Nephrology

G214 HEPARIN AND RENAL ALLOGRAFT THROMBOSIS: DOES HEPARIN SIGNIFICANTLY REDUCE THE INCIDENCE OF THROMBOSIS IN PAEDIATRIC RENAL ALLOGRAFTS?

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Aim: To establish whether heparin reduces the incidence of renal graft thrombosis in children aged 0 to 16 years.

Method: Retrospective study of 306 transplants undertaken in 274 children between 1987 to 2000. Heparin was given to all patients after 1993. Repeat grafts (n=32), >16 years of age (n=12), recurrence of HUS (n=1) and insufficient data (n=7) were excluded. The 254 children studied (84 (33%) girls) had a mean age of 8.83 (SD 4.7) years at transplant. The children were divided into 2 groups: Group 1 (n=128) did not receive heparin, and Group 2 (n=126) received heparin s.c, tds, dose: <15kg-1000 units, <20kg-1500 units, 20kg–40kg-2500 units (APTT maintained < twice control.) Recipient characteristics were similar in both groups. Mean age of Group 1 was 8.5 (SD 4.6) years and Group 2 was 9.1 (SD 4.7) years. Immunosuppression was cyclosporine, prednisolone and azathioprine in both groups, 15 patients in Group 2 received FK506 instead of cyclosporine. The incidence of graft thrombosis between the 2 groups was compared and logistic regression analysis was used to assess the effect of variables previously identified with increased risk of graft thrombosis i.e. donor and recipient age and sex, cold ischaemia time (CIT), multiple donor vessels and side of kidney graft donation.

Results: There were fewer grafts lost to thrombosis in Group 2, but this was not statistically significant (14 in Group 1 and 10 in Group 2, OR 0.7 (95% CI 0.3–1.6.), There were also 2 losses due to haemorrhage in Group 2. The mean time to graft loss was similar in Groups 1 and 2, (6.6 (SD 3.9) (range 2–12) days and 7.9 (SD 4.4) (range 1-14) days respectively.) Young age of recipient (p=0.006) and increasing CIT (p=0.007) were associated with increased risk of graft thrombosis.

Conclusion: This retrospective analysis has demonstrated that heparin does not significantly reduce the incidence of renal graft thrombosis. In agreement with previous studies we have shown that young recipient age and prolonged CIT are significantly associated with an increased risk of graft thrombosis.

G215 DOSAGE AND ADVERSE EFFECTS OF MYCOPHENOLATE MOFETIL IN PAEDIATRIC RENAL TRANSPLANTATION

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Aims: Mycophenolate Mofetil (MMF) is increasingly used as a substitute for Azathioprine in patients post renal transplant for steroid resistant rejection or toxicity from calcineurin inhibitors. We report our experience with MMF in view of the adverse side-effects noted with the suggested dosing levels (600mg/m^2 per dose twice a day)

Method: The records of all transplant children receiving MMF in our tertiary nephrology centre since August 1999 were reviewed

Results: MMF has been prescribed in 23 post transplant children (14 male) at a median age of 14.4 yrs (range 2.3–16 yrs). 3 children received MMF immediately post transplant for primary immunosuppression but 20 received it at a mean of 2.9 yrs (range 0.5–8.4 yrs) post transplant for resistant rejection and/or Cyclosporin/Tacrolimus toxicity.

On MMF 43% of patients had a mean weight loss of 10.3% (range 4.9–22.2%); 39% diarrhoea; 22% anaemia, 8.6% neutropenia; 4.3% lymphopenia and 4.3% recurrent infections. In 6 patients the MMF has been discontinued after a mean of 4.3 months because of adverse effects. The mean initial dose of MMF was 300mg/m^2 per dose twice a day with the maximum mean dose being 450mg/m^2 per dose twice a day. Only 7 patients received the recommended target dose of 600mg/m^2 twice a day.

Conclusion: MMF has been a valuable addition to the immunosuppressive regimen but appears to have marked gastrointestinal side effects with significant weight loss noted in a number of patients. The optimal dosing level needs to be established but would appear to be lower than the current recommended target dose.

G216 NEONATAL PERITONEAL DIALYSIS—OUTCOME IN A REGIONAL CENTRE

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Background: Only in the last ten years has continuous peritoneal dialysis been advocated in neonates. Limited information is available on its use in acute renal failure.

