DRUG THERAPY AND (MODEL-BASED) METABOLIC MARKERS: IS TIGHT GLUCOSE CONTROL IN CRITICAL CARE AFFECTED BY DRUG CHOICES?

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Introduction: Hyperglycaemia is prevalent in critical care due to the stress of condition, even without a previous history of diabetes. Tight glycaemic control is associated with significantly improved patient outcomes. However, providing tight control is difficult due to evolving patient condition and interactions with common drug therapies resulting in recurring hyperglycaemic episodes. Quantifying the impact of drug therapies on blood glucose and metabolic control would enable optimised delivery of these drugs and facilitate tight control. This research quantifies the impact of common steroid and inotrope drug therapies on a clinically validated measure of metabolic function – insulin sensitivity – over the critical first 2 days of ICU patient stay. The goal is to quantify the impact of these common drug therapies on the ability to provide tight control and thus balance these affects clinically.

Methods: A clinically validated, model-based measure of insulin sensitivity ($S_i$), is used as the marker of metabolic function. Blood glucose, insulin and nutrition data from 53 hyperglycaemic subarachnoid haemorrhage patients who received steroids (dexamethasone) and/or inotropes (noradrenaline) in the Christchurch ICU from 2003-2007 were used to determine $S_i$ over the first 48 hours of stay. This cohort possesses little co-morbidity so changes in $S_i$ can be assumed due to the drug therapies alone. Patients were classified on outcome (survivors, non-survivors) and therapy (steroids, inotropes, both or neither). $S_i$ is compared over 48 hours for each of the 8 patient groups.

Results: Four main results emerged:

4. Insulin sensitivity increases gradually for all patients over the 48 hour period ($p < 0.05$)
5. Insulin sensitivity was significantly suppressed in survivors given steroids (versus survivors not given steroids), by a factor of approximately 2x ($p < 0.005$)
6. Inotropes had no significant affect on the change in $S_i$ over time regardless of outcome
7. Insulin sensitivity was always suppressed in all non-survivors regardless of drug therapy.

Discussion: Suppressed insulin sensitivity appears to be a consistent marker of mortality and it is of particular concern that steroids cause similar suppression. These results may also indicate the reason that many studies on steroid administration report mixed reports with respect to mortality. Finally, a reduction of 50% in insulin sensitivity for patients on steroids will also have a significant impact on the tight glucose control regime and effort required to maintain euglycaemia, creating a much more difficult clinical control problem.

Conclusion: Model-based metabolic markers ($S_i$) can provide significant insight into the clinical impact of common critical care drug therapies. The initial results from this study will begin to enable clinicians to optimise the tradeoffs between tight glycaemic control and the metabolic impact of steroid and inotrope drug therapies.