Abstracts from the Hong Kong Society of Nephrology Annual Scientific Meeting 2005

Effect of Rapamycin on Renal Ischemia Reperfusion Injury

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Background: The aim of this study was to determine the effect of rapamycin (Rapa), a relatively new immunosuppressive drug, on renal ischemia reperfusion injury (IRI) in the mouse.

Methods: Renal IRI was induced in male Balb/c mice by clamping both renal pedicles for 45 minutes. The mice were treated with either vehicle or Rapa (2 mg/kg/day) by oral gavage, starting 2 days before the IRI and continued daily until sacrifice. The mice were sacrificed at 1, 3, and 7 days after the operation. The severity of the IRI was assessed by serum creatinine levels and renal histology. Proliferation of renal tubular cells was quantified by immunohistochemical staining for proliferation (PCNA).

Results: One day after the IRI, the serum creatinine levels of Rapa-treated mice were significantly higher than those of vehicle-treated mice. Kidney sections from Rapa-treated mice also showed more marked tubular damage on day 1. The number of PCNA-positive cells in Rapa-treated mice was significantly lower than that in vehicle-treated mice on days 1 and 3 after IRI. By day 7 after IRI, there was no significant difference between Rapa- and vehicle-treated mice in terms of serum creatinine levels, renal histology and positive PCNA staining.

Conclusion: We conclude that Rapa treatment aggravates renal IRI during the first 1 to 3 days after the insult. This effect might be partly mediated through inhibition of renal tubular cell regeneration.

Role of PPAR-γ Agonist in Diabetic Nephropyathy: An In Vitro Study

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Background: We have previously shown that advanced glycation end products (AGEs) in the form of glycated bovine serum albumin (gBSA) incite a proinflammatory phenotype in proximal tubular epithelial cells (PTECs). Emerging data suggest that peroxisome proliferator-activated receptor-γ (PPAR-γ) agonists may possess anti-inflammatory properties in addition to their insulin-sensitizing effect in diabetic nephropathy.

Methods: We investigated the intracellular signal transduction mechanism of gBSA and the impact of the PPAR-γ agonist in an in vitro model of diabetic tubulopathy. Human PTECs, obtained from primary culture, were exposed to medium alone, or supplemented with BSA (0.5 mg/mL) or gBSA (0.5 mg/mL) with or without prior addition of rosiglitazone (0.1-0.5 µM).

Results: Exposure to gBSA, but not BSA, significantly upregulated both mRNA gene and protein expression of IL-8 (p = 0.009 and p < 0.001 vs BSA, respectively) and sICAM-1 (p = 0.017 and p = 0.05 vs BSA, respectively), which were dose-dependently attenuated by rosiglitazone. Also in a dose-dependent fashion, gBSA, but not BSA, caused nuclear translocation of nuclear factor-kappa B (NF-κB) and activation of mitogen-activated protein kinases (MAPK) p44 and p42. Both NF-κB and MAPK signals were unaffected by concurrent treatment with rosiglitazone. Conclusion: AGEs potentiate tubular inflammation that may be modified by PPAR-γ ligation independent of NF-κB transcriptional activity and MAPK signaling. The anti-inflammatory effects of PPAR-γ agonists in diabetic nephropyathy may lie downstream to NF-κB and MAPK pathways.

Antibody Response to Hepatitis B Vaccine in End-stage Renal Disease Patients

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Background: This retrospective and comparative study evaluated the relationship between different factors which may contribute to suboptimal immunologic response to intramuscular recombinant hepatitis B vaccine in end-stage renal disease subjects. Methods: From a cohort of 64 dialysis subjects undergoing primary vaccination with Engerix-B, we determined the predictive factors that impinged on patients’ response to vaccine, as defined by anti-HBs level ≥10 mIU/L. Dose efficacy was further evaluated by comparing three historical cohorts vaccinated with the regimens of 20 g, 40 g and 80 g per dose respectively.