Aims: (1) To describe the profile of dialysed neonates, the duration and complications of treatment, morbidity and outcome. (2) To determine pre-dialysis assessment.

Method: All cases of neonatal peritoneal dialysis, from March 1996 to March 2001, were reviewed for the following data: indication for dialysis, gestation, corrected age and weight at dialysis, presence of cranial and renal ultrasound assessment, duration of dialysis, complications and outcome.

Results: 19 neonates were referred for consideration of dialysis. 7 were unsuitable: necrotizing enterocolitis (2), anorectal abnormality (1), ileostomy (1), and extremely poor prognosis (3).

12 were dialysed. Median (range) gestational age was 29 (23–41) weeks. Median (range) age at dialysis was 33 (28–41) weeks. Median (range) duration of dialysis was 3 (1–231) days. Indications for dialysis included hyperkalaemia (3), oliguria/anuria (4), hyperammonaemia (1), persistent acidosis (2), bilateral renal vein thrombosis (1) and renal fungal balls (1). Pre-dialysis cranial ultrasound scans were performed in 11 of the dialysed patients, 2 subsequently developed periventricular leucomalacia. 8 babies had complications including catheter blockage (4), leakage (3) and peritonitis (3). 6 required one or more catheter replacements. 9 (75%) babies died; 7 in the neonatal intensive care unit (NICU) and 2 post-discharge. Median (range) age at death in NICU 27 (6–59) days. Of the 3 survivors 1 required long-term dialysis and all are developmentally delayed.

Conclusion: Morbidity and mortality are extremely high and are related to the underlying co-morbidities. Careful parental counseling and patient selection needs to be undertaken prior to treatment.

G217 EDUCATIONAL DIFFICULTIES AND SUPPORT NEEDS OF CHILDREN FOLLOWING RENAL TRANSPLANTATION

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Aims: Improving the educational experiences and attainments of children with chronic illness is an important aspect of their care. Our study sought to i) investigate the educational difficulties and problems of children following renal transplantation, and ii) identify the support necessary to promote their effective educational and social inclusion.

Methods: Semi-structured interviews were conducted in the homes and schools with 12 children (all >2 yrs post transplant), their parents, their teachers and their non-ill school friends. Drawing on multiple informants enabled data to be triangulated. Interview transcripts were content-analysed on the basis of key themes. Schools were contacted for statistical information on school attendance and achievement.

Results: Analysis of 39 interviews indicates that post-transplant children are likely to experience peer relations difficulties at school, including bullying/name-calling. Other difficulties include i) issues of school absence and re-integration, ii) low motivation for school work due to tiredness or worry and iii) lack of teachers' awareness and knowledge about the child's health condition. Liaison between hospital and mainstream school staff was regarded as essential, especially at times of crisis or transition. Parents also acknowledged their difficulties in maintaining a balance between being supportive or over-involved in their child's schooling. Analysis of data on school attendance for 8 children to date revealed an average attendance of 83% (range 66–93%).

Conclusions: Minimising the barriers to children's effective educational and social inclusion post-transplant, will require i) providing support to help the children deal with academic and social difficulties (in particular, peer relations problems), ii) raising teacher-awareness and information levels, iii) enhancing hospital-school liaison, and iv) addressing parents' support needs in relation to their children's education.

G218 CATCH-UP GROWTH CAN OCCUR WITH NORMAL PARATHYROID HORMONE LEVELS IN CHILDREN WITH CHRONIC RENAL FAILURE

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Aims: Parathyroid hormone (PTH) levels of 2 to 4 times normal have been recommended to maintain normal growth in children on dialysis. We aimed to assess the effect of circulating PTH levels on the growth of children with chronic renal failure (CRF).

Methods: The renal unit database was used to identify patients who presented after 1989 (when current immunometric PTH assays where introduced) under the age of 5 years, with a glomerular filtration rate (GFR) of <41ml/min/1.73m^2 and with ≥2 years of 3 monthly data. Children with co-morbid features affecting growth were excluded and data collection was stopped if renal replacement therapy (n=9) or growth hormone (n=6) was commenced. The departmental policy is to optimise dietary intake, correct acidosis and salt depletion and to maintain a normal PTH by phosphate control (using dietary restriction and calcium carbonate or acetate) and prescription of activated vitamin D.

