarenal manifestations.

Materials and methods: Following ethical approval, whole exome sequencing (Illumina, USA) was performed on blood samples from patients with CNS presenting at centers collaborating in a nationwide study. Following sample processing (HiSeq analysis software; genome analysis toolkit), variants annotated by wANNOVAR were filtered to focus on reported (Clinvar, HGMD) mutations or rare, novel, deleterious and conserved variations in NPHS1, NPHS2 and WT1 (ACMG 2018). Allelic segregation was confirmed by Sanger sequencing in parents.

Results: During 2017-2018, 26 patients (58% boys) presented with CNS; all were undernourished, hypoalbuminemic and with preserved renal function. One child had Galloway-Mowat syndrome and another albinism with hypotonia. Consanguinity and family history were present in 31% and 15% cases, respectively. Homozygous or compound heterozygous pathogenic or likely pathogenic variations were found in NPHS1 in 19 cases, and NPHS2, PLCE1 and OSGEP in one case each. Two variants in NPHS1 (exon 19, c.G2600A: p.G867D and exon 27, c.C3478T:p.R1160X) were seen in 5 and 3 cases, respectively.

Conclusion: A genetic cause was determined for 84.6 (95% CI, 66.5-93.9) % patients with CNS. Testing for variations in NPHS1 is most important, and population hotspots may be present. Mutations in NPHS2, PLCE1 and OSGEP are uncommon and associated with extrarenal manifestations. WES enables genetic counselling and development of stepwise approach to testing in patients with CNS.
Assessment of Autonomic Function during Ictal and Interictal Period of Migraine

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Affiliation: Presenting Author- Name- Dr. Shivam Bansal

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INTRODUCTION:
A large number of migraineurs have nausea or vomiting and other gastrointestinal symptoms like diarrhoea, which led to the genesis of “autonomic theory” of pathophysiology of migraine. Studies suggest a degree of autonomic dysfunction which gets implicated in pathophysiology of migraine but none has ever commented on differences among ictal and interictal (headache free) period of migraine.

AIMS AND OBJECTIVES:
This study aims at assessing and comparing autonomic dysfunction during ictal and interictal period of migraine.

METHODOLOGY:
Patients with migraine according to ICHD 3rd edition β version criteria were recruited for the study. Tests of sympathetic function (beat to beat blood pressure changes in Head-Up-Tilt test) and parasympathetic function (heart rate responses to Deep Breathing and Valsalva Manoeuvre) were performed, each during ictal and interictal period. The results of the ictal period were then compared with that of interictal period.

RESULTS:
Ten patients [Eight female (80%), 20-58 years, mean 34.6] were studied.
Nine patients (90%) showed Expiration:Inspiration [E:I] ratio {Ratio of maximum RR interval during expiration phase with minimum RR interval during inspiration phase} in Deep Breathing test below 1.24 (p=0.008) and four patients (40%) showed 30:15 ratio {Ratio of RR interval during 30th heart beat with that during 15th heart beat} in Head-Up-Tilt test below 1.04 (p=0.045), thus indicating significantly impaired vagal response. These results were in ictal period. All patients exhibited normal parasympathetic response during interictal period and intact sympathetic function during both ictal and
interictal periods.

**CONCLUSION:**
There is **significant parasympathetic dysfunction in ictal state** as compared to headache-free periods. Parasympathetic dysfunction is observed in E:I ratio (p=0.008), ΔHR (p=0.014), 30:15 ratio (p=0.045). There is no objective evidence of sympathetic dysfunction in ictal period as compared to headache-free periods. Therefore, this study provides newer insight into the pathophysiology of a migraine attack- the genesis of the ictal state, which is attributed to parasympathetic dysfunction.
Functional outcomes in Children with Severe Sepsis – A Prospective Observational Study

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Keywords: Severe sepsis; POPC and PCPC scores

Functional outcomes in Children with Severe Sepsis and Septic Shock – A Prospective Observational Study

Background

There is paucity of data on the functional outcomes in children with severe sepsis and septic shock admitted to the Pediatric Intensive Care Unit (PICU).
Objective

To evaluate functional outcomes in children with severe sepsis and septic shock admitted to the PICU using Pediatric Overall Performance Category Scale (POPC) and Pediatric Cerebral Performance Category (PCPC) scales at discharge in comparison to score obtained at admission.

Methods

We conducted this prospective observational study from Jan 2018 to November 2018. Children aged 2 months to 17 years admitted to PICU with severe sepsis and septic shock were enrolled. Data collection included demographic and clinical details and POPC and PCPC scores. Data was analyzed using stata 11.

Results

A total of 96 children were enrolled. Sixty nine % had septic shock and 31% had severe sepsis. Twenty four (25%) died. The Median (IQR) POPC and PCPC scores at admission were −3 (1 to 4). The POPC and PCPC scores at discharge/death were 2 (1 to 5) and 2 (1 to 6) respectively. At admission 49% had a baseline POPC and PCPC score of ≥ 2 and at discharge/death 59 (61%) had a POPC and PCPC score of ≥ 2.

Conclusion

The functional outcomes of children admitted to the PICU with severe sepsis and septic shock were poor with more than half having mild to severe disability or death.