Results: We identified 64 end-stage renal disease patients (mean age, 43 ± 12 years; 81% receiving peritoneal dialysis) who received primary vaccination from April 1997 to September 2004. Median follow-up was 6.5 years. They achieved a seroconversion rate of 81%. Older age, diabetes mellitus, obesity and low Engerix-B dose were risk factors of inadequate anti-HBs level at one year for every 5.6 patients treated (number needed to treat to benefit, 5.6; 95% CI, 5.4-5.8). Conclusion: Our results suggest the potential for the three-dose schedule of recombinant vaccine Engerix-B 80 µg to prolong the immune response among end-stage renal disease patients.
PREVALENCE OF PSYCHOLOGICAL PROBLEMS IN CHINESE PERITONEAL DIALYSIS PATIENTS

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Background: Psychological problems are common among dialysis patients. We studied the prevalence of psychological problems in a cohort of Chinese peritoneal dialysis (PD) patients.

Methods: We studied 167 unselected adult PD patients from a single dialysis unit. Psychological status and social support were assessed by the Hospital Anxiety and Depression Scale (HADS) and the Medical Outcomes Study Social Support Survey, Chinese Version (MOS-SSS-C) questionnaires, respectively.

Results: With the HADS questionnaire, 33 (20.0%) and 76 (45.5%) patients had at least mild anxiety and depression symptoms, respectively. With the MOS-SSS-C questionnaire, 13.8% of patients had borderline social support, and 4.2% had poor social support. There was a close internal correlation between the HADS and MOS-SSS-C scores. A higher HADS score was noted in male patients (8.19 ± 6.80, p = 0.038), elderly patients (r = 0.224, p = 0.011), patients partly dependent with regard to their daily activities (8.352 ± 4.63 vs 7.08 ± 4.12, p = 0.08), those with no full-time job (7.47 ± 4.31 vs 4.45 ± 2.16, p = 0.005), those not on transplant waiting lists (7.90 ± 4.33 vs 5.71 ± 3.82, p = 0.008), and those with poor drug compliance (7.80 ± 4.44 vs 4.25 ± 4.17, p = 0.016).

Conclusion: Psychological symptoms are common in elderly male patients without full-time jobs and patients not on transplant waiting lists. On the other hand, anxiety symptoms and poor social support are associated with poor compliance to various aspects of treatment.

HAEMODIALYSIS TWICE PER WEEK - SINGLE POOL KT/V, UREA REDUCTION RATIO, BLOOD-BASED NORMALIZED PROTEIN CATABOLIC RATE AND THEIR CORRELATION

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Background: In Hong Kong, the majority of haemodialysis (HD) patients dialyse twice a week. We examined the single pool KT/V (spKt/V), urea reduction ratio (URR) and blood-based normalized protein catabolic rate (nPCR), and their correlation in this particular group of patients.

Methods: This was a retrospective study of 43 anuric patients who were receiving HD twice weekly. The data from one dialysis session of HD was collected. spKt/V was calculated by the Daugirdas second generation equation using the 15 seconds post-dialysis blood urea level (Stop Pump Technique).

Results: Excellent correlation existed between spKt/V and URR, whereas weak correlation was shown between spKt/V and nPCR, and between URR and nPCR.

Conclusion: In our patients receiving HD twice weekly, the mean spKt/V, URR, and nPCR were 2.0, 79% and 1.1 g/kg/day, respectively. spKt/V and URR correlated well, but spKt/V and URR correlated poorly with nPCR determined from blood-based parameters.

