Study UHL Ref: 09321 The pharmacokinetics of oral corticosteroids in refractory asthma: Final Report.

The above study completed by intercalated BSc student Maria Raja under the supervision of Dr Ruth Green in the department of respiratory medicine was completed in June 2005. The aims of the study were successful and the results attached below in the form of an abstract. The BSc thesis was awarded a pass with first class honours and the findings were published in abstract form in The American Journal of Respiratory and Critical Care Medicine 2006 and presented at the American Thoracic Society annual Congress 2006. The study findings have also directly impacted on clinical practice and the methodology have allowed Prednisolone assays to be introduced as part of the clinical service in Leicester for patients attending the Glenfield Difficult Asthma Clinic.

Abstract from BSc Thesis: The pharmacokinetics of oral corticosteroids in refractory asthma: Maria Raja

The poor response to regular oral corticosteroid treatment seen in a minority of patients with refractory asthma could be due to non-compliance, abnormal pharmacokinetics or impaired tissue responses. We have compared the pharmacokinetics of oral prednisolone and the cutaneous vasoconstrictor response to topical beclomethasone diproprionate (BDP) in 10 patients with refractory asthma and 8 healthy controls. Subjects were randomised to receive 30mg enteric-coated, 30mg plain or 10 mg plain prednisolone in a single blind manner. Blood samples were taken at baseline and at intervals of 1,2,3,4,5,6, and 24 hours after ingestion of prednisolone and were analysed for prednisolone concentration by high performance liquid chromatography. The study was repeated with the remaining doses of prednisolone separated by a one-week washout period. Cutaneous vasoconstriction was measured 18 hours after the topical administration of BDP at concentrations of 3,10,30 and 100 mcg/ml. There were no significant differences in the area under the prednisolone concentration time curve (AUC) between patients and controls for any of the prednisolone doses, although the maximum prednisolone concentration (Cmax) was significantly lower in patients than in controls following the 10mg dose of prednisolone (table). One patient had no demonstrable prednisolone at any time point after witnessed ingestion of 30mg enteric-coated prednisolone. A dose related vasoconstrictor response to BDP was seen in both groups but the total vasoconstriction score was significantly lower in patients than controls (median(IQR) score 4.00(2.25) v 5.75(5.63), p=0.035). These results suggest that resistance to oral corticosteroids in refractory asthma is likely to reflect impaired tissue response rather than altered pharmacokinetics, although prednisolone malabsorption should be considered where enteric-coated preparations are used.