Sildenafil for treatment of nephrogenic diabetes insipidus

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Introduction: Congenital nephrogenic diabetes insipidus (NDI) characterized by inability to concentrate urine in response to arginine vasopressin (AVP), is caused by mutations in vasopressin receptor 2 (V2R) gene (90%) or mutations in the aquaporin 2 (AQP2) water channel (10%). Current conventional treatment regimen including adequate hydration, low sodium diet, hydrochlorothiazide (HCTZ) and nonsteroidal anti-inflammatory drugs (NSAIDs) can only partially control the NDI symptoms. Recent experimental studies have suggested that treatment with sildenafil citrate, a PDE5 inhibitor, may enhance cyclic adenosine monophosphate (cAMP)-mediated apical trafficking of AQP2 and may be effective in increasing water reabsorption in patients with congenital NDI.

Methods: A 4-year old boy with x-linked NDI (12bp-deletion, delta R247-G250 at Xq28 position) resistant to conventional therapy (HCTZ-amiloride and indomethacin) treated with sildenafil citrate 2mg/kg/day for 10 days after a 2-day washout period between the two treatment regimen. Aliquots of 24-hr urine collections before and after sildenafil treatment were analyzed for urine volume, osmolality and cAMP determination. Blood samples were also obtained for sodium and osmolality measurements. The primary endpoint was 24-hour urine volume after 10 days of sildenafil and conventional treatments.

Results: Compared to conventional therapy, treatment with sildenafil resulted in significant reduction in 24-hr urine volume (1698 mL vs. 851 mL) and serum sodium (164 vs. 148 mEq/L) and an increase in osmolality (101 vs. 687 mOsm/L) and cAMP concentration (759 vs. 1501 nmol/day). Patient tolerated sildenafil well and experienced no adverse effects.

Conclusion: Sildenafil citrate should be considered as an alternative agent in treatment of x-linked NDI resistant to conventional therapy.
Outcome of Immediate Use of the Permanent Peritoneal Dialysis Catheter in Children with Acute and Chronic Renal Failure

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Introduction: Peritoneal dialysis remains the only available option for patients which need immediate dialysis and it could be a bridge between end-stage renal failure (ESRD) and transplantation. There is a paucity of published experience of children with immediate use of permanent Tenckhoff Catheter for peritoneal dialysis from developing countries. In this study we report our experience on immediate use of permanent peritoneal access and continued peritoneal dialysis for a prolonged time.

Methods: Fifty six patients were studied including 30 males and 26 females within the age range of 1 month to 14 years with mean age of 6.5 years in Urmia, Northwest, Iran.

Results: No operative morbidity was seen. During a total of 499.5 continuous ambulatory peritoneal dialysis months, 16 patients had 28 episodes of peritonitis, which means an overall result of one episode per 17.8 months. There were 3 patients (5.35%) with catheter site leakage, 12 (21.4%) catheter obstructions (which led to omentectomy), 4 (7.2%) exit site infections (2 patients in the early postoperative period and 2 patients during follow up). Death due to catheter related complications occurred in 1 per 56 patients and due to non-catheter related causes in 10 per 56 patients.

Conclusion: Present results indicate that catheter-related complications were not higher than those previously reported and peritoneal dialysis could be initiated immediately after catheter implantation and could be a safe bridge between end-stage renal failure (ESRD) and transplantation.
Evaluation of prostaglandin E1 infusion on urinary calcium excretion in neonates with congenital heart disease

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Introduction: Congenital heart disease is one of the most important life-threatening conditions in neonatal period. Administration of prostaglandin E1 to keep the ductus arteriosus open before corrective surgery is necessary. Despite the life-saving role of prostaglandin E1, numerous and dangerous side effects are considered; including the effect of prostaglandin E1 on generation of hypercalciuria. This study aimed to assess the effect of intravenous administration of prostaglandin E1 on urinary calcium excretion of newborns with congenital heart disease.

Methods: Ten neonates with congenital heart disease related to patent ductus arteriosus were enrolled in this study. Three random urine samples; once before injection as well as 24 and 72 hours after prostaglandin E1 infusion were taken from each patient. Urine samples were examined for calcium, sodium and creatinine.

