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Review

The challenge of intra-abdominal sepsis

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ABSTRACT

An overview of intra-abdominal sepsis is necessary at this time with new experimental studies, scoring systems and audits on management outcomes. The understanding of the pathophysiology of the peritoneum in the manifestation of surgical sepsis and the knowledge of the source of pathogenic organisms which reach the peritoneal cavity are crucial in the prevention of intra-abdominal infection. Inter-individual variation in the pattern of mediator release and of end-organ responsiveness may play a significant role in determining the initial physiological response to major sepsis and this in turn may be a key determinant of outcome. The ability to identify the presence of peritoneal inflammation probably has the greatest influence on the final surgical decision. The prevention of the progression of sepsis is by early goal-directed therapy and source control. Recent advances in interventional techniques for peritonitis have significantly reduced the morbidity and mortality of physiologically severe complicated abdominal infection. In the critically ill patients there is some evidence that the prevention of gut mucosal acidosis improves outcome.

The **aim** of this review is to ascertain why intra-abdominal sepsis remains a major clinical challenge and how a better understanding of the pathophysiology may enable its prevention and better management.

Method: Electronic searches of the medline (PubMed) database, Cochrane library, and science citation index were performed to identify original published studies on intra-abdominal sepsis and the current management. Relevant articles were searched from relevant chapters in specialized texts and all included.

1. Introduction

Intra-abdominal sepsis is one of the most challenging situations in surgery and usually presents as peritonitis.[1–5] Gastrointestinal perforation, with leakage of alimentary contents into the peritoneal cavity, is a common surgical emergency and may have life-threatening sequelae. The mortality of perforated viscus increases with delay in diagnosis and management.[1–3,9–12] The recently reported 12-fold variation in the 30-day mortality rate following emergency abdominal surgery in Britain ranged from 3.6% in the best performing hospital to 41.7% in the worst.[5] This would be alarming in the developing world where an overall mortality rate of less than 17% is reported.[12] This shows that surgical outcome depends on a complex interaction of many factors and the success obtained with the early onset of specific therapeutic procedures. Mortality is lower when operations are conducted by consultant anaesthetists and surgeons rather than trainees and, where patients have ready access to treatment in intensive care following surgery.[9–11] The 'surgeon factor' i.e. decision making on surgical management of the acute abdomen is a critical determinant of outcome.[5] 'Patient factor' is also important as most patients are over 65 with co-morbidity and often seriously ill with internal haemorrhage or a bowel perforation.[5,13,14] Perhaps the variation in surgical management outcome may also be partly explained by the demography and health of the local population.[5,12] A better understanding about susceptibility to infections (patient factor) will explain why a patient with minimal bacterial contamination at surgery may develop a pelvic abscess whereas another patient with massive faecal contamination after stercoral perforation of the colon may not develop infective complications. Inter-individual variation in the pattern of mediator release and of end-organ responsiveness may play a significant role in determining the initial physiological response to major sepsis and this in turn may be a key determinant of outcome.[1–5] Other key determinants of outcome are the initial severity of infection e.g. colonic perforation, the timeliness and adequacy of attempts at treatment and the

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patient's general health and consequent ability to withstand the process.[9–16] Surgical peritonitis may emanate from perforation, ischaemia (mesenteric or strangulation), pancreatitis and anastomotic leakage.[11] Intra-abdominal abscesses may also occur within an intra-abdominal organ. These include pyogenic abscess in the liver from portal pyaemia when in a septicaemia organisms and neutrophil polymorphs embolize to the liver e.g. following appendicitis or a perforation (now fortunately rare because of the use of antibiotics); pancreas from acute pancreatitis, and in the fallopian tube (pyosalpinx) following adhesions in the fimbrae from an ascending infection.[19] Infections above an obstructing calculi may include an empyema of the gallbladder or in the renal pelvis. A complicated abdominal infection extends beyond the hollow viscus of origin into the peritoneal space and is associated either with peritonitis or abscess formation.

Acute appendicitis is the most common surgical emergency with a life time risk of ~7%, and it is one of a relatively dwindling number of conditions in which a decision to operate may be based solely on clinical findings.[10] There are undoubtedly specific features associated with all acute abdominal conditions which are well established. The aim of both the history and examination is to determine a diagnosis and clinical decision. It remains the ability to identify the presence of peritoneal inflammation which probably has the greatest influence on the final surgical decision.[7,18] Regular re-assessment of patients and making use of the investigative options available will meet the standard of care expected by patients with acute abdominal pain.[7]

2. Pathophysiology of sepsis

Sepsis is an evolving process. It is the systemic inflammatory response to infection frequently associated with hypoperfusion followed by tissue injury and organ failure. Therefore, its sequelae reflect increasing severity of the systemic response to infection and *not* severity of infection.[1–3] Infection is enhanced by the synergy between aerobes e.g. *Escherischia coli* which reduce oxygen content and facilitates growth of obligate anaerobes e.g. *Bacteroides fragilis*, and by the presence of adjuvant substances e.g. faeces, bile or urine.[25]