A SINGLE CENTER STUDY ON PERITONITIS IN APD PATIENTS

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Background: The optimal treatment for peritonitis in APD is not known. Methods: Retrospective review of hospital and OPD notes. Results: A total of 47 patients were examined: 38.3% were diabetic; 25 patients required helpful. The duration of therapy ranged from 6 to 97 months. The total therapy time was 1,695 patient-months. There were 32 episodes of peritonitis reported. The peritonitis rate was 1 in 53 patient-months. The mean time to first peritonitis was 21.9 months. The causative organisms were: Gram-positive bacteria, 37.5%; Gram-negative bacteria, 37.5%; culture negative, 12.5%; TB, 6.25%; and mixed organisms, 6.25%. The breakdown of the bacterial cultures were: Staphylococcus spp, 6/32; MRSA, 4/32; Klesbiella spp, 4/32; Pseudomonas aeruginosa, 3/32; Escherichia coli, 2/32; Actinobacter spp, 2/32; Staphylococcus aureus, 1/32; and Enterococci, 1/32. Four patients died during the same peritonitis episodes: two were related to TB peritonitis; the third died of AMI; the fourth patient had PD catheter removal and died after prolonged hospital stay. Twenty-four episodes (85.7%) responded to antibiotics: 22 patients were treated with in-hospital CAPD followed by antibiotics in APD day-dwell; one was prescribed outpatient antibiotics in day-dwell at the start; and the last patient was continued on CAPD until completion of antibiotics. Three of four catheter removal cases had successful catheter reinsetion. The relative risks for peritonitis were 2.35, 1.41 and 1.34 for helper status, NIPD and DM respectively.

Conclusion: A regimen of CAPD followed by day-dwell antibiotics was successful in 85.7% of APD peritonitis. DM, requirement for a helper, and NIPD were risk factors for the development of peritonitis.

PRISMARS AS SUPPORT FOR LIVER AND MULTI-ORGAN FAILURE

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Background: The MARS system was first described in 1993 as a non-biological system for liver support. PRISMARS is the coupling of such an albumin absorbent circuit with a continuous haemodialysis machine which was designed to tolerate intermittent haemodialysis or who require multi-organ support therapy in the intensive care unit. PRISMARS was first introduced to Hong Kong in September 2003. From 1 September 2003 to 15 November 2004, eight patients (male:female, 6:2) received 47 PRISMARS treatments at the Hong Kong Sanatorium and Hospital. Two patients had multi-organ failure, three had primary and two had secondary CA; one patient had fulminant hepatic failure (FHF) due to hepatitis E.

Treatment protocol: Multi-lumen haemocatheter as vascular access; 8-hour session at BFR 150 mL/min and UFR 50-150 mL/hr. Hemosol-Bo solution as replacement fluid at 600-1,000 mL/hr given before haemofilter; Enoxaparin Na 20 mg at start and 10 mg at 4 hour iv for anti-coagulation. Results: No mortality or complications were directly related to PRISMARS therapy. Thirty-day survival was 85%. Total serum bilirubin was reduced by 20% (425.6 vs 338.4 mol/L, p = 0.0262). Direct bilirubin was reduced by 33.4% (330.2 vs 219.8 mol/L, p = 0.00216). The ammonia level was reduced by 23.3% (63.2 vs 48.5 mol/L, p = 0.082). Haemoglobin level dropped insignificantly from 9.65 to 9.25 g/dL (p = 0.2). Platelet count dropped insignificantly from 51,774 x 10^9 to 47,573 x 10^9 (p = 0.6). Mean arterial blood pressure improved from 60.98 to 66.5 mmHg (p = 0.0177) during PRISMARS treatment.

Conclusion: PRISMARS offers effective, well-tolerated support to multi-organ failure patients, with a significant reduction in bilirubin levels and improvements in the haemodynamic and fluid status of critically ill patients. However, its impact on patient survival remains to be further evaluated.
A Simple Citrate Anticoagulation Protocol for Haemodialysis (HD) Using a Commercial Calcium-containing Dialysate

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Background: By chelating ionised calcium (iCa), regional citrate anticoagulation for HD has been proven to reduce bleeding complication in high risk patients. However, the complexity of the HD circuit and the citrate associated metabolic complications impeded the popularity of this approach. In the present study, we attempted to use low dose citrate and to simplify the circuit by using a conventional calcium-containing dialysate.

Methods: Twelve patients (8 male, 4 female; mean age, 59 ± 14 years) with high risk of bleeding requiring HD treatment were studied. Each patient was dialysed for 4 hours using a Polyflux 8L dialyser. Blood flow was kept at 200 mL/min. A dialysate containing 1.25 mmol/L calcium was used, and the sodium and bicarbonate content were set at 135 and 32 mmol/L, respectively. Anticoagulant citrate dextrose-formula A solution was infused into the afferent blood line at a rate of 340 mL/hr (citrate, 25.4 mmol/hr). Calcium infusion was not required. Acid-base status, electrolytes, iCa, dialyser urea clearance (UrCl) and creatinine clearance (CrCl) were collected. Wilcoxon’s signed rank test was used for comparison of paired data.