Results: Data have been collected for a mean (range) of 3.6 (2.0–4.9) years from 59 patients age 2.0 (0.4–4.9) years, GFR 21 (6–41) ml/min/1.73m^2. The mean (SEM) height standard deviation score (Ht SDS) at inclusion was –1.77 (0.18), which is significantly different from normal (p<0.001). The overall mean change in Ht SDS (ΔHt SDS) per year was 0.11 (0.04), which is a significant (p=0.012) improvement on normal growth. This catch-up growth was independent of age and occurred during the first 2 years of treatment (ΔHt SDS 0.4 (0.14)) (p<0.005); in subsequent years there was no further change in Ht SDS. Overall, age corrected, mean calcium and phosphate levels were 0.97 (0.91–1.03) and 0.83 (0.72–0.95) times the upper limit of the normal range (ULN) respectively and the median PTH level was equal to the ULN (inter-quartile range (IQR) 0.8–1.3 times ULN).

Conclusion. Children with a GFR <41 ml/min/1.73m^2 who are managed conservatively maintain excellent growth with normal PTH levels, suggesting that normalisation of PTH levels in this patient group is appropriate.

G219 THE INCIDENCE OF HYPERTENSION FOLLOWING VESICO URETERIC REFLUX

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Aims: Hypertension in children with vesico ureteric reflux (VUR) and renal scarring is reported in at least 10%. The prevalence in adults with renal scarring is up to 50%. Studies to date have concentrated on those with the highest risk of developing hypertension (i.e. those with bilateral renal scarring) but have not compared the outcomes between those with no scarring, unilateral and bilateral scars. This study investigated the development of hypertension in all patients with VUR regardless of scarring status.

Method: A total of 771 patients with VUR, reflux nephropathy or both were identified from our paediatric nephrology-urology database. 512 (66%) records have been scrutinised to date for grade of VUR, severity of renal scarring, surgical intervention and length of follow up. In addition, each blood pressure measurement together with height and age was recorded. Hypertension was defined as 2 or more blood pressure readings greater than the 95 th centile for height or age or treatment with antihypertensive medication at any stage of follow up.

Results: 474 patients were followed up for a median of 54 months. 448 (94.5%) were normotensive (no scars 236, unilateral scars 160, and bilateral scars 52). 26 (5.5%) were hypertensive including 18 who had a florid presentation (no scars in 1, unilateral scars in 8 and bilateral scars in 17). The median age at onset of hypertension was 84 months (IQR 4-133 months). The numbers of patients who were hypertensive by grade of scarring was as follows: VUR alone (1 out of 237 (0.4%)), VUR + unilateral scars (8 out of 168 (4.7%)) and VUR + bilateral scars (17 out of 69 (24.6%)). There was a significant association between the detection and severity of scars and the presence of hypertension.

Conclusion: This analysis would suggest that the incidence of hypertension following VUR is dependent upon the presence and severity of renal scarring.

G220 A NEW URINE COLLECTION METHOD BY ABSORBENT PAD AND MOISTURE SENSITIVE ALARM

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Background: Collecting a 'clean' urine sample in young children to rule out urinary tract infection (UTI) is difficult. Urine collection pads (U.C.P.) are inexpensive and easy to use but about 25% of samples have a high rate of local flora (>10^5 mixed growth organisms/ml) contamination. We hypothesised that reducing the contact time between the wet urine pad and skin might reduce the risk of contamination. We decided a new U.C.P. method incorporating an enuresis alarm sensor.

Aims: To compare the mixed growth (>10^5 mixed growth organisms/ml) of urine samples obtained from U.C.P. and U.C.P connected to a moisture sensitive alarm.

Methods: Febrile children under the age of 2 years with suspected urinary tract infection were randomised to 2 groups, U.C.P alone and U.C.P with enuresis alarm.

Results: 91 children were enrolled in the study and 71 adequate samples were obtained (UCP group—37, UCP & alarm group—34). U.T.I occurred in 7% (UCP—3/37, UCP & alarm 2/34). The overall incidence of any mixed growth (>10^3 mixed growth organisms/ml) was 49% (35/71), which was not significantly different between the 2 groups; UCP 16/37 (45%), UCP & alarm 19/34 (55%) (Odds ratio 1.66, 95% CI 0.6–4.2). Excluding those with UTI, the rate of heavy mixed growth (>10^5/ml) was similar in both groups, UCP 7/34 (21%), UCP & alarm 7/32 (22%) (Odds ratio 1.08, 95% CI 0.3–3.5). There were no adverse effects from the use of alarms & one false alarm.

