

## **NRI-01 Anti-beta2 glycoprotein I (beta2GPI) antibodies facilitates phagocytosis of apoptotic neutrophils in patients with systemic lupus erythematosus (SLE)**

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**Background :** Increased apoptosis provides a continuous source autoantigens and has been suggested to have a pathogenic role in SLE. We have previously shown patients with SLE have impaired clearance of apoptotic bodies. In this study, we evaluated whether anti-beta2GPI antibodies, a subset of antiphospholipid antibodies, may have an effect on the phagocytosis of apoptotic bodies by macrophages in these patients.

**Methodology:** Patients satisfying the 1982 revised ACR criteria for SLE and normal controls were recruited for study. Peripheral blood mononuclear cells were separated into neutrophils and monocytes by double gradient centrifugation. Neutrophils were left to undergo spontaneous apoptosis while macrophages were derived from monocytes growing in culture medium. Apoptotic neutrophils were fed to macrophages from SLE patients or normal controls with or without beta2GPI (100 µg/ml) in the presence or absence of goat anti-human beta2 GPI antibodies (10 µg/ml) and examined for the number of macrophages with ingested apoptotic neutrophils under light microscopy (phagocytic index).

**Results:** beta2GPI alone was not shown to increase phagocytosis of apoptotic neutrophils by macrophages ( $33.2 \pm 9.5\%$  vs.  $31.8 \pm 9.4\%$ ,  $p=0.67$ ). However, the addition of anti-beta2GPI antibodies enhanced macrophage phagocytosis of apoptotic neutrophils from  $31.8 \pm 9.4\%$  to  $49.7 \pm 6.8\%$  in SLE patients ( $p=0.03$ ). Anti-beta2GPI alone had no effects on the macrophage phagocytosis index. Anti-beta2GPI antibodies plus beta2GPI were also found to facilitate phagocytosis in normal controls but the changes did not reach statistical significance ( $51.1 \pm 14.8\%$  vs.  $25.7 \pm 12.6\%$ ,  $p=0.07$ ). Fcγ receptor blockade by mouse immunoglobulin IgG1 (50 µg/ml) did not reverse the facilitation in phagocytosis by anti-beta2GPI antibodies ( $49.7 \pm 6.8\%$  vs.  $37.1 \pm 20.4\%$ ) ( $p=0.47$ ).

**Conclusion:** Anti-beta2GPI antibodies significantly enhance phagocytosis of apoptotic neutrophils by macrophages in patients with SLE. This process is dependent on the presence of beta2GPI and the uptake is not mediated by Fcγ receptor on the surface of macrophages.

## **NRI-02 Efficacy of chemoprophylaxis for tuberculosis infection in patients with systemic lupus erythematosus in an endemic area**

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**Background:** Chemoprophylaxis has been advocated for protection against tuberculosis (TB) in immunocompromised hosts. Evidence for the efficacy of chemoprophylaxis in patients with systemic lupus erythematosus (SLE) receiving immunosuppressive doses of corticosteroid is lacking. In this study, we examined the efficacy of isoniazid (INH) prophylaxis in SLE patients in Hong Kong.

**Methodology:** Records of patients from an inception cohort (1989-2001) of Chinese patients with SLE were reviewed. Episodes of TB that were diagnosed before or after the onset of SLE but before the commencement of immunosuppressive drug treatment were identified. Because of the previous lack of consensus on the use of chemoprophylaxis, INH (300 mg/day) prophylaxis was prescribed to some patients (chemoprophylaxis group) and not others (non-chemoprophylaxis group) at the discretion of the attending physician when the patient had an exacerbation of SLE requiring immunosuppressive doses of corticosteroid equivalent to prednisolone  $\geq 15$ mg daily. The outcome of these 2 groups of patients was followed for recurrence of TB. A chi-square test was used for statistical analysis.

**Results:** There were 652 patients in the cohort. The mean  $\pm$  SD (range) age of patients at the time of study was  $44.6 \pm 11.3$  (22-78) years and the age at onset of SLE was  $32.4 \pm 12.1$  (13-71) years. The mean duration of disease of these patients was  $14.2 \pm 7.4$  (median 13.0; range 1-31) years. 101 episodes of TB from 84 patients were identified. The female to male ratio was 76:8. 44 episodes were prophylactically treated with INH while 57 episodes were not. The rates of recurrence of TB in the chemoprophylaxis and non-chemoprophylaxis groups were 1.56 and 1.51 per 100-patient-year after  $13.1 \pm 7.6$  and  $10.4 \pm 5.8$  years of follow up respectively ( $p=0.61$ ). However, extrapulmonary TB has higher preponderance for recurrence than pulmonary TB (0.89 and 2.82 per 100-patient-year respectively). Patients in the chemoprophylaxis group were also found to have a higher rate of relapse of SLE ( $0.26 \pm 0.26$ /patient-year) and had higher cumulative dose of corticosteroid than those in the non-chemoprophylaxis group ( $0.15 \pm 0.23$ /patient-year) ( $p=0.01$ ). A further case-control analysis were therefore carried out matching 30 prophylactic INH treated and 30 non-INH treated episodes for these 3 factors. No difference in the rates of recurrence of TB could be detected between these 2 groups (1.55 and 2.17 per 100-patient-year for chemoprophylaxis and non-chemoprophylaxis groups respectively) ( $p=0.73$ ).

**Conclusion:** INH is ineffective as a prophylactic agent in the prevention of recurrence of TB infection in SLE patients requiring the use of immunosuppressive drug treatment.