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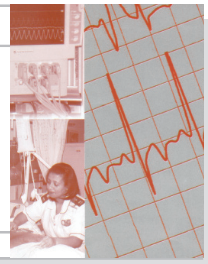
Enterocyte protection – a new goal in ICU nutrition



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Enterocytes are among the most metabolically active cells in the body but are the least well supplied with blood even under resting conditions.[1] Maintaining function of enterocytes has benefits that are becoming apparent in terms of improved outcomes from such diverse diseases as colorectal cancer[2] and pneumonia.[3]

Basic enterocyte physiology

Enterocytes are either secretory or absorptive. Secretory function is reduced in times of physiological stress such as critical illness but the basal metabolic activity of both types of cells still requires a supply of nutrients. Seventy per cent of the nutrition required by enterocytes is obtained from the gut lumen. As critical illness is almost invariably accompanied by a period of starvation, this source of nutrition is markedly diminished.[4]

Not only are luminal nutrients reduced, but the blood supply to the splanchnic circulation is also reduced in critical illness as blood flow is diverted to vital organs such as the heart, kidneys and brain.[5] Blood flow to the enterocytes is intended for absorption rather than delivery of nutrients so is sluggish even under resting conditions. Under stress, flow is markedly diminished.[4]

The challenge of maintaining enterocyte integrity is therefore to provide luminal nutrients and maintain splanchnic blood flow. Maintenance of blood flow is central to many other therapeutic approaches in ICU so this review will concentrate on maintenance of luminal nutrient levels.

Minimise pre-operative starvation

One of the major bones of contention between the anaesthetic and surgical teams in many hospitals is the period of fasting prior to surgical procedures. Keeping patients 'nil per mouth' (NPM) arose from the findings of Mendelson[6] that obstetric patients undergoing mask anaesthesia were at risk of regurgitation and aspiration. Fasting has been advocated to reduce the risk of aspiration during anaesthetic induction, prior to airway control, and emergence from anaesthesia. A simple formula is advocated by the American Society of Anesthesiologists (ASA), the 2/4/6/8 rule (Table I).[7]

Table I. Period of fasting prior to anaesthesia related to food consumed

Food consumed	Period of fasting (hours)
Large, fatty meal	8
Solid food (including dairy)	6
Breast milk/formula	4
Clear fluid (including black tea/coffee)	2

This rule has a number of caveats, firstly regarding the timing of emergency surgery in relation to fasting status:[8]

- Patients who have undergone recent trauma or received opioids remain at risk irrespective of fasting period.
- Patients may have metabolic (diabetes, pregnancy) or mechanical (gastric or bowel obstruction) reasons that will result in risk irrespective of fasting period.

Patients in the groups above should be anaesthetised with necessary precautions to prevent aspiration, including awake intubation or rapid sequence induction with application of cricoid pressure.

The second group of caveats relates more specifically to the maintenance of the enterocytes:

- Patients SHOULD receive clear fluids up to 2 hours before surgery.
- Patients who are in the ICU with airway control by endotracheal tube or tracheostomy do not need to be fasted UNLESS the procedure contemplated involves the gastrointestinal (GI) tract or airway. Fasting for radiological investigations IS NOT required.[9]

Pre-operative oral fluids

Fluids administered pre-operatively have a number of beneficial effects depending on their constituents:[9]

- Water: maintains hydration and reduces the requirement for intravenous fluids that have been implicated in the generation of postoperative oedema. Adequate hydration also improves patient comfort and satisfaction.

- Carbohydrates: reduce the catabolic response generated by starvation and surgery. Insulin sensitivity and tissue integrity are maintained.[10]
- Peptides: maintain enterocyte function and muscle strength.[11]

Lipids are not recommended as lipid emulsions are unstable in the acid environment of the stomach and may become particulate with a risk of aspiration.

Early postoperative enteral nutrition

Patients who undergo elective abdominal surgery do not necessarily develop an ileus requiring postoperative fasting with nasogastric drainage. Work from Copenhagen,[2] replicated in other centres,[12] has demonstrated that patients can undergo colonic resection with a period of fasting of only 8 - 10 hours and re-establishment of full enteral nutrition within 24 hours of surgery. This approach has become known as 'fast-track colonic surgery' and relies on a multimodal approach including:

- Clear fluids up to 2 hours pre-operatively, including carbohydrate and peptides
- Limiting intra-operative IV fluids to maintenance plus losses
- Laparoscopic dissection with specimen retrieval via Pfannenstiel incision
- NO nasogastric tube/abdominal drains
- Thoracic epidural analgesia
- Stop IV fluids on discharge from recovery room
- Commence sip feeds within 6 hours of admission to ward
- Aim for full enteral nutrition within 24 hours.

The success of programmes such as this requires a team approach with contributions from members including, but not limited to, surgeons, anaesthesiologists, intensivists, physiotherapists and dieticians. This has been supported by the ESPEN guidelines, which state that there is no reason to fast elective surgical patients postoperatively.[1]

Early enteral nutrition after emergency surgery

Emergency surgical procedures involving the abdominal contents and elective operations involving the upper GI tract (including gastrectomy and pancreatectomy) do not allow for early enteral nutrition via the stomach. In these cases, a fine-bore feeding tube placed via the nose beyond the pylorus (or surgical anastomosis) into the proximal jejunum (nasojejunal tube) as part of the laparotomy may be very useful. This tube is preferable to the placement of a feeding jejunostomy as the potential for morbidity is reduced.[13]

The nasojejunal tube is extremely useful in maintaining enterocyte integrity. With the tube in place, a low dose (10 - 30 ml/h) of a semi-elemental feed may be commenced as soon as the patient arrives in the ICU. Semi-elemental feeds are absorbed in the absence of peristalsis and do not require an increase in secretory or digestive function.[14] The enterocytes can thus receive nutrition without an increase in oxygen requirement.