Results: The results (median ± SD) are shown in the table below. All the dialysis treatments were uneventful and well tolerated. Manifestations of citrate toxicity or hypocalcaemia were not observed. There was no significant difference in the 15-minute and 4-hour dialysate UrCl and CrCl. All the dialysers passed the fibre bundle volume test after reprocessing and could be reused.

Conclusion: Our results suggest that the present citrate protocol is simple, safe, effective, and will be useful in dialysing patients with a high risk of bleeding.

Mycophenolate Mofetil Alleviates Persistent Proteinuria in IgA Nephropathy

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Background: Mycophenolate mofetil (MMF) is increasingly used to treat primary glomerulopathies. Its effectiveness in IgA nephropathy (IgAN) remains unclear.

Methods: Forty IgAN patients with persistent proteinuria (> 1 g, 24 hours) despite conventional treatment with blockers of the renin-angiotensin system were randomised to receive MMF for 24 weeks (group 1) or continue conventional therapy (group 2), and followed for 72 weeks. The primary end point was reduction of proteinuria by 50% or more over entry level. Results: Sixteen patients (80%) in group 1 versus 6 patients (30%) in group 2 reached the primary end point (p = 0.0019). Time-averaged change in proteinuria showed a significant decline in group 1, while control subjects displayed a modest rise (p = 0.003). By 72 weeks, the median proteinuria was 62.0 ± 77% (p = 0.003) and 120.5 ± 14.1% (p = 0.031) that of the corresponding baseline value in group 1 and group 2, respectively. There was a concomitant increase in serum albumin and a decrease in serum iCa levels in group 1 but not group 2 patients. Baseline histologic grades, blood pressure control, and the rates of change of serum creatinine and creatinine clearance were not different between the two groups. Normalisation in binding of polymeric IgA to cultured mesangial cells and serum interleukin-6 levels, which sustained to study end, was observed in group 1 but not group 2 patients.

Conclusion: In selected patients with IgAN, MMF is effective in lowering proteinuria and ameliorating some of the putative pathogenic abnormalities.

Lamivudine in Hepatitis B-associated Membranous Nephropathy

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Background: Although lamivudine is effective for the treatment of chronic hepatitis B (HBV) infection, its potential therapeutic impact on HBV-related membranous nephropathy (MN) in adults has not been characterised. Methods: We treated 10 HBsAg-positive patients with biopsy-proven MN, elevated serum alanine aminotransferase (ALT), and HBV-DNAemia (group 1), and compared their clinical course with 12 patients diagnosed to have HBV infection, elevated serum ALT, and MN in the pre-lamivudine era (group 2). Results: Baseline demographic and clinical parameters were not significantly different between the 2 groups. In group 1, lamivudine treatment was associated with significant reduction in proteinuria, increase in serum albumin, normalisation of ALT levels and disappearance of circulating HBV-DNA during the first year. Four (40%) and six (60%) patients went into complete remission after 3 g/day and 6 to 12 months respectively. In group 2, significant proteinuria persisted during the first year. Eight (83.3%) and three (25%) patients went into remission. Cumulative 3-year renal survival (using end-stage renal disease as the primary end point) was 100% in group 1 and 58% in group 2 (p = 0.024, log rank test). Blood pressure control reached the target of < 130/85 mmHg in both groups. Lamivudine was well tolerated and not associated with any adverse events. Hepatic decompensation or malignancy was not observed during follow up in both groups. Conclusion: HBV-related MN led to end-stage renal disease in a significant proportion of patients before the advent of anti-viral therapy. Lamivudine treatment improves renal outcome in HBV carriers with MN and evidence of liver disease.

Spirolonactone Enhances Antiproteinuric Effect of Angiotensin-converting Enzyme Inhibitor (ACEI)

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Background: It has been suggested that aldosterone may contribute to progression of kidney disease. We attempted to investigate whether the antiproteinuric effect of ACEI could be enhanced by co-administering spironolactone to aldosterone receptor blockade.