Conclusion: The use of moisture a sensitive alarm with UCP to reduce the contact time of wet pad with skin does not reduce the likelihood of contamination of the urine sample. However, the alarm method was faster and easier to use and was the preferred method by the nursing staff.

G221 ETHNICITY AND RELAPSE RATES IN CHILDREN WITH NEPHROTIC SYNDROME

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Nephrotic syndrome (NS) affects children throughout the world. There are clear racial differences in incidence, histology and prognosis. In the U.K. there is a higher prevalence of MCNS in Asian children.

Aims: To study the demographics, clinical course and outcome of children with nephrotic syndrome in Leicestershire, over a seven year period.

Methods: Data was obtained from case note review. Follow up data were available for at least one-year post diagnosis. Features at presentation, racial variations in steroid response, relapse rates and biopsy findings were studied.

Results: 57 children presented within this period. Male to female ratio, 1.7:1.Asian: Caucasian, 1.2:1. Estimated incidence of NS in Leicestershire Asians 13/100 000. Haematuria was present in 51% of children at presentation. Relapse rates were significantly higher in Asians *v* Caucasians 97% *v* 70% Chi square p=0.002

Conclusion: Our study confirms the higher prevalence of NS in Asians. All Asians were steroid responsive at first presentation but were significantly more likely to relapse than Caucasians. Caucasians had a higher incidence of steroid resistant NS at presentation.

G222 PROGNOSTIC FACTORS AND OUTCOME IN CHILDHOOD MESANGIOCAPILLARY GLOMERULONEPHRITIS (MCGN)

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MCGN is uncommon in children, and reported to have poor long-term renal survival. We present results of a two centre retrospective analysis of 53 children with MCGN diagnosed on renal biopsy.

The children (21 females and 32 males) presented at a mean of 8.8 years (range 13 mo–15 yr). Classification by renal histology identified 31 type I, 14 type II, 2 type III and 6 undetermined. Presenting features included proteinuria 92%, haematuria 87% (microscopic 70%, macroscopic 17%), hypoalbuminaemia 81%, hypocomplementaemia 74%, renal impairment (eGFR<80ml/min/m^2) 72%, hypertension 49% and nephrotic syndrome 40%.

They were followed for a mean of 4.9 years (range 2 mo–17 yr). Mean renal survival time was estimated at 12.2 years (CI 9.7–14.6yr). Five year renal survival was 92% (CI 88–100%) and ten year renal survival 83% (CI 74–92%). MCGN type, sex, age at presentation, hypertension and low complement at presentation were not predictive of outcome. Nephrotic syndrome was a significant adverse prognostic factor with mean renal survival of 8.9 years (CI 7.1–10.7 years) vs 13.6 years (CI 10.8–16.5 years) (p=0.047). The degree of proteinuria at presentation and at one year, however, had no significant association with renal survival. Renal impairment at one year was a poor prognostic factor for renal survival at five years (87% (CI 70–100%) vs 100% if normal eGFR at one year, p=0.037). Mean renal survival at follow-up was 13 years when eGFR was normal at one year vs 11.3 years (CI 8–14.7 years) when abnormal (p=0.065). The mean difference in eGFR at one year in those who progressed to ESRF compared to those who did not was 46 ml/min/1.73m^2 (CI 23-69, p<0.001).

We conclude that nephrotic syndrome at presentation and abnormal eGFR at one year predict poor renal outcome.

G223 THE INFLUENCE OF TREATMENT UPON OUTCOME IN MESANGIOCAPILLARY GLOMERULONEPHRITIS PRESENTING IN CHILDHOOD

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Aims: To determine the effect of presentation upon the treatment used and the influence of treatment upon outcome in children presenting with mesangiocapillary glomerulonephritis (MCGN).

Methods: Data were collected retrospectively from patient notes. Details of 19 patients were collected in Bristol and 34 in Birmingham.

Results: 53 patients were identified presenting between 1980 and 2000. The range of follow-up time was 1–17 years with 45% having data to 5 years. Treatment varied within and between centres. 29 received Prednisolone or Methylprednisolone, 12 Azathioprine, 6 Cyclophosphamide and 4 Plasma exchange. There were no demographic differences between the group to receive steroids (treated) and the non-steroid group (non-treated) and the types of MCGN were similar in each group. Within the treated group (29/53), there was a higher proportion (76%) with a reduced glomerular filtration rate (GFR) at presentation compared to the non-treated group and there was a significant difference in the presence of hypertension (p=0.037) and nephrotic syndrome (p=0.002) at presentation between the groups. There was no significant difference in outcome measured by GFR, hypertension and proteinuria between the two groups.

