The relevance of Th1/Th2 paradigm to the pathogenesis of lupus nephritis

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Background: Lupus nephritis (LN) is characterized by intrarenal infiltration and activation of T-lymphocytes. Since T-bet and GATA-3 are the key transcription factors mastering the differentiation of Th1 and Th2 lymphocytes, we studied their intrarenal expression and correlated their expression with the severity of kidney lesions in LN patients. **Methods:** Glomerulus and tubulointerstitium were isolated from the snap-frozen biopsied kidney tissue of 37 LN patients by laser capture microdissection. The mRNA expression of T-bet and GATA-3 were studied by real-time quantitative polymerase chain reaction. **Results:** T-bet expression in glomerulus and tubulointerstitium of LN patients were 53.9 ± 9.9 and 23.8 ± 6.7 folds higher than the normal kidney controls. In contrast, GATA-3 expression in glomerulus was 1.9 ± 0.3 folds elevated, but depressed by 3.0 ± 0.5 folds in tubulointerstitium as compared to normal control. Both T-bet and GATA-3 showed a strong internal correlation between their expression in glomerulus and tubulointerstitium ($r = 0.59$ and $r = 0.69$, $p < 0.001$ for both). The T-bet-to-GATA-3 expression ratio in glomerulus significantly correlated with serum creatinine ($r = 0.36$, $p = 0.03$), glomerular filtration rate ($r = –0.41$, $p = 0.01$) and degree of renal fibrosis by morphometry ($r = 0.40$, $p = 0.04$). In addition, the degree of glomerulosclerosis and cortical fibrosis inversely correlated with GATA-3 expression in glomerulus ($r = –0.47$, $p = 0.006$) and tubulointerstitium ($r = –0.44$, $p = 0.01$) respectively. The degree of leukocyte infiltration significantly correlated with tubulointerstitium expression of T-bet ($r = 0.44$, $p = 0.01$). The total histologic chronicity index inversely correlated with GATA-3 expression in glomerulus ($r = –0.42$, $p = 0.02$) and tubulointerstitium ($r = –0.37$, $p = 0.03$). **Conclusions:** LN patients have a shift of T-bet/GATA-3 expression in the kidneys, and the expression correlates with the severity of histologic involvement. Our result suggests that Th1/Th2 imbalance may be important in the pathogenesis of renal damage in LN.

Hong Kong study using valsartan in IgA nephropathy (HKVIN): a double-blind randomized placebo-controlled study

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Background: We conducted a double-blind, randomized, placebo-controlled multicenter study on the use of the angiotensin II receptor blocker (ARB) valsartan 80–160 mg in reducing proteinuria and retarding the progression of renal failure in patients with IgA nephropathy. **Methods:** One hundred and nine patients, from six centers, with IgA nephropathy, characterized by either (i) proteinuria more than 1 g daily and serum creatinine less than 250 μmol/L, or (ii) serum creatinine between 120 and 250 μmol/L irrespective of proteinuria magnitude were randomized to receive either valsartan 80 mg (titrated up to 160 mg for blood pressure control) or placebo for 104 weeks. Additional antihypertensives were allowed to control blood pressure in both groups. **Results:** Fifty-four patients [(41 females) mean age 40.2 ± 9.2 years] were randomized to active treatment, and the placebo group consisted of 55 patients [(38 females) mean age 40.5 ± 9.2 years]. No discernible difference was noted in the baseline creatinine clearance or proteinuria between the treatment and placebo groups. Baseline blood pressure and lipid profile were also comparable. After adjustment for the blood pressure and baseline proteinuria, annual decline in glomerular filtration rate was 4.3 mL/min/year (95% CI 0.2–8.6 mL/min/year, $p = 0.038$) slower in the active treatment group after 52 weeks. Treatment benefit was maintained until the end of study period, with the glomerular filtration rate annual decline difference being 4.6 mL/min/year ($p = 0.028$). After 104 weeks, the proteinuria of the treatment group reduced from 1.8 ± 1.2 to 1.2 ± 1.2 g/day ($p = 0.03$), and from 2.3 ± 1.7 to 2.0 ± 1.7 g/day in the placebo group ($p = 0.72$). Valsartan treatment resulted in significant reduction in proteinuria compared with placebo ($p = 0.001$). No severe adverse event was encountered in both treatment and placebo groups. **Conclusions:** The angiotensin II receptor blocker valsartan is a safe and effective treatment that leads to slower renal deterioration and more reduction in proteinuria in patients with IgA nephropathy.

