WHAT'S HOT WHAT'S NEW - AN UPDATE FROM THE IPNA 2016 MEETING

Dialysis

1. This study has shown that oral paricalcitol is safe and well tolerated in children aged 10–16 years with stages 3–5 CKD. A significant reduction in iPTH levels was seen, with risk of 'clinically meaningful' hypercalcaemia in 15% of CKD 5 children.

FP-S31-1 - Oral paricalcitol is effective and well-tolerated in children with stages 3 to 5 chronic kidney disease

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Objectives: Elevated intact parathyroid hormone (iPTH) levels can contribute to morbidity and mortality in children with chronic kidney disease (CKD). The present studies evaluated the pharmacokinetics, efficacy, and safety of oral paricalcitol in the reduction of iPTH levels in children with stages 3–5 CKD.

Methods: Two phase 3 studies enrolled children aged 10–16 years with stages 3–5 CKD. The first study evaluated oral paricalcitol pharmacokinetics, efficacy, and safety in children with stage 3/4 CKD with an initial 12-week doubleblind period followed by a 12-week (minimum) open-label period wherein all children received paricalcitol. The second study evaluated the efficacy and safety of oral paricalcitol (no comparator) for 12 weeks in children with stage 5 CKD undergoing hemodialysis or peritoneal dialysis.

Results: In the stage 3/4 CKD study, 12 children received 3 µg paricalcitol and were assessed for intensive pharmacokinetics (mean Cmax, 0.13 ng/mL; AUC0–∞, 2.87 ngâ'h/mL). Population pharmacokinetic analysis showed that CKD stage does not influence the pharmacokinetics of paricalcitol in children. Thirty-six children were randomized (baseline iPTH, 150 mg/dL) and 27.8% of the paricalcitol group achieved two consecutive iPTH reductions of ≥30% from baseline vs no childrenin the placebo group (P=0.045). Adverse events were observed in a higher proportion of the placebo group compared with the paricalcitol group in the double-blind (88.9% vs 38.9%; P=0.005) portion of the stage ¾ CKD study. In the stage 5 CKD study, 8 of the 13 (61.5%) children enrolled had two consecutive iPTH reductions of ≥30% from baseline (baseline iPTH, 884 pg/mL, n=13), and 5 (38.5%) had two consecutive iPTH values between 150 and 300 pg/mL. Clinically meaningful hypercalcemia occurred in 2 (15.3%) paricalcitol-treated children in the stage 5 CKD study.

Conclusions: Oral paricalcitol dosing in children aged 10–16 years with stages 3–5 CKD reduced iPTH levels and was well tolerated.

2. This multicentre prospective survey of exit site infections in PD patients has shown that monthly surveillance of exit site care may reduce the risk of exit site infections.

FP-S07-1 - Exit SIte Infections (ESI) in Children on Chronic Peritoneal Dialysis (PD): Findings from the Standardizing Care to Improve Outcomes in Pediatric End Stage Renal Disease Collaborative (SCOPE)

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Objectives: Although ESI has been linked to peritonitis in pediatric PD, little data exists as to ESI frequency and clinical factors influencing its manifestation. SCOPE aims to reduce PD-associated infections through the systematic implementation of standardized care practices, including stipulated ES care and an ES-scoring tool. We sought to elucidate ESI rates, predisposing clinical factors, and ESI outcomes in children on PD.

Methods: SCOPE data collected10/1/11-9/30/14 were analyzed, including demographic and infection detail. ESI was defined as purulent drainage or exit site score >4 or treatment for ESI.

Results: 857 catheter insertions (56% boys; 44% white, 27% Hispanic, 18% black; mean age at catheter insertion 7.7 yo) contributed 10,110 months of PD in 734 children. 207 ESIs occurred in 124 children (14%), with ESI rate 0.25/yr. Median time to ESI was 329 days (IQR 161-629 days) post-insertion. At ESI diagnosis, 67% involved ES only; 21% tunnel only, 2% both. 6% had concomitant peritonitis. Among all ages, ESI incidence was lowest in children <2 yo at enrollment and highest in children 6-12 yo (p=0.003). Failure to review ES care and ES score >0 in the prior month were associated with subsequent ESI (p<0.001). ESI was not associated with gender, race, ESRD etiology, exit site orientation, catheter cuff number or mobilization, and presence of G-tube, urinary stoma, or vesicostomy. At ESI, median ES score was 4 (IQR 2-5). ESI cultures obtained in 84% grew staph and pseudomonas most frequently. 71% ESI resolved with treatment although 24% required hospitalization, 2% developed tunnel infections and 1 child developed peritonitis. 9% required catheter removal, most often with tunnel infections.

Conclusions: ESI occurs at annualized rate of 0.25, typically well into PD course. Younger age and monthly review of ES care is associated with lower ESI rates. Although most ESIs resolve, hospitalization is frequent and catheter loss and tunnel involvement noteworthy.

3. This unique study on PD biopsy samples has shown complement activation in the omental vessels, particularly with low GDP dialysate, and that the complement activation preceeds the development of overt arteriolopathy.

FP-S25-02 - The complement system is highly activated in PD associated arteriolopathy

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Objectives: Cardiovascular disease is the leading cause of death in children on peritoneal dialysis (PD), underlying mechanisms are still incompletely understood.

Methods: Omental arterioles covered with fat, i.e. located beyond PD fluid penetration level were microdissected from non-uremic children, age and gender matched children at time of first PD catheter insertion and children treated with low GDP PD fluids [PD vintage 26; 2-72 months). Childrenwith diseases potentially affecting vessel integrity were excluded. 3-4 arterioles per patient with similar structural dimensions (as defined by Aperio®automated image analysis after EVG staining vessels) were selected, neighboured sections were used for whole transcriptome and proteome analysis.

Results: Uremia induced up-regulation of 173 and down-regulation of 117 arteriolar genes ($p<0.01$) compared to age and sex matched healthy controls. In patients on low GDP PD, 88 genes were up- and 11 genes down regulated compared to respective uremic controls, while in children on high GPD PD 139 genes were up- and 17 genes downregulated. Intima media thickness was comparable in all groups. Gene ontology analyses demonstrated activation of various inflammatory, immunological and stress response cascades with uremia and even more with PD. In children treated with low GDP fluid the complement system and respective regulatory pathways were upregulated most significantly. 14 complement factors demonstrated comparable upregulation on RNA and protein level, CD55 was suppressed. Findings were validated immunohistochemically in an independent cohort of 15 children per group; C1q and C3c were 5 and 2.6 fold increased with low GDP PD compared to uremic controls.

Conclusions: Omental arterioles are uniquely suited for global assessment of molecular pathomechanisms of uremia and PD associated arteriolopathy. We for the first time demonstrate specific activation of the complement cascade in arterioles from children on low GDP peritoneal dialysis, prior to overt arteriolopathy.

Also see abstract FP-S07-3 - The PD Membrane Microvasculature in Uremia and PD – Recent Findings from the International Pediatric PD Biobank from B. Schaefer et al