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Symposium 3: Nutrition is the cutting edge in surgery: peri-operative feeding

Pre-operative nutrition and carbohydrate loading

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An optimal nutritional state is an important consideration in providing successful operative outcomes. Unfortunately, many aspects of surgery are not constructive to providing this. In addition, the metabolic and immune response to injury induces a catabolic state and insulin resistance, a known risk factor of post-operative complications. Aggressive insulin therapy post-operatively has been shown to reduce morbidity and mortality but similar results can be achieved when insulin resistance is lessened by the use of pre-operative carbohydrate loading. Consuming carbohydrate-containing drinks up to 2 h before surgery has been found to be an effective way to attenuate insulin resistance, minimise protein losses, reduce hospital stays and improve patient comfort without adversely affecting gastric emptying. Enhanced recovery programmes have employed carbohydrate loading as one of several strategies aimed at reducing post-operative stress and improving the recovery process. Studies examining the benefits of these programmes have demonstrated significantly shorter post-operative hospital stays, faster return to normal functions and lower occurrences of surgical complications. As a consequence of the favourable evidence they are now being implemented in many surgical units. Further benefit to post-operative recovery may be found with the use of immune-enhancing diets, i.e. supplementation with *n*-3 fatty acids, arginine, glutamine and/or nucleotides. These have the potential to boost the immune system, improve wound healing and reduce inflammatory markers. Research exploring the benefits of immunonutrition and solidifying the use of carbohydrate loading is ongoing; however, there is strong evidence to link good pre-operative nutrition and improved surgical outcomes.

Pre-operative nutrition: Carbohydrate loading: Immunonutrition

Nutrition support has long been considered an integral part of improving surgical outcomes. Malnutrition is known to be associated with high levels of post-operative complications and delayed recovery. Impaired wound healing, loss of muscle tissue and power, reduced immunocompetence, depression, apathy, immobility, longer hospital stays, greater readmission rates and increased health care cost have all been linked to poor nutrition status pre-operatively. Benefits have been found when severely malnourished patients received nutrition support for 10–14 d prior to surgery[1].

Unfortunately, the very nature of surgery (be it from the underlying disease, surgical procedures, arising complications or a combination) does not promote adequate nutritional practices and thus impacts negatively on nutritional stores, increasing the risk of malnutrition. Surgical trauma results in release of hormones that stimulate the body into a catabolic state, increasing metabolism and diverting nutrients away from their original uses. An anabolic state is essential for repair and recovery and any measure that helps reduce catabolism post-operatively could ultimately help speed recovery[1].

Malnutrition and surgical stress also leads to the suppression of immune function through atrophy of lymph nodes, decreased lymphocyte and IgA production and inhibition of cellular immunity[2]. Surgery itself is known

Abbreviation: ERAS, enhanced recovery after surgery.
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to bring about a decrease in T-lymphocytes and natural killer cells[2]. The result of this suppression is an increased risk of infection.

The foundation of effective nutrition support encompasses route, timing and composition. Pre-operative nutrition support can benefit malnourished patients but sufficient time must be allowed for the benefits to be realised. Identification of malnutrition with nutrition screening and assessment must be in place so that interventions can be started without delay. There is also potential for nutritional measures to be implemented regardless of nutritional state that will reduce post-operative metabolic changes and result in better, faster surgical recovery.

The aim of this article is to review pre-operative nutritional management strategies that may help reduce catabolism, maintain immune function and improve recovery with particular focus on carbohydrate loading and immunonutrition.

Surgically induced insulin resistance

A series of events occur within the body in response to surgery that leads to a release of stress hormones and inflammatory markers (e.g. cytokines, cortisol, catecholamines and glucagons)[3]. These hormones diminish the action of insulin (which is the body's main anabolic hormone) thus leading to a boost in energy substrate mobilisation, i.e. catabolism[1,3].

With the anabolic effect of insulin hindered glucose uptake in peripheral tissue is reduced while production of glucose via gluconeogenesis is enhanced. Both these changes lead to hyperglycaemia. In addition, insulin resistance will also cause an increase in lipolysis and proteolysis resulting in loss of fat stores and contributing to a negative nitrogen balance. The combination of protein breakdown, increased gluconeogenesis and inability to utilise glucose leads to a reduction in muscle function. This phenomenon can last for several weeks and is a major cause of prolonged fatigue following surgery[3].

