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Editorial

Oral carbohydrate preload drink for major surgery – the first steps from famine to feast

'Nil by mouth' is a cornerstone of pre-operative care. Soon after the first anaesthetics were administered, regurgitation and pulmonary aspiration of gastric contents were described. Nearly 70 years ago, in one of the most widely cited of all medical papers, Mendelson [1] described how aspiration occurred in 66 women from over 44 000 obstetric deliveries. Although only two mothers died, he also highlighted a more common problem of liquid aspiration, causing cyanosis and dyspnoea. With its description of morbidity (from aspirated liquid) and mortality (from solid food), this paper helped to shape anaesthetic practice for over a generation as nil by mouth, often for many hours, became standard.

Twenty years ago, this approach was revisited. Not only is excessive periods of being 'nil by mouth' unpleasant (causing dehydration, anxiety and even relative hypoglycaemia), it is also unnecessary. Studies suggested that allowing patients to drink clear fluids until two hours before surgery neither increased residual gastric volume nor reduced pH [2] – two determining factors in the severity of any pneumonitis. Although the evidence may not be powerful (due in part to the low incidence of severe harm arising from aspirated material), fasting guidelines were nevertheless changed to include water until two hours pre-operatively and it seemed as if no further progress would be made.

At the same time, intensivists [3, 4] were describing how the outcome after major surgery was improved if there was an increase in tissue oxygen delivery, without a build-up of an oxygen debt from anaerobic metabolism. Whilst not universally accepted, this interest in tissue oxygen delivery by optimisation of cardiac output was the harbinger of individualised goal-directed fluid therapy. Independently, physiologists using a different method (expired gas analysis) were also able to quantify maximum oxygen consumption ($\dot{V}O_{2max}$) and anaerobic threshold in athletes during exercise [5].

The consequences of inadequate oxygen delivery with anaerobic metabolism and accumulation of lactate is seen as highly undesirable in both areas: with patients, it is associated with a higher mortality; and in athletes, with significantly impaired performance and early fatigue. In this respect, there seem to be physiological similarities between major surgery and a major athletic endeavour. Therefore, could a significant factor in reducing the onset of anaerobic metabolism in athletes – nutritional preparation – have a parallel with optimising surgical patients?

Recently, there has been increased interest in, and enthusiasm for, sport nationally, perhaps triggered by hosting of high-profile events such as the Olympic and latterly Commonwealth games as well as the Tour de France, together with the way in which these world-class athletes prepare for major events. Since the 1960s, studies have shown that several days of dietary carbohydrate loading in athletes increases muscle glycogen stores [6–8], with a corresponding increase in performance time during endurance exercise at 75-85% of $\dot{V}O_{2max}$ [7, 8]. Medicine has moved rather more slowly, but we have known for nearly 25 years that carbohydrate loading to avoid pre-operative fasting has several benefits, including reducing insulin resistance [9] and preserving nitrogen metabolism and muscle mass [10]. Perhaps we can give our patients something better than water?

The preparations for athletes and for our surgical patients, on the face of it so diverse, have therefore converged. We should no more starve our patients for prolonged periods of time than we would our athletes.

What carbohydrate is suitable? Currently, the most popular are specific commercial preparations such as Preload® (Vitaflo® International Ltd, Liverpool, UK) and preOp® (Nutricia Ltd, Trowbridge, Wiltshire, UK). These clear carbohydrate drinks contain maltodextrins, complex carbohydrates that empty readily and predictably from the stomach (unlike glucose or milk). The Enhanced Recovery After Surgery (ERAS) programme has acted for many anaesthetists as an introduction to the concept of oral preload, with the first dose given as an 800-ml volume (containing 100 g carbohydrate) around 12 h before surgery (or the night before) and the second dose given as a 400-ml volume (containing 50 g carbohydrate) 2-3 h before surgery (or the morning of surgery) for maximum benefit. The rationale behind giving oral preload is threefold:

- to avoid dehydration before surgery and improve patients' well-being [11];
- to allow safe general anaesthesia with an empty stomach, without the increased risk of pulmonary aspiration of gastric contents [12] (see below);
- to give a large enough carbohydrate load to allow the patient to be in a metabolically fed state before surgery, which has beneficial effects on reducing insulin resistance [13, 14] and catabolism, and preserving muscle function as measured by grip strength [15, 16].