Keywords: Severe sepsis; POPC and PCPC scores
Changes in muscle thickness in critically ill children during their initial 7 days’ stay in PICU: an observational study

Authors: Jain Agam, Lodha Rakesh, Kabra Sushil, Jana Manisha, Sankar, Jhuma, Jat Kana Ram

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Abstract Body

Introduction:
Significant muscle wasting occurs in patients surviving ICU, causes being multifactorial. Various preventive strategies have not yielded significant result. One of the hindrances for developing a successful therapy is the lack of a reliable tool to monitor the muscle mass. Preliminary studies have shown that quadriceps muscle thickness correlates with the muscle mass of the body. We hypothesised that monitoring the muscle thickness of quadriceps using bedside ultrasound can be reliable tool for monitoring wasting.

Aims & Objective:

To measure the changes in muscle thickness of quadriceps femoris in critically ill children aged 1 - 18 years over initial 7 days of their PICU stay

Materials And Method:
The study was a prospective bedside observational study in the PICU. Transverse and longitudinal axis measurements of quadriceps femoris anterior thickness were undertaken using a bedside ultrasound machine - Philips CX-50 with the linear transducer. The average of four measurement values was recorded. The location of measurement for consistency was taken as midpoint of Anterior superior iliac spine to patella of right leg. Serial measurements were undertaken on D1 and D7.
RESULTS:

One hundred and eleven children were screened out of which 19 were enrolled to assess loss of muscle mass by Day 7. The median age of the population was 7 years, out of which there were 13 boys and 6 girls. The median muscle thickness at baseline was 1.58cm (IQR = 1.41cm - 2cm). The median muscle thickness at Day 7 was 1.66cm (QR 1.42cm - 2.04cm). The median decrease in muscle mass was 8.6%(IQR = -21.2 to 27.5%) over 7 days, which shows high variability. Linear regression applied between cumulative fluid balance and muscle mass change shows, muscle mass did not vary significantly with positive fluid balance, (regression coefficient= 7.8, p=0.44. There was a median increase in thickness of subcutaneous tissue by 16.3% (IQR = -4.3% to 26.7%)

CONCLUSIONS:

There was no significant decrease in muscle mass over 7 days, as measured by ultrasonography, in this study. A plausible explanation is there was concomitant positive fluid balance, leading to tissue edema, leading to overestimation of muscle thickness. An increase in subcutaneous tissue thickness supports this explanation. The results of this study do not corroborate with similar studies published. Further studies are required to validate the role of muscle ultrasonography as a tool to monitor muscle wasting.
CHARACTERIZATION OF BONE MARROW INVOLVEMENT IN PEDIATRIC HODGKIN LYMPHOMA USING $^{18}$F-FDG PET/CT AND ITS COMPARISON WITH BLIND BONE MARROW BIOPSY

ABSTRACT

Background: Bone marrow involvement in Hodgkin lymphoma upstages the disease and is associated with poor prognosis. Bone marrow biopsy of bilateral iliac crest, which is the standard to diagnose bone marrow involvement, is an invasive procedure which is likely to miss focal bone marrow involvement elsewhere. The role of whole body FDG PET CT in baseline staging for detection of bone marrow involvement in pediatric Hodgkin lymphoma was explored in this study.

Methods: Pathologically confirmed cases of pediatric Hodgkin lymphoma ($\leq 16$ years) were prospectively recruited. All patients underwent a whole body FDG PET CT scan along with blind bone marrow biopsy from bilateral iliac crest. FDG PET CT scans were interpreted by 2 nuclear medicine physicians and bone marrow biopsies were interpreted by a pathologist who were blinded to findings of second modality. Semiquantitative analysis of FDG PET CT were also explored. The difference of median between 2 groups were calculated using Mann Whitney U test and p value $<0.05$ was considered significant.

Results: Of the 37 patients who underwent both bone marrow biopsy and PET CT scan, bone marrow biopsy were positive in 6 patients (16.2%). True positive bone marrow involvement was seen in 14 (37.9%) patients while 6 patients (26.2%) showed false positive diffuse homogenous marrow uptake. The sensitivity, specificity, PPV, NPV of FDG PET CT in identifying bone marrow involvement scan were 100%, 73.9%, 70%, 100% respectively. Semiquantitative analysis showed the median values of SUVmax marrow to liver ratio [3.409;IQR 2.149-6.87 vs 1.339; IQR1.041-2.162; $p =0.0003$] as well as SUVmax marrow to mediastinal blood pool structure ratio [8.097; IQR 3.273-9.489 vs 1.35;IQR 1.041-3.04; $p=0.0001$] were significantly higher in those with actual bone marrow involvement. Area under ROC curve SUVmax marrow to liver ratio and SUVmax marrow to mediastinal blood pool structure ratio were 0.846 (95%CI: 0.718-0.974) and 0.863 (95%CI: 0.741-0.986) respectively suggesting good discrimination value of these parameters.

Conclusion: FDG PET CT is a highly sensitive test to detect bone marrow involvement at baseline in pediatric Hodgkin lymphoma which is especially important as the marrow involvement is often focal. High negative predictive value suggests in presence of negative involvement in FDG PET/CT, bone marrow biopsy may be omitted at baseline. Semiquantitative analysis of PET/CT scan can also be added on to visual interpretation for detecting true bone marrow involvement.