Insulin resistance occurs in some degree after any type of surgery and regardless of nutritional status. The magnitude of resistance is influenced by the size of the operation and amount of blood lost[3,4]. It can last up to 3–4 weeks post-surgery and has been found to be an independent factor in determining the length of post-operative stay[3]. Insulin resistance following surgery is associated with a greater inflammatory response, increased complications, poor wound healing, longer hospital stays and higher morbidity and mortality rates in both diabetics and non-diabetics alike[3,5]. Better surgical outcomes have been shown when intensive insulin therapy has been used post-operatively but attention is becoming more focused on prevention.

How surgically induced insulin resistance causes complications is uncertain. It has been proposed that it is due to an increase in free radicals that occur when glucose metabolic pathways become saturated[3]. Insulin resistance causes glucose to be directed away from insulin-sensitive cells to non-insulin-dependent cells (such as the liver and brain) that can increase their uptake of glucose independently of insulin[3]. When hyperglycaemia occurs these non-insulin-dependent cells have an excess of glucose feeding into glycolysis resulting in production of free radicals that may contribute to the development of post-operative complications[3].

No matter what mechanisms are involved, reducing insulin resistance is central to producing an anabolic state following surgery and thus allowing repair and recovery.

Reducing pre-operative fasting periods

Traditionally, pre-operative practice has been to fast the patient for up to 12 h prior to surgery. The rationale for this is to reduce gastric acidity and volume with a consequent decrease in the risk of gastric content aspiration during surgery. However, even this amount of fasting has been associated with greater catabolism and prolonged recovery as a fasted state places the body under greater metabolic stress and reduces its ability to cope with complications[1,4–6].

A Cochrane review found no increased risk of aspiration in patients who were allowed fluids 2–3 h prior to surgery compared to patients having undergone a traditional fasting period[7]. Additionally, patient comfort in terms of thirst was improved with shorter fasting times[7].

Guidelines have been adapted to reflect these findings with the European Society for Parenteral and Enteral Nutrition supporting the ingestion of solid foods 6 h prior to surgery and clear fluids until 2 h before surgery[1]. The American Society of Anaesthesiologists changed their guidelines in 1999 to recommend patients be allowed to eat up to 6 h before surgery and drink clear fluids until 2 h before surgery. Exceptions to this are emergency cases and those with delayed gastric emptying[8]. The recommendations made by the Association of Anaesthetists of Great Britain and Ireland developed in 2001 mimic those made by their American counterparts[9].

Most clear fluids, however, will not provide a substantial nutritional value. Thus, carbohydrate loading has been investigated as a means of inducing an anabolic state prior to surgery while still allowing sufficient stomach emptying.

Carbohydrate loading

Theoretically if insulin resistance is reduced, carbohydrate uptake, utilisation and storage will be improved and protein losses minimised thus helping establish the essential anabolic state[3]. Surgically induced insulin resistance can be treated post operatively with intensive insulin therapy. However, there are also preventative measures that can be implemented prior to and during surgery to help minimise its occurrence. Key in these measures is nutritional strategies such as avoiding long periods of starvation and using carbohydrate loads pre-operatively.

The amount of carbohydrate required to induce an effect must be enough to shift the body from a fasted to a fed state. Oral ingestion of 50 g carbohydrate has been shown to produce a release of insulin similar to that seen after ingestion of a mixed meal and therefore current recommendations have been based around this value: a loading

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dose the night before surgery of 100 g to be followed up with another 50 g dose 2 h before surgery[10].

There are now specialist oral supplements available that provide this as a hypo-osmolar 12·5% carbohydrate drink. Intravenously this equates to a rapid infusion of a 20% glucose solution[3,5]. Commonly used low-concentration glucose solutions do not cause significant insulin release to cause an effect[3,5]. The specialist supplement drinks have been studied extensively in the surgical setting without any adverse effects reported[4]. They have been developed with a low osmolarity (240 mosmol/l solution) to promote effective gastric emptying and dispel initial concerns over aspiration[10].