Safety concerns

Safety is paramount before any change in guidelines. However, it is worth remembering that a number

of steps/prerequisites are required before significant patient harm occurs. A significant volume of stomach contents, of sufficiently low pH, has to be regurgitated, then aspirated into (or obsruct) the trachea or distal airways; in addition, the patient has to be vulnerable to these events, either because of the magnitude of the aspiration or his/her poor physiological reserve. Thus, one area of concern is that the apparent relaxation in fasting guidelines may predispose to larger residual gastric volume before induction of anaesthesia, thereby increasing the risk of pulmonary aspiration. However, a large meta-analysis confirmed the safety of reduced fasting times for water, with significantly smaller gastric volumes and no increased risk of aspiration, regurgitation or related morbidities [17]. As there is a move away from clear water to other liquids, the evidence on safety is also required for these, and the use of ultrasound measurement of antral cross-sectional area (which correlated with measured volume of gastric aspirate) is being advocated as a useful tool in this area [18]. To date, however, there is only little evidence; for example, the addition of milk to tea was always assumed to be comparable to solid food. Recently, Hillyard et al. investigated this, both by gastric ultrasound and the co-administration of paracetamol (and measuring the time to its peak concentration), and demonstrated that tea with milk made no difference to gastric emptying times and reduced the time to peak paracetamol concentrations [19]. This study would also lend support to the safety of administering patients' normal medication pre-operatively. However, given the relative rarity of aspiration of gastric contents – approximately 1:7000, with a mortality of 1:100 000 anaesthetics [20] – very large studies would be required to provide further information.

A second concern is the use of oral preload in diabetic patients, who might be expected to be at risk of both hyperglycaemia and pulmonary aspiration if there is co-existing autonomic neuropathy. Gustafsson et al. found that in type-2 diabetic patients, a carbohydrate preload with paracetamol (the latter to determine gastric emptying) was not associated with a delay in gastric emptying nor a risk of hyperglycaemia or pulmonary aspiration [21]. The current recommendations are to give type-2 diabetic patients a preload along with their usual diabetic medication [21].

The current position

Oral preload is one of the 17 key elements (described by Fearon et al. in 2005 [22]) of the ERAS protocol for colorectal surgery. This was recently updated by Gustafsson et al. [23]. It is the first element in the surgical pathway to reduce stress and metabolically condition a patient with the aim of early return to oral diet, mobility and recovery as soon as possible after surgery. A review of all of the ERAS elements by Gustafsson et al. [24] concluded that oral preload was one of the two ERAS elements that independently had a significant effect on reducing complications and improving wellbeing. The other element was the amount of intravenous fluid given on the day of surgery, with fluid excess increasing the incidence of complications. Oral preload also reduced the need for intravenous fluid [24].

Whilst much of the evidence is for ERAS protocols for colorectal surgery, there is evidence from other specialities to support enhanced peri-operative nutrition for patients. Using dietetic assistants to administer additional nutritional support improved the outcome of patients with hip fracture, with significantly better daily energy intake and, crucially, reduced mortality on the acute ward and at four months [25].

Suboptimal implementation of preload

Whilst compliance with most ERAS elements in the UK is above 70%, the use of oral preload is around 50% [26]. The reason for this is probably multifactorial:

- some clinicians may not feel that it is important or relevant to their specialty;
- anaesthetists may challenge its use and safety before induction of anaesthesia;
- nurses may be uneducated in its use and worried about giving it so soon before scheduled surgery in case the operation is cancelled by the anaesthetist;
- the logistics of giving it to patients in the pre-operative clinic;
- funding comes from a different department that sees no cost benefit; and

- administration via pharmacy or dietetics may be disputed on the grounds of whether the drink needs to be prescribed or not.