Results: The calcium level and calcium-to-creatinine ratio of the third sample was higher in comparison to the second and first samples (p<0.05). The average of calcium-to-creatinine ratio in half of the patients in third sample was above the normal range (p<0.05). The sodium-to-creatinine ratio was higher than normal range (p<0.05).

Conclusion: Increased urinary calcium excretion after PGE1 infusion might be suggestive of the role of prostaglandin E1 in generation of hypercalciuria in newborns with congenital heart disease and increased risk of kidney stone and nephrocalcinosis in future.
Association of E-selectin with hematological, hormonal levels and plasma proteins in children with end stage renal disease

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Introduction: Hypercoagulable state is a common serious problem in patients with end-stage renal disease (ESRD). ESRD patients are in a condition of chronic inflammation. An increased level of E-selectin, “a key adhesion molecule that regulates leukocyte bindings to endothelium at damaged sites,” accompanies the higher risk of inflammation in ESRD patients. We aimed to investigate the possible correlation among E-selectin as an adhesion molecule, coagulation factors, and inflammatory factors in children with ESRD.

Methods: Thirty-five children with ESRD who had been on regular dialysis treatment were registered in our study. Nineteen sex- and age-matched healthy volunteers were used as the control group. Laboratory tests were requested for the evaluation of hematological and biochemical parameters, and parathyroid hormone (PTH), and for coagulation state; fibrinogen, protein C, and protein S were measured. The enzyme-linked immunosorbent assay (ELISA) (Biomerica, CA, and IDS, UK) for serum E-selectin assay was provided by R and D Systems (Abingdon, UK).

Results: Hemoglobin (Hb), blood urea nitrogen (BUN), creatinine, calcium, PTH, triglyceride (TG) concentrations in serum as well as E-selectin showed significant difference between the two study groups. Serum E-selectin was significantly higher ($P$ value = 0.033) in dialysis patients than in healthy subjects. E-selectin was positively correlated only with phosphorus in ESRD children ($r = 0.398$, $P = 0.018$). No association was found for other parameters.

Conclusion: Although in our study circulating E-selectin concentration “as an inflammatory maker” is independently positively associated with limited blood markers, for better evaluation, well-designed cohort studies should be examined in ESRD children.
Can Duplex Doppler Ultrasound Predict the Complete Obstruction in Children with Unilateral Ureteropelvic Junction Obstruction?

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Introduction: Duplex Doppler ultrasound is a safe and useful modality for evaluation of children with hydronephrosis. It may be used to improve the ability of conventional ultrasound in distinguishing between obstructive and non-obstructive hydronephrosis. Resistive index (RI) is the most valuable duplex index reflecting the renal obstructive conditions.

Methods: In a prospective study between January 2014 and March 2015 children referred to radiology department of Emam Hossein Children hospital (a tertiary center in Isfahan, Iran) for evaluation of unilateral hydronephrosis were enrolled, consecutively. The patients with the evidence of UPJO in gray-scale ultrasound were offered for supplementary Doppler study. In duplex Doppler study mean RI of arcuate arteries in upper, middle and lower parts of both kidneys of each patient were obtained. Then RI ratio and difference of RI between kidneys of each patient (dRI) were calculated and recorded. Voiding cystourethrogram was done for the exclusion of the cases with concomitant vesicoureteral reflux. In the next step, standard diuretic renal scintigraphy with Tc 99m diethylenetriaminepentaacetic acid (DTPA) was performed for the patients.

Results: Of the 51 patients with primary diagnosis of UPJO in grey scale ultrasound, 27 were confirmed as UPJO by diuretic renal scintigraphy, and the others had various degrees of decrease in renal function and perfusion or had a normal scan. Patients with UPJO were 16 (59.3%) male and 11 (40.7) female aged 2 months to 9 years. The Rate of non-complete and complete UPJO was 85.2% and 14.8%, respectively. Mean RI in kidneys with complete UPJO was 0.77 ± 0.09 and in kidneys with non-complete UPJO was 0.68 ± 0.05 (p=0.009). For evaluating the ability of the indices in order to differentiate between the complete from non-complete UPJO, the area under the ROC curve for RI was 79.8% (95% CI 46.1, 100), for RI ratio was 90.8% (95% CI 77.9, 100.0) and for dRI was 92.4% (95% CI 79.4, 100.0).

