Determination of a critical level of tissue oxygenation in acute intestinal ischaemia

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Abstract

Tissue oxygen tension (PtO₂) was measured using a miniaturised polarographic oxygen electrode in 134 segments of rat small intestine of varying degrees of ischaemia. Without knowledge of the PtO₂ levels, the viability of each segment was scored using clinical parameters and tissue damage scored by independent histological examination. Histologically non-viable bowel had significantly impaired tissue oxygenation when compared with viable bowel (t test, p<0.001). Marked degrees of tissue hypoxia were frequently tolerated before major histological damage became apparent, a critical PtO₂ level of 1.9 mmHg being identified. The overall accuracy rate of PtO₂ measurement in the operative prediction of intestinal viability was 92.5%, which contrasts with a rate of only 57.7% for clinical criteria alone.

Intuition says that an adequate supply of oxygen is the most important determinant of tissue viability. The technology to measure intestinal tissue oxygen tension (PtO₂) per operatively is now available, having been developed from the original Clark type polarographic oxygen electrodes,1 designed for use in cardiopulmonary bypass machines. This has been used in experimental animals2,3 and, more recently, in man,4-7 principally to evaluate the levels of tissue oxygenation necessary to allow intestinal anastomotic healing. Patterns of tissue oxygenation in ischaemic bowel and the relationship of oxygenation to tissue damage and therefore subsequent viability have, however, never been established in a systematic study.

In many cases of acute intestinal ischaemia, resection of the ischaemic bowel is the only treatment option. The assessment of intestinal viability in such cases remains an ongoing problem, one of the main difficulties being the unreliability of clinical parameters at operation.8,9 The result is a tendency to err on the cautious side, leading to the resection of excessive amounts of potentially viable bowel, with the familiar gastroenterological and nutritional sequelae of short bowel syndrome. Attempts at bowel preservation, on the other hand, frequently necessitate the performance of a ‘second look’ laparotomy 24–48 hours later. The desire to avoid such ‘second look’ laparotomies, often in very ill patients, has been the stimulus to the evaluation in the past of a large number of techniques for the objective assessment of bowel viability, most of which have not been found to be of practical value in patients.

If measured tissue oxygenation, however, could be related to subsequent viability, then knowledge of per operative PtO₂ levels may allow greater conservation of potentially viable bowel. The aim of this study, therefore, was to investigate the relationship between PtO₂ and histological tissue damage in segments of intestine of varying clinical viability.

Methods

ANIMALS

Twenty five male Wistar rats (weight 150–200 g) were used for this study. General anaesthesia was induced by ether inhalation and, through a short midline laparotomy incision, a segment of ileum was rendered ischaemic by ligating and dividing the main mesenteric artery branch to that segment (Fig 1). The ileum was returned to the peritoneal cavity, which was then closed, and an injection of 10 ml normal saline was given subcutaneously into the back, after which the animal was allowed to recover. By ligating the arterial supply in this way, it was hoped to create a segment of intestine of variable viability, ideally consisting of a central markedly ischaemic area, bounded at the proximal and distal margins by areas of intestine of questionable viability, the remaining bowel being normal.

Twenty four hours later, during a second laparotomy, the relevant segment of ileum was identified and a series of PtO₂ and surface temperature measurements were taken from the serosal surface. PtO₂ was measured using a specially built miniaturised Clark type oxygen probe (Fig 2). This 2.4 mm diameter probe consisted of a central platinum cathode (diameter 0.12 mm) and a concentric silver anode, cast in an epoxy resin body. The tip of the probe was covered with a Teflon membrane, which was
Table I: Scoring system for clinical assessment of viability

<table>
<thead>
<tr>
<th>Score</th>
<th>Clinical impression</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td>1</td>
<td>Uncertain, probably viable</td>
</tr>
<tr>
<td>2</td>
<td>Ischaemic</td>
</tr>
<tr>
<td>3</td>
<td>Necrotic, gangrenous or perforated</td>
</tr>
</tbody>
</table>

Table II: Scoring system for histological damage

<table>
<thead>
<tr>
<th>Score</th>
<th>Histological appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td>1</td>
<td>Ischaemic necrosis of mucosal villus tips only</td>
</tr>
<tr>
<td>2</td>
<td>Ischaemic necrosis of mucosal villus and crypts</td>
</tr>
<tr>
<td>3</td>
<td>Ischaemic necrosis extending into submucosa and inner muscle layers, but not full thickness muscle necrosis</td>
</tr>
<tr>
<td>4</td>
<td>Full thickness necrosis of bowel wall</td>
</tr>
</tbody>
</table>

Results

Two rats died shortly after induction of anaesthesia for the second laparotomy and so were excluded from the study. From the remaining 23 rats, a total of 134 histological specimens were examined and scored for macroscopic appearance and histological damage.

Although on clinical assessment the 134 specimens were fairly evenly distributed between viable (n=40), uncertain viability (n=56), and non-viable (n=38), histological examination revealed that the majority or the specimens (n=111) were potentially viable, as evidenced by no (grade 0) or minimal (grade 1) tissue damage. The mean (SD) stomach PtO2 of the 23 rats was 38.4 (7.8) mmHg, which was significantly higher (t test, p<0.05) than the mean PtO2 of the control small intestinal segments (33.4 (11.3) mmHg). PtO2 levels recorded within the devascularised segment (14 (13.7) mmHg), however, were significantly lower than either stomach or control small intestine (t test, both p<0.001). PtO2 changes across the ischaemic segments in the 23 animals are shown in Figure 3.