Future use of preload and peri-operative nutritional supplements

The physiological stresses of undergoing major surgery and of competing as a top-level athlete have obvious parallels. We are starting to see the benefits of oral preload as part of a multimodal treatment strategy to improve the metabolic response to surgical injury. The success of enhanced recovery has been described in the first of two recent editorials in this journal as the 'aggregation of marginal gains' of its individual elements [27]. The benefits of one of those elements – carbohydrate loading – are starting to be translated into shorter postoperative hospital stays and a faster return to normal functions [28], perhaps also contributing to lower occurrences of peri-operative complications. Furthermore, the second editorial [29] is also relevant here – as patient cooperation and compliance is fundamental if the perceived benefits of preload are to be consistently reaped. We may not have found the ideal nutritional recipe for either yet, but the fact that simple and cheap nutritional input has such demonstrable benefits in patients merits further research. Indeed, in years to come we may be adding immunonutrients such as n-3 polyunsaturated fatty acids, glutamine, arginine or nucleotides to improve wound healing and reduce inflammatory markers [30]. Moreover, given that rapid return to normal muscle function is pivotal for enhanced recovery (permitting mobilisation and optimal respiratory function in the absence of fatigue and malaise), then muscle metabolism and efficiency is of paramount importance. Again, if we look to athletes as a physiological model, where optimal muscle metabolism has understandably generated much interest, then the future looks more fascinating. The key pathway is plentiful nitric oxide (NO) within muscles, particularly at times of reduced oxygen availability. The production of NO was thought to be solely through the endogenous NO synthase-dependent oxygenation of L-arginine. The discovery that there is an alternative oxygen-independent NO production pathway from nitrites and nitrates *and* that these latter compounds can be increased in muscle by exogenous oral compounds containing inorganic nitrates (found in beetroot and spinach, for example) is currently topical. There is growing evidence to suggest that at low oxygen levels, exogenous administered nitrates not only reduce the oxygen cost of exercise but also improve exercise tolerance and performance. This has recently been expertly reviewed by Jones [31]. If this improved muscular efficiency in athletes could be transferred to patients there would be obvious benefits, minimising the duration and severity of postoperative muscular dysfunction and maybe even reducing cellular oxygen consumption during the peri-operative period.

If the present sounds tasty, the future is tantalising. We should be able to broaden these ideas to address not just carbohydrate loading immediately pre-operatively, but to develop the concept of 'nutritional peri-operative medicine'. This would include not only the current practice of nutritional supplementation for a period pre-operatively for those severely malnourished (e.g. patients undergoing oesophagogastric or pancreatic surgery) and early postoperative feeding, but targeted dietary supplementation (e.g. nitrates) to increase efficiency of oxygen utilisation. In addition, a more formalised structure of when to exercise and what to feed patients for maximal anabolic effect to improve healing and reduce muscle catabolism needs to be developed, just as in muscle-centric sports [32].

We have a long way to go and there are still unanswered questions, including the ideal pre-operative drink and whether or not it can be substituted for other cheaper and more simple alternatives, especially as some patients complain of the unpleasant taste and of feeling very bloated. In addition, there is little information to date on the place of carbohydrate loading for patients receiving regional anaesthesia alone, for whom the metabolic upset is rather less, with concerns of pulmonary aspiration also reduced. Lastly, the precise risks and benefits for insulin dependent diabetics need to be clarified. Nevertheless, it is both surprising and disappointing that carbohydrate preload – one of the easiest and cheapest elements within the enhanced recovery pathway to improve surgical outcomes – has one of the lowest implementation rates. There is a need to

develop a structured research programme during peri-operative care, integrating and optimising the triad of metabolic, cardiopulmonary and muscle performance to benefit patients undergoing surgery. It is time not only to end the famine, but to start planning the feast.

Competing interests

No external funding and no competing interests declared. MJS is secretary of ERAS-UK and MJS and WJF are both on the committee of ERAS® Society.

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