The nasojejunal tube is not intended to provide systemic nutrition as this would require an increase in the digestive and secretory functions of the enterocytes with a resultant increase in oxygen requirements. In the early postoperative phase, splanchnic circulation may be reduced.[5] This reduction may be exacerbated by pre-existing vascular disease or the use of inotropes, such as dopamine and adrenaline, which promote splanchnic vasoconstriction. Attempting to feed a full dose of enteral nutrition via a nasojejunal tube will result in feed intolerance, diarrhoea and even perforation of the terminal ileum. This perforation arises as a result of an increase in oxygen requirements that cannot be met by increased blood flow, as the terminal ileum lies in a watershed area between the superior and inferior mesenteric circulations, making it particularly vulnerable to ischaemia, progressing to perforation, a process with the acronym of NOMI (non-occlusive mesenteric ischaemia).[15]

Systemic nutrition

With enterocyte nutrition being maintained by nasojejunal feeding, systemic nutrition may be provided by the route most likely to prove successful. Systemic nutrition during the initial phase of ICU admission is most commonly confined to 5 - 10% dextrose to limit ketosis. During this phase emphasis is placed on resuscitation with restoration of circulation and oxygenation. Within 48 - 72 hours the condition of the patient should have stabilised to the extent that systemic nutrition should be considered.

A nasogastric tube will be in place so gastric feeding is also an option. Tolerance of gastric feeding is deemed to indicate that the distal ileum is no longer at risk of NOMI.[15] Gastric feeding may be considered if gastric aspirate within a 6-hour period is less than 150 - 200 ml.[16] The protocol followed at Addington Hospital is shown in Fig. 1.

In the early stages of ICU admission a central line is still likely to be in place. Should gastric feeding be unsuccessful, the use of parenteral nutrition should be considered at this stage. Commencing parenteral nutrition does not preclude continued attempts to feed enterally. The aim should be to establish gastric feeding with reduction of parenteral feeding as goals are met.[17]

Once full gastric nutrition is established, both nasojejunal and parenteral feeding can be stopped.

Gastric residual in previous 6 hours < 150 ml

↓

Commence standard gastric feed at 40 ml/h

↓

Stop feeding after 5 hours and spigot NG tube

↓

Wait for 1 hour and then aspirate NG tube

↓

Response dependent on volume of aspirate:

< 150 ml – repeat

> 150 ml – repeat after 6 hours

When aspirate is < 50 ml on two occasions:

Feed for 11 hours – spigot for 1 hour and aspirate (check for feed intolerance)

Increase feed rate by 20 - 40 ml/h every 12 - 24 hours

Fig. 1. Approach to gastric feeding at Addington Hospital.

Parenteral supplementation with glutamine may be continued as glutamine is avidly taken up by enterocytes, leaving limited amounts to provide systemic benefit.[18]

Refeeding syndrome[19]

Patients fed following a period of starvation exceeding 48 hours are at risk of the refeeding syndrome, the main component of which is acute hypophosphataemia. Phospate is an essential component of all high-energy energy-transfer molecules such as adenine triphosphate (ATP). Synthesis of these compounds is reduced in starvation with increased urinary phosphate losses. On refeeding there is an increased demand for phosphate that may not be met by the slow mobilisation of phosphate from bone. It is therefore essential to check phosphate prior to and within 6 hours of commencing feeding. Phosphate is supplemented intravenously in the form of potassium-hydrogen-phosphate by the same protocol as for potassium choride (KCl) – 40 mmol K^+ in 200 ml 0.9% sodium chloride (NaCl)/5% dextrose. Magnesium is also a major cofactor for energy transfer that may be low in critical illness, so 2 g magnesium sulphate ($MgSO_4$) is added to this supplement at Addington.

Advantages of enterocyte nutrition

Early enteral nutrition does not place patients at risk of bowel perforation after surgery and bowel anastomosis. Early use of a semi-elemental feed (which does not increase enteral oxygen demand) is, by contrast, associated with a reduced rate of anastomotic dehiscence.[20] There is also an earlier return of bowel function and a reduced rate of both wound and pulmonary infections.[21] The reduction in pulmonary infections led to an animal study, where mice were fed either enterally or parenterally for 2 weeks. At this stage all animals received a similar intratracheal inoculation of *Escherichia coli*. Parenterally fed mice had a rate of subsequent pneumonia 50% greater than the enterally fed mice.[22] It therefore appears that maintaining enterocyte, and thus gut-associated lymphoid tissue (GALT), function results in maintenance of barrier function at other epithelial surfaces, including the skin and respiratory epithelium.

Conclusion

Enterocytes have not commanded great attention but should be considered central to maintenance not only of bowel function, but of epithelial integrity throughout the body. Maintaining luminal nutrients will require fresh approaches to some of the 'holy cows' of peri-operative patient management, including pre-operative fasting and early enteral nutrition.

Consideration should be given to reducing pre-operative fasting and providing oral feeds as soon as possible.

Where tube feeding is required, differentiation should be made between enterocyte and systemic nutrition. Low-dose, nasojejunal, semi-elemental feeds may be used for enterocytes while either gastric or parenteral feeding may be used as appropriate for systemic nutrition.[23]

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