Meta-analysis of prospective control trials has shown a reduction in length of stay by 20% in those receiving pre-operative carbohydrate-rich drinks when compared with a traditional overnight fast and up to 50% reduction in insulin resistance following surgery including abdominal and orthopaedic surgery[4,5,10,11]. Improvements in protein metabolism have also been found with a 50% reduction in loss of lean body mass reported when carbohydrate loading was used prior to major abdominal surgery[3]. Carbohydrate loading has also been shown to reduce patient discomfort with regard to thirst, hunger and anxiety while lessening reports of fatigue following surgery[4,6,12].

A randomised controlled trial comparing a pre-operative carbohydrate drink (100 g carbohydrate the evening before and 50 g on day of surgery) against a placebo in patients undergoing total hip replacement found an improvement in glucose oxidation rates both pre- and post-operatively in the carbohydrate group. A reduction of up to 25% in insulin resistance was observed in their small sample population but these results did not equate to any change in length of stay[10]. They suggested that improved recovery could be procured from carbohydrate loading due to the reduction in surgical-induced altered metabolism thus allowing nutrition provided post-operatively to be better utilised[10].

Another randomised controlled trial demonstrated shorter post-operative stays of 2·5 d in those taking pre-operative carbohydrate compared to a fasted group before colorectal surgery. An observed trend towards quicker return of gastrointestinal function was also noted although this was not statistically significant[6]. The same study found better preservation of muscle strength in the carbohydrate group as demonstrated by a handgrip measurement[6]. Those fasted before surgery had a significantly reduced grip strength of 11% compared to 5% who received carbohydrate prior to surgery[6].

Preservation of muscle function is another beneficial outcome of attenuating insulin resistance with carbohydrate loading. Reduced protein breakdown has been shown with ingestion of large amounts of carbohydrate (175–200 g) prior to colorectal surgery when compared with a low carbohydrate dose (35–40 g)[13].

As insulin secretion is stimulated by both the presence of carbohydrate and protein, could the benefits to glycaemic control and muscle preservation be better still with the inclusion of protein? This theory was investigated in a randomised controlled trial comparing a carbohydrate only fluid (100 g carbohydrate), a combined carbohydrate and protein drink (100 g carbohydrate and 28 g protein) and water. All groups were allowed fluids until 3 h before surgery with no difference observed in gastric emptying between the groups. In the first week post-operatively a reduction in pre-operative muscle strength of 10–11% was observed in both intervention groups compared to 16% in the control group[14]. After one month, a 5% reduction was observed in the intervention groups and 13% in the control[14]. At 2 months, both intervention groups had surpassed initial strength measures while the control group still remained below[14]. These results were not significant when compared individually; however, they became significant when the intervention groups were combined[14]. Here provision of carbohydrate-rich drinks is supported; however, whether further benefit from the inclusion of protein can be obtained is not clear and further investigations are required.

Use of carbohydrate-rich drinks prior to surgery in diabetic patients has caused some debate and many studies have excluded diabetic patients on the grounds of slower gastric emptying and impaired glycaemic control. There is limited knowledge therefore on the effect pre-operative carbohydrate loading could have on this group of high-risk patients. Gustafsson explored the feasibility of using this strategy with type 2 diabetics and found gastric emptying was not delayed when compared with healthy individuals (in fact emptying times were slightly faster in the diabetic subjects)[15]. No difference was observed between diet/oral medication-controlled diabetes and insulin-controlled diabetes[15]. No association was found between gastric emptying, glucose concentrations or HbA1c[15]. Further trials in this area are needed to establish the metabolic effects and surgical outcomes of carbohydrate loading in the diabetic patients especially given the increasing number of diabetic surgical candidates.

Available data show carbohydrate loading prior to surgery is an effective, simple approach to reducing surgically induced insulin resistance and thus improving post-operative muscle strength, reducing fatigue and speeding recovery times. While there is still scope for future studies current guidelines have suggested its inclusion into surgical protocols and it has become an integral part of Enhanced Recovery Programmes.

Enhanced recovery

Enhanced recovery after surgery (ERAS) programmes have become an important focus on improving the peri-operative course and accelerating the recovery process. ERAS programmes include multiple evidence-based interventions aimed at minimising surgical stress, speeding recovery, reducing hospital stays and lessening health care costs[5,16]. ERAS incorporates many recommendations around nutritional care including avoidance of prolonged fasting, carbohydrate loading, limited use of naso-gastric tubes for gastric decompression and quick progression to diet following surgery[5,16]. In addition to nutritional measures the programmes also make recommendations relating to pain control, anaesthesia and mobility.

