

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Glucocorticoid-induced hyperglycaemia

Glucocorticoids such as prednisolone and hydrocortisone have long been known to increase blood glucose levels. They do not seem to interfere with glucose uptake by the cell, but probably interfere with one or more of the intracellular mechanisms of glucose metabolism or insulin resistance. No single defined mechanism has yet been elucidated to explain exactly why glucocorticoids raise blood glucose levels. Their administration is associated with increased insulin production in subjects with functioning pancreatic cells, but despite the increased levels of insulin, normal blood glucose levels cannot be maintained.

There may be marginal, if any, changes on the fasting state blood glucose levels, while the greatest impact occurs on the post-prandial blood glucose levels. This typically involves doubling of the normal post-prandial blood glucose concentrations. The effect appears to be related to age (and therefore perhaps pancreatic insulin producing ability), low-insulin responders (the 20% of the population who have a low initial insulin response and may be considered to be pre-diabetic), and related to the dose of glucocorticoid administered.

Using a case-control format one group investigated the odds ratio for those patients commencing an oral hypoglycaemic agent of taking concurrent glucocorticoids. The table below shows the clear dose-response relationship seen in this study.

Hydrocortisone dose (mg)	Approximate equivalent prednisolone dose (mg)	Odds ratio for developing hyperglycaemia requiring drug therapy
1-39	1-10	1.8
40-79	10-20	3.0
80-119	20-30	5.8
>120	>30	10.3

The rapidly increasing dose-related risk for prednisolone may be related to its limited protein binding capacity. At higher doses, the amount of prednisolone exceeds the capacity of the protein binding, thus releasing a significantly greater proportion of prednisolone into the unbound, active state.

For patients receiving shorter courses of glucocorticoid therapy hyperglycaemia has long been considered a relatively benign side-effect. In recent times the consequences of accepting short-term hyperglycaemia for hospitalised patients, regardless of its origin, has become apparent. Hyperglycaemia during hospitalisation is now known to be associated with increased in-hospital mortality in both the intensive care and post-coronary artery bypass grafting surgical settings. There is increased morbidity in other hospitalised patient groups, such as increased infection rates and lengths of stay, and this now extends to nondiabetics with stress hyperglycaemia.

In this light, the possible impact of glucocorticoid-induced hyperglycaemia needs to be further assessed. The Departments of Respiratory Medicine and Pharmacy are currently investigating the effects of glucocorticoid-induced hyperglycaemia on clinical outcomes in patients admitted with exacerbations of chronic obstructive pulmonary disease. Progress is also being made towards optimising management strategies for hyperglycaemia in the intensive care setting.

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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