Methods: Twelve patients (malefemale, 5:7; mean age, 49 ± 7) on ACEI with refractory proteinuria were studied. A fixed low dose of spironolactone (25 mg daily) was added to the ACEI treatment. Patients were monitored for 8 weeks. Data on serum potassium (K), serum albumin (Alb), proteinuria (Uprotein) and creatinine clearance (CrCl) were collected. Wilcoxon’s signed rank test was used for comparison of paired data.

Results: The results (median, interquartile range) are shown in the table below. All patients tolerated the treatment except for one who developed hyperkalaemia that required stopping of spironolactone. A significant improvement in Alb and reduction in proteinuria was observed. A transient decrease in CrCl was noted but there was no difference in CrCl values between Week 0 and 8. There was no significant difference in blood pressure during the study.

Conclusion: Our findings suggest that the combination of ACEI and spironolactone may exert an additive antiproteinuric effect. Patients should be monitored closely for the development of hyperkalaemia. Further study is warranted to confirm the finding.
Glomerular Pathology of Allograft Kidneys

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Background: To review glomerular diseases diagnosed in allograft kidneys and to correlate them with clinical parameters.

Methods: Eight hundred and ninety-one renal graft biopsies and 43 graft nephrectomies filed in Queen Mary Hospital from 1980 to 2004 were studied. They came from 442 allograft transplant recipients. Results: Glomerular diseases were diagnosed in 33.0% of kidney grafts. Indications for biopsy were baseline assessment (23 biopsies, 2.5%), renal dysfunction (790 biopsies, 88.7%), proteinuria (154 biopsies, 17.3%), and hematuria (11 biopsies, 1.2%), and by protocol (4 biopsies, 0.4%). The median time post-transplant when the biopsies were procured was less than 8 months. The mean time post-transplant for diagnosing IgA nephropathy (IgAN), transplant glomerulopathy (TG), focal segmental glomerulosclerosis (FSG), mesangiocapillary glomerulonephritis (MCGN), membranous GN, mesangial proliferative GN, and diabetic nephropathy was 70, 66, 65, 55, 45, 49, and 101 months, respectively. Specific glomerular diseases were diagnosed by biopsies in 106 of 119 (89.1%) proteinuric allografts. Recurrent glomerular disease was documented in 31 (7.0%) grafts. Conclusion: Glomerulopathy was common in allograft biopsies. A higher proportion of grafts from donors related to the recipients than from unrelated donors had IgAN (p < 0.05), and there was no difference in the time to diagnose IgAN post-transplant between the two groups, suggesting that genetic factors might play a role in its pathogenesis. Recurrence of glomerulopathy underlying end-stage renal disease was frequent for IgAN, FSG, and MCGN, but this was rare for membranous GN.

Clinical Outcome of Hepatitis C Virus (HCV) Infection on Renal Transplantation

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Background and Methods: In order to understand the clinical outcome of HCV-infected renal allograft recipients, a retrospective review was conducted in July 2005 to study the clinical course of renal allograft recipients followed-up in the renal unit of Princess Margaret Hospital since January 2002.

Results: In 2002, 23 out of 404 renal transplant recipients were HCV-infected. The male:female ratio was 12:11; 82.6% of HCV-infected patients had cadaveric renal transplantation in China; 69.6% of HCV-infected patients were HCV-RNA positive. The predominant HCV genotype was 1b (56.3%). Other genotypes were: 1a, 18.8%; 2a, 12.5%; 3b, 6.2%; and 6a, 6.2%. Only two patients had co-hepatitis B virus infection. Two patients had liver biopsy before transplantation; both showed features of chronic hepatitis but they had stable graft and liver functions. None of them had acute flare up of hepatitis or hepatocellular carcinoma. One patient developed liver cirrhosis, while two eventually resumed dialysis due to graft failure. The mortality rates of HCV-infected and non-HCV-infected renal allograft recipients were 17.4% and 1.6%, respectively. Four HCV-infected recipients died: two died of severe sepsis with multiple organ failure; one died of perforated bowel; and one died from an unknown cause.