Meta-analysis of enhanced recovery in colorectal surgery has found reductions in length of stay by 3–4 d and lower morbidity, while no significant difference was found in readmission or mortality rates[17,18]. Individual studies examining the benefits of these programmes have demonstrated significantly shorter post-operative hospital stays, faster return to normal functions and lower occurrences of surgical complications[16].

There is strong evidence and support for ERAS in the setting of colorectal surgery; however, there is potential for similar benefits to be found in other surgical settings. Of course, the benefits of ERAS cannot be attributed to pre-operative nutritional measures alone but they are a fundamental part of the programme and implementation of these programmes could potentially raise the profile of nutritional measures in some settings. They highlight the need for combined interventions for optimal results.

Immunonutrition

An additional area of nutrition which has potential to convey benefits on surgical recovery is the concept of immunonutrition. Nutrients such as glutamine, arginine, *n*-3 fatty acids and RNA have the potential to reduce inflammatory markers, enhance the immune response, improve wound healing, reduce post-operative complications and ultimately speed up recovery[19].

Arginine, a conditionally essential amino acid, supports T-cell maturation and activity while glutamine (also conditionally essential) plays a vital role in nitrogen transport, acid–base regulation, antioxidant defence, rapidly dividing cell function and as a source of fuel for gut mucosa[20,21]. *n*-3 Fatty acids modulate the inflammatory response by altering the production of inflammatory markers such as IL, eicosanoids and cytokines[20,21]. Nucleotides (such as RNA) improve protein synthesis, help intestinal cell maturation and regulate T-cell-mediated immune responses[20]. Speciality supplements containing these nutrients in combination have been designed for both oral and enteral use.

Systematic review of immune-enhancing supplementation has shown improvements in infectious complication rates and shorter hospital stays but no differences in mortality rates[22]. The studies included in the analysis, however, were not specific to pre-operative supplementation and it was acknowledged that results are variable dependent on the intervention, sample population and methodology of the trials[22].

Results of randomised clinical trials using combined immune-enhancing supplements (containing arginine, *n*-3 fatty acids and nucleotides with or without glutamine) have been conflicting. One trial involving 150 patients undergoing gastrointestinal surgery for malignancy found the development of post-operative complications was significantly lower in the group receiving an immunonutrient supplement for 7 d pre- and post-surgery compared to a control group (18 % compared to 42 %)[23]. Furthermore, the mean length of hospital stay was reduced by 3 d[23]. A subsequent trial with sixty patients undergoing elective surgery for gastric cancer investigated the benefits of using a similar supplement for 7 d prior to surgery (but not following) against a conventional supplement. Significant reductions were found in post-operative infectious complications (28 % compared to 7 %) and duration of systemic inflammatory response syndrome (1·34 d compared to 0·77 d) in the group receiving immunonutrition[19].

In contrast, a trial using an immune-enhancing supplement for 7 d pre-operatively only, found that while pre-albumin levels were significantly improved in the immune enhanced group there were no differences in T-lymphocyte counts, post-operative complications or length of stay[2]. A further trial using the same supplement for 5 d pre- and post-operatively found no significant differences in infectious complications, mortality or length of stay when compared with a group receiving no nutrition support[20].

Recommendations on the use of immune-enhancing supplementation have been included into current guidelines on nutrition in surgery[1]. They advocate their use pre-operatively if possible and continued for 5–7 d post-operatively in those undergoing surgery for cancer of the neck and abdomen as well as after severe trauma. They specify the combination of arginine, *n*-3 fatty acids and nucleotides as the preferred supplement[1].

Conclusion

Based on the current evidence, the optimal pre-operative nutritional approach to surgical patients involves a combination of interventions. Improving the nutritional state in severely malnourished patients has been shown to improve post-operative outcomes. Regardless of nutritional status, reducing pre-operative fasting periods and increasing carbohydrate loading can be beneficial in reducing surgically induced stress, attenuating insulin resistance, preserving muscle function and improving patient comfort. Combining nutritional measures in an ERAS programme can help reduce post-operative stay and complications. There is support for the use of immune-enhancing supplementation in certain population groups but more evidence is required. Nutritional support must not be overlooked when considering optimal surgical care.

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