There is a *balance* between excessive and inadequate responses to infection. Some production of mediators is needed to combat infection but an excessive or prolonged activation of such cellular/humoral mediator pathways is thought to contribute to the development of multiple organ failure (MOF) in patients with major sepsis.[1–3,42] Mortality increases with the degree of the systemic inflammatory response syndrome (SIRS). The mortality following a *bacteraemia* is ~5%, *sepsis* (infection + SIRS) ~15%, *septic shock* (sepsis + hypotension (systolic BP < 90 mmHg) ~50%, *severe SIRS* ~80%, *multiple organ failure* (MOF) ~90%.[1–3] SIRS is a massive systemic response comprising an evolution of a cytokine cascade (TNF, IL-1, IL-6, IL-8), and a sustained activation of the reticuloendothelial system. It finally leads to the elaboration of secondary inflammatory mediators causing cell damage. These mediators include arachidonic metabolites (prostaglandins and leukotrienes), nitric oxide (vasodilator), oxygen free radicals, platelet activating factor causing increase platelet deposition, vasodilatation, increase capillary permeability and activation of coagulation pathways which results in end-organ dysfunction by formation of microthrombi. When three or more systems have failed the ensuing mortality approaches 80–100% and once one organ system has failed, others typically follow (organ failure amplification).[5] Thus it is important to strive to support as far as possible each organ system to avoid each further adverse event (e.g. ventilation, haemofiltration/haemodialysis, inotropic support, use of blood products).

Organs vary in their ability to maintain their own perfusion (through autoregulation) and generally, measurements relate the total body picture, rather than adequacy of perfusion of specific viscera. Renal failure is common in MOF and often established during the early stages. Renal function will return when perfusion and oxygenation are adequate and until this occurs, renal replacement therapy is needed.[1–4,23] Certain organs, notably the gut, are more prone to covert hypovolaemia and the consequent hypoxia may continue to drive the inflammatory process (including multiple organ failure) probably via bacteria translocation even when the initial causal factors are dealt with.[1] To overcome this, one approach has been to try and ensure that the critically ill patient with MOF has a circulation which provides an oxygen delivery greater than normal, thus minimizing the chance of occult hypoxia. A related approach has been to monitor plasma lactate and/or negative base excess as elevated values suggest that tissue hypoxia may be present.[2,3] An alternative strategy is to try and measure specific visceral perfusion in suspect viscera such as gut mucosa pH tonometry particularly in the preoperative preparation of the critically ill surgical patient.[4]

2.1. The Mannheim peritonitis index score

Many scoring systems have been created for assessing patient risks of death during an event of peritonitis. The *Mannheim peritonitis Index* (MPI) is a reliable predictor of the peritonitis outcome as the increase of MPI scores is proportional to that of morbidity and mortality. MPI adverse factors include presence of organ failure, time elapsed >24 h, presence of malignancy, origin of sepsis, the presence of faecal peritonitis and generalized peritonitis.[12,13]

3. Early goal-directed therapy

It is not possible to practice fully the ideal management of early diagnosis and surgery for the acute abdomen, thus reducing morbidity and mortality to zero, because patients and the disease are variable. However, because *infection*, *inadequate tissue perfusion* and *a persistent inflammatory state* are the most important risk factors for development of multiple organ failure it seems logical that initial therapeutic efforts should be directed at their early treatment or prevention (early goal-directed therapy).[20,21]

Early initiation of broad spectrum antibiotics has been shown to be critical during the SIRS phase for prevention of sepsis and septic shock. It has been shown clearly that patient mortality is significantly lower when appropriate antibiotics are prescribed early in the course of the patient's illness.[24] It is also important to appreciate that fungi and atypical organisms can contribute to the sepsis syndrome, and to take cultures and prescribe appropriately.[17] Prolonged 'prophylaxis' is detrimental as superinfection by fungi, antibiotic-resistant *Pseudomonas, Enterococci* and *Staphylococci* is encouraged.[17,41] These infections carry a high mortality and are difficult to treat. Enteric streptococci account for 10–20% of severe infections related to the abdomen and are not sensitive to all common prophylactic antibiotics.[15–17]

Early goal-directed resuscitation during the first 6 h after recognition of shock has moved towards the use of whole blood as it appears to eliminate the problems of expansion of extravascular volume and marked fluid retention seen with crystalloid on a background of leaky capillaries, and also appears to provide a lower incidence of organ failure.[20]

Adequate replacement of fluid loss via oesophageal doppler monitoring of left atrial filling, stroke volume and aortic flow (goal-directed fluid management) avoids the complications of fluid overloading or under-filling and thus favour faster recovery.[42–44] Critically ill patients who are either physiologically unstable or at high risk of failed source control especially following septic shock