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# Preoperative carbohydrates to prepare metabolism for surgery

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Already in 1848 overnight fasting was suggested as the routine to prepare patients for anaesthesia and elective surgery. This was suggested to ensure an empty stomach to avoid the risk of vomiting and aspiration. Studies over the last few decades questioned this routine and showed that it was unnecessary. Instead of fasting from midnight many anaesthesia societies now recommend only a 2 hour fast for clear fluids before elective surgery, as reviewed in (1). This change was brought about primarily to avoid the discomfort of thirst that many patients suffer from.

More recently the metabolic effects of the overnight fast has also been studied. Many animal studies in experimental stress showed that even a brief fast, sufficient to cause a change in metabolism from a fed to fasted state and reduce the glycogen reserves, was sufficient to alter the reactions to stress, as reviewed elsewhere (2). These studies showed that even a brief fast before stress caused a stronger catabolic stress hormone response and it was also shown to be detrimental by reducing survival. These ideas were then transferred to the clinical situation, and in several studies it was shown that preparing the patients with either iv or oral carbohydrates markedly reduced postoperative insulin resistance (3).

Postoperative insulin resistance has recently caught a lot of attention. A large randomised trial showed that treating insulin resistance targeting to normalize glucose levels to 4.5-6.0 mmol/l had a remarkable effect on outcome in patients in need of ventilatory support after surgery (4). In this study morbidity was markedly reduced by 30 to 50% by this treatment compared to the traditional regime of giving insulin only when glucose levels exceeded 12 mmol/l. This was the underlying cause for a remarkable reduction in ICU mortality by 43%. In a follow up analysis it was shown that it was bringing down the glucose levels rather than the insulin treatment per se that was the main underlying factor for these improvements (5). Interestingly enough, tight glucose control has a universal effect on whole body metabolism, since BRANDI and coworkers showed that when glucose levels were normalised so were circulating levels of free fatty acids, protein losses and substrate utilization (6), confirming metabolic effects described by Allison and co-workers already 25 years ago (7). So from these data it seems clear that insulin resistance is a major sign of metabolic derangement after surgery, and that its presence imposes a risk for the surgical patient.

Post operative insulin resistance develops in almost all kinds of surgery, and the degree of change is directly related to the magnitude of the operation (8). This state of metabolism remains for about 2-3 weeks even after an uncomplicated open cholecystectomy. It occurs to the same degree independently of gender, age or preoperative insulin sensitivity. Insulin resistance is the main cause behind hyperglycemia. Insulin resistance occurs both in the liver and in extrahepatic tissues, mainly muscle, but also in fat tissues. These disturbances cause a dual effect that supports the elevation of glucose levels. Endogenous glucose production is increased and the uptake of glucose in the periphery is reduced. The latter is associated with a disturbance in the activation of specific glucose transporting proteins that facilitate glucose uptake upon insulin stimulation. This does not occur in the postoperative situation.

The risk of hyperglcymeia and insulin resistance can be acted upon in two ways : As described above, insulin treatment can be given to overcome an already existing state of insulin resistance. The other way is to try to avoid insulin resistance to develop in the first place. There are four different ways by which this can be done. The use of epidural anaesthesia placed at levels that block the adrenal release of catecholamine have been shown to reduce insulin resistance (9). Reducing pain also reduces insulin resistance (10). Furthermore, minimal invasive surgery results in less postoperative insulin resistance than open surgery (11). Lastly, preparing the patient with carbohydrates instead of overnight fasting (3).

Preoperative carbohydrates can be administered intravenously using a 20% glucose infusion in a large peripheral vein. By giving it at a rate of

5 mg/kg/min sufficient glucose is given to stimulate insulin release to levels that simulate those seen after a meal. Although this is plausible, it has some disadvantages in that the patients do complain about discomfort from the fairly concentrated glucose given. Another way to administrate the carbohydrates is to use a drink containing sufficient amounts of carbohydrates. This has been shown to be safe to use in that 400 ml of a 12.5% solution of primarily polymers of carbohydrates pass the stomach in 90 minutes (12). Both the glucose infusion and the preoperative carbohydrate rich drink markedly reduces postoperative insulin resistance in several different types of surgery including cholecystectomy, colorectal surgery and hip replacement (3). Importantly, the preoperative metabolic modulation by carbohydrates has additive effects on top that of an epidural (13).

The mechanisms behind this effect is not fully explained as of yet. However, evidence from animal studies that indicate that depending on the metabolic state at the time of injury, the endocrine response will differ. In general, an animal subjected to stress in a fasted state has a more pronounced release of catecholamines and corticosteroids. These two hormones have been shown to cause insulin resistance. This finding has also been conformed to some extent in patients undergoing surgery. Hence, if patients undergoing hip replacement were treated with insulin and glucose at the time of the operation there was no release of cortisol, and the IGF-I levels were higher than in those fasted before the same operation. An additional piece of information just recently presented shows that the treatment with a carbohydrate rich drink in the morning before surgery causes an elevation of insulin sensitivity by about 50% at the time when surgery is about to begin (unpublished data). In addition, glycogen synthesis is stimulated, and the opening of these pathways before the onset of surgical stress may impact these system also after the operation.