Conclusion: Although there is a higher mortality rate in HCV-infected renal allograft recipients, HCV infection is not a contraindication to renal transplantation. Transplantation is the best option for patients with HCV-infected end-stage renal failure. Adjustment of immunosuppression and careful follow-up are mandatory in order to detect infection and worsening of liver disease earlier.

Impact of Parathyroidectomy on Renal Graft Function: A Single Center Perspective

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Background and Methods: In this study, we retrospectively evaluated the impact of parathyroidectomy (PTX) on renal graft function in stable renal transplant recipients treated for persistent post-transplant hyperparathyroidism in our centre. All renal transplant recipients receiving PTX after renal transplant from 1999 to 2005 were recruited. Serum creatinine (SCr) levels were measured at pre-PTX, 1 month, 3 months and 6 months post-PTX. Changes in serum [Ca] and [P], parathyroid hormone level (PTH), hemoglobin (Hb) and BP were also studied. Data were expressed in mean ± SD or median (IQR). Results: Thirteen patients (MF = 7:6) with a mean age of 44.0 ± 9.0 years were recruited. PTX was performed at a median of 35.9 (68.6) months post-transplant. Mean SCr before PTX was 142.5 ± 49.7 μmol/L. All patients received calcium and vitamin D supplements post-PTX. Serum [Ca] and PTH levels improved significantly after PTX (Table 1). Significant increases in patients’ SCr were observed at 1 month, 3 months and 6 months post-PTX (Table 2). No significant changes in Hb (12.5 vs 12.3 g/dL, p = 0.36), mean arterial pressure (91.1 vs 89.0 mmHg, p = 0.40) and number of anti-HI drugs used before and after PTX were observed.

**Table 1**

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<th>Pre-PTX</th>
<th>Post-PTX</th>
<th>p</th>
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<tr>
<td>Ca (mmol/L)</td>
<td>2.90 ± 0.12</td>
<td>2.49 ± 0.28*</td>
<td>&lt; 0.005</td>
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<tr>
<td>PO4 (mmol/L)</td>
<td>0.96 ± 0.11</td>
<td>1.33 ± 0.17*</td>
<td>&lt; 0.005</td>
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<tr>
<td>PTH (pmol/L)</td>
<td>33.5 ± 27.6</td>
<td>4.3 ± 7.2*</td>
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**Table 2**

<table>
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<tr>
<th></th>
<th>Pre-PTX</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
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<tr>
<td>SCr (μmol/L)</td>
<td>142.5 ±49.7</td>
<td>157.0 ±40.9*</td>
<td>160.7 ±44.8</td>
<td>161.1 ±46.0*</td>
</tr>
<tr>
<td>% Change</td>
<td>13.3 ± 14.6*</td>
<td>15.2 ± 12.6*</td>
<td>15.2 ± 9.4*</td>
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*p < 0.05; **p < 0.005**

Conclusion: PTX was effective in the management of post-transplant hyperparathyroidism but was associated with deterioration in renal graft function that persisted at 6 months post-PTX. The mechanism of the deterioration remains to be elucidated.