Conclusion: Duplex Doppler ultrasound (RI, RI ratio and dRI) can provide a non-ionizing convenient method for predicting complete UPJO and may be used for supporting the results of DPTA scan especially in challenging diuretic renograms. Larger studies are needed to validate our findings.
Which pediatric patients with vesicoureteral reflux need cystorethrography after anti-reflux surgery?

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Introduction: Vesicoureteral Reflux (VUR) is a common urinary problem in children. Postoperative imaging is one of the most controversial challenges of follow up for these patients.

Methods: In this observational study 40 patients with primary VUR underwent anti-reflux surgery with Gil-vertnet method. Clinical manifestations, urine culture, ultrasonography of urinary system and VCU of all patients before and after surgery were carefully studied. Data collected by questionnaire and were analyzed by SPSS 18 software.

Results: Thirty four patients were free of reflux after surgery and 6 patients showed variable degrees of reflux in postoperative VCU. All 6 patients were in high risk group. In postoperative assessment 5 patients had positive urine culture. All 6 patients had variable degrees of hydronephrosis. All of patients in low risk group and 77% of high risk group were completely improved, although 23% of high risk patients had reflux after surgery.

Conclusion: This study showed that postoperative VCU is not mandatory in all patients with reflux and it is better to be performed in the high risk group who has postoperative urinary tract infection or hydronephrosis.
Nephrocalcinosis in children: Its effect on renal function and body growth

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**Introduction**: Nephrocalcinosis (NC), is defined as tubulointerstitial calcification of the kidneys. NC is a complication of metabolic disturbances, underlying renal disorders, vitamin D excess, medications and prematurity. The body growth and renal function in children with NC have rarely been investigated. In this study, we aimed to assess the etiology of NC, retrospectively and to evaluate the growth and kidney function of patients with NC.

**Methods**: This cross-sectional study performed on 30 patients with NC aged 2-27 years old who had been admitted or referred to Loghman Hakim Hospital between 2006 to 2013. The patients’ charts were reviewed for age, gender, etiology of NC, clinical manifestations, GFR, Height and weight standard deviation scores at presentation and follow-up periods. Data analyzed by statistical tests with SPSS software version 18.

**Results**: Mean age at presentation was 2.2±2.5 (range: 0.1-9.7) years. Fourteen patients (47%) were male. Mean follow-up duration was 7.1±5.2 (range: 1.0-20.9) years. The most common symptoms were urinary tract infection (25%) and growth retardation (18%). The etiology of NC included distal renal tubular acidosis (dRTA) in 34.5%, idiopathic hypercalciuria (IHC) in 17.2%, Bartter syndrome in 10.3% and unknown in 6.9%. Mean GFR was 75.6±29.1 ml/min/1.73m\(^2\) at presentation and 105.7±21.9 ml/min/1.73m\(^2\) at follow-up. Four of 30 (14.3%) patients had hSDS<-2 at presentation that remained the same at the last follow up.

**Conclusion**: The results of this study indicate that the etiology of nephrocalcinosis was almost similar to the other studies and in long term, nephrocalcinosis per se do not have significant influence on growth indices and GFR.
Fanconi Syndrome: Case presentation

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Introduction: Fanconi syndrome (FS) is characterized by multiple defects in renal proximal tubular reabsorption: glucosuria, phosphaturia, generalized aminoaciduria, and bicarbonaturia. FS can be hereditary or acquired. The commonest cause of hereditary FS is cystinosis, but it may also be seen with Wilson disease, hereditary fructose intolerance, galactosemia, Fanconi-Bickel syndrome, Lowe syndrome, Dent’s disease, mitochondrial cytopathies, tyrosinemia and idiopathic FS.

Case report: Here, we report 2 rare cases of primary FS. The first one was a neglected 10.5 year-old girl who referred due to severe respiratory failure (oxygen dependent) secondary to chest deformity and muscle weakness. She was the first child and product of a consanguineous marriage. Her growth and development were relatively normal up to 12 months of age. At 2 years old, she was not able to walk due to severe weakness and limb fractures. She had received several injections of Vitamin D with the impression of rickets and admitted repeatedly for pneumonia. By the age of 7, she was candidate for surgical correction of the limb deformities but she was inoperable because of severe osteoporosis. She was treated as a case of refractory rickets and also received citrate solution for metabolic acidosis by endocrinologist with insignificant improvement. More investigations showed polycythemia (Hb:17.8 g/dl, RBC:6.3), biochemical and radiological evidences of advanced rickets, normal anion gap metabolic acidosis with hypokalemia, glucosuria and hyperphosphaturia. Eye examination and the other tests were normal. The 2nd case was her younger brother presenting with FTT and marked rickets in infancy. Both were successfully treated as primary FS with better outcome in the second case.

