Effects of glucocorticoids on platelet functions in rheumatoid arthritis

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Appreciation of the non-genomic effects produced by glucocorticoids (GC) has led to the investigation of the effects these drugs could produce on platelets. Previous data indicate that platelets express the glucocorticoid receptor (GR), and that pre-incubation with prednisolone inhibits adenosine di-phosphate (ADP) - and collagen-induced platelet aggregation. We have since confirmed these results using whole blood aggregation, measuring 23.7±5.5% (n=6) inhibition by 10µM prednisolone on the ADP response. The aim here is to investigate the consequences of prednisolone on platelet aggregation and activation during a human inflammatory pathology such as rheumatoid arthritis (RA).

RA patient blood samples (n=7) were harvested before and after daily oral treatment (prednisolone - 15mg) at 1, 7 and 14 days. ADP (6.4-3.2 µM), collagen (3.2-1.7µg/ml) or arachidonic acid (AA) (0.25-0.1 mM) induced aggregation was analysed in whole blood (multiple platelet function analyser, Dynabyte medical, Munich). Changes in P-selectin surface and fibrinogen expression were studied by flow cytometry.

RA platelet aggregation (56.3±5.7%) was lower than the response observed in healthy volunteers, with values of 69.4±8.6 and 39.6±8.8 units for healthy and RA platelets respectively, during collagen (3.2 µg/ml)-induced aggregation (P<0.05, Mann-Whitney test). No difference was observed for ADP-induced aggregation. Fibrinogen and P-selectin surface expression following ADP and thrombin receptor-activating peptide (TRAP)-activation were not altered in RA, compared with healthy control. When patients entered the treatment regimen, a significant increase in platelet aggregation to both collagen and AA was measured by day 1 and 7 post-treatment: (p<0.05, Mann-Whitney test); such an effect was lost at day 14. For the RA patients, platelet counts were also monitored, with values before treatment of 400±44 10⁹/L (n=5). After 14 days of steroid intake the number was reduced to 335±33 10⁹/L, suggesting an effect of prednisolone either on thrombocytopoiesis or platelet disruption.

This translation study underlies the importance of GC treatments on platelet functions in vivo. The rapid increase in platelet aggregation following prednisolone (day 1) requires further investigations to determine if this mechanisms underlies GC induced increase in the risk of thrombosis. Experiments with several GC might allow identification of a specific ligand with less pro-thrombotic activities in RA.