Mannose binding lectin gene mutation and incident rate of peritonitis in long-term peritoneal dialysis patients

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Background: Mannose binding lectin (MBL), a calcium dependent C-type lectin, is an important first line defence mechanism to protect the body from infection, by its capability to activate the complement system and phagocytosis. A low serum MBL may lead to an opsonic defect, which impairs phagocytosis by polymorphonuclear leukocytes. Study has shown low serum MBL level was associated with a higher incidence of spontaneous bacterial peritonitis in chronic viral hepatitis patients. Peritoneal dialysis (PD) related peritonitis is one of the major factor causing technique failure and mortality in patients on long-term dialysis. It is important to investigate any risk factor for peritonitis and related complication. Herein, we study any association between the peritonitis rate and MBL gene mutation in our long-term PD patients and investigate whether patients with peritonitis related technique failure associated with higher rate of MBL gene mutation. **Methods:** Long-term PD patients were recruited from two dialysis centers. Patients with repeated episodes of peritonitis classified as peritonitis group (RP). Patients without any history of peritonitis but having been on PD for more than 2 years were recruited as non-peritonitis group (NP). It was because the peritonitis rate was average once every 24 patient-months in our centers. For patients who developed technique failure secondary to peritonitis, currently on long-term hemodialysis were also recruited as HD group. Blood samples and peritoneal fluid were collected for analysis. Serum and peritoneal MBL levels were measured by the enzyme-linked immunoassay. MBL gene mutation at codons 52, 54 and 57 was detected by polymerase chain reaction assay. **Results:** There were 68 patients (NP), 51 patients (RP) and 46 patients (HD) recruited with mean age of 56.5 ± 15.8 years (M = 87). Thirty-four patients (21%) were diabetic. The median of duration of PD was 4.43 years (range, 0.8–9.9). There were 35 patients (21.2%) who had codon 54 mutations, but no patient had codons 52 and 57 gene mutations. Serum (575.6 ± 381 ng/mL) and peritoneal (36.2 ± 11.8 ng/mL) MBL levels of patients with mutations were significant lower compared to other patients without mutations (2,311 ± 1,030 ng/mL and 54.0 ± 26.6 ng/mL, $p < 0.001$). Nevertheless, the mutation rate of codon 54 among different study groups was similar (NP: 23.5% vs RP: 23.5% vs HD: 15.2%). **Conclusions:** Patients with MBL gene mutation had a lower level of serum and peritoneal MBL levels. However, it did not suggest a higher incidence of peritonitis or technique failure associated with MBL gene mutation.

A continuous quality improvement (CQI) project: improve fluid compliance in chronic peritoneal dialysis (PD) patients

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Background: Fluid overload increases chronic dialysis patient morbidity and mortality. A CQI project on improving fluid compliance in PD patients was done in 2002 to 2003. **Objectives:** *T*o identify the group of PD patients with fluid compliance problems, to explore the causes of fluid non-compliance, and to develop strategies to improve fluid compliance. **Methods:** All the PD patient records were reviewed. Patients with history of fluid overload were identified. A checklist was developed to collect information on patient physical status and eating habits. All the identified patients were arranged to have intensive patient education program on fluid compliance. Renal nurses performed periodic assessment on the patients. Number of episodes of fluid overload and the extra dialysis required due to poor fluid compliance were compared in the 12 months before and after the CQI program. **Results:** Ninety-nine (35.5%) out of the 279 chronic PD patients were identified to have a history of fluid overload. Sixty-nine patients had stayed in the CQI program for 12 months. Significantly fewer patients had ankle edema after the CQI program ($p = 0.018$). When compared with the 12 months before and after the CQI program, the group of patients required less extra dialysis ($p = 0.01$) and there was a decrease in episodes of fluid overload due to poor fluid compliance ($p < 0.001$). **Conclusions:** One-third of the chronic PD patients experienced fluid overload. A majority of the fluid overload patients underestimated their daily total fluid intake. Appropriate patient education such as dietary counseling and reinforcement on educating patients on the harmful effects of fluid overload can improve fluid compliance in chronic peritoneal dialysis patients.