So what are clinical effects of preparing patients with carbohydrates instead of fasting or placebo ? For the preoperative situation it is worth while that the change in fasting guidelines was instituted to avoid unnecessary thirst. Adding carbohydrates to the drink the patient is taking preoperatively will additionally reduce hunger and preoperative anxiety (14) as well as preoperative nausea (15). For the minor surgery such as laparoscopic cholecystectomy one study found no difference in postoperative sleep behaviour or well being (15), while another similar study found that preoperative carbohydrates resulted in less post operative nausea and vomiting compared to fasted patients (16). In medium to major size operations the effects on metabolism become more pronounced and in these situations insulin resistance is markedly reduced, as described above. This occurs by minimising both the disturbances that lie behind postoperative hyperglycaemia. Hence, endogenous glucose production is less pronounced and glucose uptake is less reduced in patients given carbohydrates compared to those fasted before surgery. These attenuations of the metabolic stress response allows complete enterla feeding without the addition of any insulin and still glucose levels can be maintained below 6 mmol/l after major colorectal surgery (17). In other studies of major surgery, it has been shown that preoperative carbohydrates minimises protein losses (18). This treatment has also been shown to preserve muscle strength for a prolonged period of time after surgery (19). In other studies, reports have indicated that the heart may benefit from preoperative carbohydrate loading in cardiac surgery, as summarised elsewhere (2). Lastly, a retrospective analysis of prospective studies indicated that recovery may be faster, as indicated by length of stay, in patients undergoing surgery in the carbohydrate fed state as opposed to the overnight fasted state (20).

In summary, preparing patients metabolically using carbohydrates has several benefits over just allowing the patient to drink clear drinks containing little or no energy or fasting. The treatment with a preoperative carbohydrate rich drink has been extensively tested and in clinical use for some years and shown to be safe. The preoperative well being is improved, and there seems to be effects on PONV in minor surgery. For major operations, minimising postoperative insulin resistance can reduce the risk of hyperglycaemia. This may have several practical implications since it may be hard to have intensive insulin treatments for hyperglycaemia in practice in a general surgical ward situation.

## References

1. Ljungqvist O., Soreide E., *Preoperative fasting*, Br. J. Surg.,**90** (4), p. 400-6, 2003.
2. Ljungqvist O., *et al.*, *Perioperative nutrition therapy - novel developments*, Scand. J. Nutr., **44**, p. 3-7, 2000.
3. Ljungqvist O., Nygren J., Thorell A., *Modulation of postoperative insulin resistance by pre-operative carbohydrate loading*, Proc. Nutr. Soc., **61** (3), p. 329-36, 2002.
4. van den Berghe G., *et al.*, *Intensive insulin therapy in the critically ill patients*, N. Engl. J. Med., **345** (19), p. 1359-67, 2001.

5. Van den Berghe G., *et al.*, *Outcome benefit of intensive insulin therapy in the critically ill : Insulin dose versus glycemic control*, Crit. Care Med., **31** (2), p. 359-66, 2003.
6. Brandi L. S., *et al.*, *Insulin resistance after surgery : normalization by insulin treatment*, Clin. Sci. (Lond.), **79** (5), p. 443-50, 1990.
7. Woolfson A. M., Heatley R. V., Allison S. P., *Insulin to inhibit protein catabolism after injury*, N. Engl. J. Med., **300** (1) : p. 14-7, 1979.
8. Thorell A., Nygren J., Ljungqvist O., *Insulin resistance : a marker of surgical stress*, Curr. Opin. Clin. Nutr. Metab. Care, **2** (1), p. 69-78, 1999.
9. Uchida I., *et al.*, *Effect of epidural analgesia on postoperative insulin resistance as evaluated by insulin clamp technique*, Br. J. Surg., **75** (6), p. 557-62, 1988.
10. Greisen J., *et al.*, *Acute pain induces insulin resistance in humans*, Anesthesiology, **95** (3), p. 578-84, 2001.
11. Thorell A., *et al.*, *The metabolic response to cholecystectomy ; insulin resistance after open vs. laparoscopic surgery*, Eur. J. Surg., **162** (3), p. 187-192, 1995.
12. Nygren J., *et al.*, *Preoperative gastric emptying. Effects of anxiety and oral carbohydrate administration*, Ann. Surg., **222** (6), p. 728-34, 1995.
13. Nygren J., *et al.*, *Preoperative oral carbohydrate administration reduces postoperative insulin resistance*, Clin. Nutr., **17** (2), p. 65-71, 1998.
14. Hausel J., *et al.*, *A carbohydrate-rich drink reduces preoperative discomfort in elective surgery patients*, Anesth. Analg., **93** (5), p. 1344-50, 2001.
15. Bisgaard T., *et al.*, *Randomized clinical trial comparing an oral carbohydrate beverage with placebo before laparoscopic cholecystectomy*, Br. J. Surg., **91** (2), p. 151-8, 2004.
16. Hausel J., Nygren J., Almström C., *Preoperative oral carbohydrates improves well being after elective colorectal surgery*, Clinical Nutrition, **18**, suppl. 1 : 80, 1999.
17. Soop M., *et al.*, *Randomized clinical trial of the effects of immediate enteral nutrition on metabolic responses to major colorectal surgery in an enhanced recovery protocol*, Br. J. Surg., **91**, p. 1138-1145, 2004.
18. Crowe P. J., Dennison A., Royle G. T., *The effect of preoperative glucose loading on postoperative nitrogen metabolism*, Br. J. Surg., **71** (8), p. 635-7, 1984.
19. Henriksen M. G., *et al.*, *Effects of preoperative oral carbohydrates and peptides on postoperative endocrine response, mobilization, nutrition and muscle function in abdominal surgery*, Acta Anaesthesiol. Scand., **47** (2), p. 191-9, 2003.
20. Ljungqvist O., *et al.*, *Preoperative nutrition – elective surgery in the fed or the overnight fasted state*, Clinical Nutrition, **20**, suppl. 1, p. 167-171, 2001.