Early Experience of C4d Staining in Renal Graft Biopsies: Two Years’ Experience

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Background and Methods: Local data are lacking on the use of C4d in renal graft biopsies. We report our experience on its application and attempt to find out its prognostic significance. Renal graft biopsies performed between 1 April 2003 and 31 March 2005 were reviewed. Results: There were 42 biopsies, 25 (59.5%) from males. Mean age ± SD at biopsy was 44.85 ± 10.83. The primary causes of renal failure included glomerulonephritis (26.2%), diabetes (16.7%), hereditary (71.4%), unknown (40.5%) and others (9.5%). Duration of follow-up was 11.4 ± 6.24 months. Histologic diagnoses included acute tubular necrosis (ATN) (28.6%), acute cellular rejection (Banff 1997) (borderline, 9.5%; type I, 23.8%; type II, 2.4%), and others (35.7%). Sixteen of 42 (38.1%) were stained C4d positive (10 focal, 6 diffuse). C4d positive and negative groups received similar immunosuppression and demonstrated similar histologic findings, except a higher
prevalence of ATN (11/26 vs 2/16; \( p = 0.084 \)) and arteriosclerosis (6/26 vs 0/16; \( p = 0.067 \)) in the latter group. C4d positive patients were more likely to receive pulse steroid after renal biopsies (7/16 vs 3/26; \( p = 0.027 \)) and to have higher serum creatinine levels at 6 months (in \( \mu \text{mol/L} \): 254.6 ± 129.7 vs 162.1 ± 63.9; \( p = 0.056 \)). Nevertheless, graft survival (in months) did not differ significantly [16.05 ± 1.73 vs 19.3 ± 1.74 (SE); \( p = 0.58 \)]. \textbf{Conclusion:} Routine C4d staining is needed as its status cannot be predicted by histologic findings. Positive C4d staining is probably associated with poorer renal outcome.

### Effects of Cyclosporine and Tacrolimus on the Pharmacokinetics of Mycophenolic Acid in Renal Transplant Recipients

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\textbf{Background and Methods:} To investigate the effects of cyclosporine (CsA) and tacrolimus (TAC) on mycophenolic acid (MPA) pharmacokinetics, we compared MPA profiles taken at 1 and 3 months post-transplant from renal transplant patients receiving mycophenolate mofetil (MMF) (2 g/day) plus CsA (\( n = 8 \)) and MMF (1 g/day) plus TAC (\( n = 7 \)). All patients received concomitant prednisolone. Blood samples were taken at 0 (trough), 20, 40, 60, 75 and 90 minutes, and at 2, 4, 6, 8, 10 and 12 hours post-dose for each MPA profile. Plasma MPA levels were determined by HPLC. \textbf{Results:} Mean MPA trough levels were higher at both 1 and 3 months in the TAC group compared with the CsA group (2.73 ± 1.20 vs 1.21 ± 0.42 \( \mu \text{g/mL} \) at 1 month, \( p < 0.005 \); 2.97 ± 2.07 vs 1.24 ± 0.69 \( \mu \text{g/mL} \) at 3 months, \( p < 0.05 \)). Mean MPA AUC0-12h in the TAC and CsA groups were 40.5 ± 9.4 and 35.7 ± 5.0 \( \mu \text{g*h/mL} \) at 1 month (\( p > 0.05 \)), and 44.4 ± 17.2 and 43.2 ± 10.8 \( \mu \text{g*h/mL} \) at 3 months (\( p > 0.05 \)), respectively. A second peak was observed in MPA profiles in the TAC but not the CsA group. When MPA levels were dose-normalised to 1 g MMF, mean MPA trough, \( C_{\text{max}} \) and AUC0-12h at 1 and 3 months were significantly higher in the TAC group compared to the CsA group.

\textbf{Conclusion:} These data suggest that CsA affects MPA pharmacokinetics by interrupting the enterohepatic recirculation of MPA. Using a 50% lower dose of MMF can achieve a similar MPA exposure when used in combination with TAC compared to CsA. MMF dose adjustment and drug monitoring may be necessary when CsA is switched to TAC or vice versa.

### Answer to Clinical Quiz

\textbf{Radiographic Findings}

A radio-opaque object with the shape of a fragmented tooth is seen in the left main bronchus. Slight loss of lung volume is noted on the left side, and the left diaphragm is also mildly elevated. Consolidation is noted at the left perihilar region, obscuring the left hilar and cardiac border. The right lung is clear. Cardiac outline is within normal limit. No obvious shifting of the mediastinum is noted.

\textbf{Diagnosis:}

Bronchial foreign body (tooth fragment) aspiration causing pneumonic change and mild atelectasis in the left upper lobe.

\textbf{Management:}

Bronchoscopy was immediately performed after diagnosis on chest film, and the fragmented tooth was removed in one-piece. Follow-up chest film showed complete clearance of the tooth fragment. Residual consolidation was still noted in the left upper lobe, and resolved completely on further follow-up.

\textbf{Reference:}


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