Conclusion: Although, cystinosis is the most common cause of hereditary FS, primary FS which is a rare disease should be considered in children with severe rickets and FTT.
The antibiotic susceptibility patterns of uropathogens in children with urinary tract infection in Shiraz, 1393

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Introduction: Urinary tract infection (UTI) is one of the most common bacterial infections in children. This study aimed to determine the frequency of bacteria that cause UTI and their antibiotic susceptibility to choose the best empirical treatment for children with UTI in Shiraz.

Methods: In this prospective study, 202 children aged 2 month to 18 years old with UTI who referred to outpatients clinics of Shiraz University of Medical Sciences, between August and November 2014, were enrolled. The evaluation of antibiotic susceptibility was performed by Kirby Bauer method. Patients’ data were collected from medical records and interview with parents.

Results: UTI was significantly more prevalent in girls (70.3%) than boys. The most frequent microorganisms causing UTI were Escherichia coli (104), klebsiella spp. (34), Enterococcus species (20) and Coagulase-negative Staphylococcus (16). There was a high rate of ESBL production among isolates of E. coli and Klebsiella spp. (69.2% and 50%, respectively). Overall, the lowest level of sensitivity was recorded for ampicillin (16.8%) and co-trimoxazole (17.8%) and the highest level of sensitivity for Imipenem (90.1%) and Gentamicin (65.3%). The most effective antimicrobial therapy for patients with Gram-negative and gram positive UTI were Colistin (98.8% susceptibility) and linezolid (100%), respectively and the least effective ones for patients with gram-negative and gram positive UTI were amoxicillin (16.2%) and Clindamycin (100%), respectively.

Conclusion: The efficacy of third generation of Cephalosporins in treatment of children with UTI was reduced because of high rate of ESBL production. Intramuscular Gentamicin is the best candidate for outpatient treatment of UTI in children in Shiraz.
Identification of Two New CTNS Mutations in Iranian Patients with Infantile Nephropathic Cystinosis

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Introduction: Nephropathic cystinosis, the most common cause of renal Fanconi syndrome, is a lysosomal transport disorder with an autosomal recessive inheritance pattern, resulting from different mutations in the CTNS gene located on chromosome 17p13. The CTNS gene contains 12 exons. The last 10 exons encode a lysosomal transmembrane protein with 367-amino acids called cystinosin. This protein consists of 7 putative transmembrane domains (TM) and 2 lysosomal targeting motifs. Cystinosin dysfunction leads to deficient cystine transport and accumulation in cells of different organs particularly the kidney, cornea and thyroid. Without treatment, patients illustrate growth retardation, proximal renal tubular acidosis (Fanconi syndrome) at 6-12 months of age, renal failure at the end of the first decade of life and different non renal problems.

Methods: In this study, PCR amplification and direct sequencing of coding regions of CTNS gene for 3 unrelated Iranian patients with infantile nephropathic cystinosis was performed. In order to confirm the novel missense mutation, ARMS PCR was performed for 100 normal chromosomes.

Results: We found 2 new mutations including one homozygous missense variant in one patient and one homozygous 24bp in-frame deletion that observed in two unrelated patients.

Conclusion: In this report, analysis of CTNS gene coding exons in 3 Iranian unrelated cystinosis patients, revealed 2 novel mutations that have not been previously reported. The first novel mutation is the missense mutation. This mutation changes the highly conserved Tyrosine at the TM2 domain of the protein to basic amino acid Histidine. The second novel mutation is the in-frame deletion identified in two unrelated patients that removes 8 of 21 amino acids from TM2 domain. Sequence analysis of the DNA surrounding deletion breakpoints revealed the presence of a 9-bp direct repeat at the both sides of breakpoints. These two short direct repeats provoke slipped strand mispairing (SSM) during DNA replication.