Conclusions: There is a paucity of literature looking at this number of children with MCGN. In this series, presentation influenced the treatment received and there were no significant differences in outcome comparing the treated and non-treated groups. Treatment varied within and between 2 units. Evidence based recommendations and treatment protocols across the UK will be discussed.

G224 PLASMA FROM CHILDREN WITH FOCAL SEGMENTAL GLOMERULOSCLEROSIS AFFECTS THE PODOCYTE CYTOSKELETON, CELL DIFFERENTIATION AND FUNCTION

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Focal segmental glomerulosclerosis (FSGS) is a form of nephrotic syndrome strongly implicated as being caused by a circulating factor. More recently, familial forms of FSGS have been defined due to inherited podocyte specific disorders, e.g. podocin defects. Using a unique cell line of conditionally immortalised human podocytes, we examined the effect of plasma collected from patients with severe FSGS on cultured, differentiated cells. Plasma was collected from 3 patients undergoing plasma exchange for severe proteinuria. 2 children were post-transplant recurrences, and a 3rd had native disease. Control samples were from the 2 transplanted patients, when in remission; a non-nephrotic patient undergoing plasma exchange; a normal subject; and 10% FCS. Cells were treated for 24hrs and 48hrs, and examined by IF and Western blotting. In cells treated with relapse plasma, at 24 hours, we observed no change in cell morphology. The only change was that expression of the actin binding protein, synaptopodin, was lost and functionally there was a difference in calcium flux studies (p<0.001) between remission and relapse samples. By 48 hours the cells had changed shape, with diminution of cell body size, and loss of peripheral processes. Nephrin was down regulated, and together with podocin, redistributed from a cell surface distribution to a granular cytoplasmic location. Actin filaments became disrupted. Control plasma treated cells displayed none of these changes. Thus, plasma from patients with FSGS and active disease causes an early loss of synaptopodin, with calcium influx, followed by disruption of the actin cytoskeleton, in conjunction with redistribution of nephrin and podocin. This provides a model to further explore the mechanisms underlying this disease, as well as a means to test disease activity *in vitro*.

G225 ENDOTHELIAL MICROPARTICLES: JUST BLOOD "DUST", OR A "MUST" FOR THE DIAGNOSIS AND MONITORING OF DISEASE ACTIVITY IN CHILDHOOD VASCULITIDES?

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Introduction: Microparticles (MPs) are released from endothelial cells in response to a variety of injurious stimuli and recently have been shown to be increased in multiple sclerosis and antiphospholipid syndrome.

Aims: This study examined endothelial and platelet MP profiles in children with systemic vasculitis (SV) to test the hypothesis that endothelial MPs may provide a tool for the diagnosis and monitoring of disease activity.

Patients: 12 children with active SV (9 with polyarteritis, 2 with Kawasaki disease, and 1 with hypersensitivity vasculitis); 8 children with inactive SV; 8 disease control children without SV; and a control group of 28 healthy subjects comprising 11 healthy children and 17 young adults were studied. Additionally, paired samples from 4 children with SV pre and post induction of remission were examined.

Methods: Plasma was centrifuged at 13000G for 60 minutes, and the pellet resuspended and prepared for flow cytometry. MPs were defined as particles less than 2 microns in diameter and with surface binding of annexin-V. Fluorescent conjugated monoclonal antibodies to several endothelial markers and platelet markers were used to identify and quantify MPs.

Results: Plasma from patients with active vasculitis contained a 12.4 fold elevation of E-selectin positive endothelial MPs compared with patients in remission (p=0.001), a 5.7 fold elevation compared with controls (p=0.000) and a 7.9 fold elevation compared with disease controls (p=0.001). A similar result was obtained for MPs expressing the endothelial marker CD105. No difference was observed for MPs of platelet origin between the groups. 4/4 patients with active vasculitis demonstrated high levels of endothelial MPs which fell to normal following induction of remission (a 10.5 fold decrease for CD105 MPs and an 8.7 fold decrease for E-selectin MPs).

Conclusion: Endothelial MPs may provide a "window" to the activated endothelium, and these preliminary data suggest that they may be useful diagnostically and for the monitoring of disease activity in SV of childhood.