The use of clinical criteria alone correctly identified all 23 of the histologically compromised segments (grades 2–4). Of the 111 histologically non-compromised segments (grades 0 and 1), however, only 40 (36%) were felt to be viable using clinical parameters, giving an overall accuracy rate for clinical assessment of 57.7%.

The relationship between PtO2 and the degree of histological damage was assessed (Fig 4). Histologically compromised tissue (grades 2–4)
The presence of adequate levels of oxygen in the tissues is a major determinant of viability and intuition says that its measurement should allow accurate assessment of the adequacy of tissue perfusion. The drawbacks noted above are minimised in tissue oxygenometry and the methodology of transserosal tissue oxygen tension measurements in the gastrointestinal tract is now well established in animals and man.\(^6\) Although applied to the serosal surface, such probes have been shown to measure oxygen from a diffusion zone, which has been calculated mathematically to be of the order of six times the diameter of the cathode tip.\(^7,8\) With a 0.12 mm diameter cathode, such as was used in this study, the predicted diffusion zone should extend through all layers of the thin rat intestinal wall and therefore allow measurement of the mean transmural \(\text{PtO}_2\). Variations in this should reflect oxygenation of the mucosal layer, which, because of its high oxygen requirements, is more prone to ischaemic damage than the other layers. Only one \(\text{PtO}_2\) measurement was taken at each site, as these probes have been shown to provide highly reproducible readings with an average variability of only (2.9) mmHg.\(^7\) The apparently large standard deviations in Figure 3 simply reflect variation in oxygenation between individual animals.

Although this technique has been used to effect in individual patients with ischaemic bowel,\(^6\) an animal model was chosen for this study because of the practical difficulties in organising a systematic study in patients presenting with this condition. These difficulties arise from the sporadic nature of the problem combined with considerable variability in its surgical management (many patients with extensive advanced ischaemia have no procedure performed at the initial laparotomy, while others may have resection, revascularisation or ‘second look’ procedures or indeed any combination of these). Furthermore, histological specimens may not always have been obtainable.

Cases of ischaemic bowel usually do not come to surgery until many hours after the initial event and often after irreversible changes have taken place in the wall of the intestine. It is common clinical practice not to attempt revascularisation/reperfusion, either because it is not felt to be feasible or because the damage is not considered to be reversible. The animal model used in this study was devised to simulate this common clinical situation, with no attempt at intestinal reperfusion being made. It is acknowledged that a different experimental model would be required to assess the ischaemia/reperfusion process.

The use of histological appearance to assess
viability, although obviously it cannot be 100% accurate, is an objective and widely accepted technique. An ischaemic time of 24 hours was chosen because preliminary studies revealed that shorter periods were frequently insufficient for the full spectrum of histological changes to develop and longer periods were associated with the development of shock states in many animals, as evidenced by control PtO₂ readings.

The results of this study suggest that by applying strict clinical criteria, potentially non-viable bowel is unlikely to be overlooked. In achieving this, an undoubtedly desirable result, however, much potentially normal intestine may be needlessly excised, as shown by the fact that 64% of the histologically non-compromised segments in this study were mistakenly designated as non-viable by standard clinical parameters. Hence the need for more accurate and objective methods.

Although PtO₂ measurement provides a more accurate overall assessment of non-reversible damage (92-95%), the occurrence of relatively high PtO₂ levels in some segments of both clinically and histologically gangrenous tissue was unexpected. Although it is not immediately clear why this should occur, it is suggested that it is artefactual and is probably caused by necrosis of cells lining the serosal surface of the intestine.

It is possible that a metabolite or metabolites released from the necrotic cells may have crossed the oxygen probe membrane and undergone electrochemical reduction at the cathode surface, such as has been reported when these electrodes have been exposed to certain anaesthetic gases.

From this study, it appears that small intestine can tolerate marked degrees of ischaemia for 24 hours before evidence of significant histological damage becomes apparent. Indeed, the calculated critical PtO₂ of 1.9 mmHg was considerably lower than expected. In other studies evaluating intestinal PtO₂, the critical level for anastomotic healing was found to lie between 20 and 25 mmHg in animals and patients. It must be emphasised, however, that the intestine in the present study was not subject to a wound which was required to heal, such as an anastomosis, unlike the studies referred to above. Presumably, in the circumstances of the present study, the requirement for oxygen for collagen synthesis is much less than in a healing anastomosis and, in the short term, oxygen may only be needed to maintain basal metabolism.

No comparable studies looking at the relationship between intestinal tissue oxygenation and histological damage exist. Workers using micro-electrodes, however, have shown that resting intracellular PO₂ is low, 4 mmHg or less and that the critical PO₂ for cellular function may be as low as 1-2 mmHg.

More recent studies, where the mitochondrial PO₂ has been measured, suggested that the critical PO₂ for this vital organ may be as low as 2 mmHg. Critical levels of this magnitude would be supported by the findings of our study, with very low PtO₂ levels being found in some segments of intestine without any significant associated histological damage. It may be, however, that more prolonged exposure to such degrees of hypoxia would lead to significant damage — for example, strictures — in the long term.

Although further studies are required to examine the relationship of PtO₂ and tissue viability with differing ischaemic times, and also to evaluate changes in tissue oxygenation after intestinal reperfusion, the potential application of this technique in clinical practice can be appreciated. It may allow more intestinal conservation and reduce considerably the requirement for second look laparotomies. The occurrence of false positive indications of viability in obviously gangrenous tissue would not be a problem from a practical viewpoint, as the need for resection of such tissues would be clinically indisputable. In tissues where the clinical viability remains in doubt, however, PtO₂ measurement should be of considerable practical benefit.

24 Gillett ER, Sheridan WG, Mansel RE. Acute intestinal failure secondary to simultaneous occlusion of the caecum and appendix.


