Mechanisms Of Post-Operative Sepsis And Renal Impairment In Obstructive Jaundice

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Abstract

After open operations to relieve obstructive jaundice, several complications are excessively common. These include renal impairment, infections and sepsis. Under some circumstances, bile components can injure the bowel wall.

The hypothesis underlying this thesis was that after such operations, bile returning to the intestinal lumen increases bowel-wall permeability, allowing potentially harmful bowel contents to enter the tissues. These contents may include agents known to be harmful, such as bacteria and endotoxin, as well as agents whose toxicity is unknown, such as urobilinogen. A second hypothesis was that urobilinogen is nephrotoxic.

The aims were firstly, to develop a method of reversible obstructive jaundice in the rat. Secondly, to use the model to measure alterations in bowel-wall permeability to labelled bacteria, endotoxin and ethylenediaminetetraacetic acid (EDTA) after the relief of obstructive jaundice. Thirdly, to assess the toxicity of urobilinogen to renal cells cultured in vitro. Finally, to measure urobilinogen in various body fluids (including serum and urine) in rats and in human patients undergoing operations to relieve obstructive jaundice.

Various difficulties were encountered with the model of reversible obstructive jaundice, which limited its usefulness in measuring bacterial translocation from the bowel to the tissues. However, modification of the model allowed it to be used to assess alterations in bowel-wall permeability after bile was returned to the intestinal lumen. No such alterations were seen with normal bile or bile from subjects with obstructive jaundice, even when the bile was infected.

Urobilinogen was found to be toxic to cultured renal cells in concentrations which may reasonably be expected in disease, although caveats apply to this conclusion.

A urobilinogen assay, previously described by other workers, was found to be unsuitable for assay of specimens from jaundiced subjects, because interference from an unknown substance or substances occurred.

In summary, bile returning to the intestinal lumen of rats with obstructive jaundice did not alter bowel-wall permeability to endotoxin or EDTA. Urobilinogen was toxic to in vitro cultured renal cells in concentrations that may be expected to occur in disease. A previously-described assay for urobilinogen was found not to be useful for assaying specimens from jaundiced subjects.

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1. INTRODUCTION AND LITERATURE REVIEW

1.1 Note on Definitions

Sepsis and renal failure have long been recognised as being excessively common after operations on patients with obstructive jaundice (OJ). However, the terms 'renal failure', 'renal impairment' and especially 'sepsis' have been used rather loosely in the past, although sepsis has recently been more precisely defined (as discussed in more detail on p. 45). This often means that when comparing papers that report these complications, only limited conclusions can be drawn. With these limitations in mind, the definitions used by previous workers have been accepted, but where necessary, comment is made on whether those definitions may have affected either the interpretation of the author's own results, or their comparison to other work.

The aim of this thesis is to investigate some of the possible mechanisms underlying these common complications of operations to relieve obstructive jaundice. It refers specifically to conventional 'open' operations, i.e. those involving laparotomy, because it is after these procedures that these problems have been most frequently reported by previous workers. However, other means of treating obstructive jaundice, such as endoscopic and percutaneous approaches, are also discussed where relevant.

Many earlier papers using the term 'jaundice' do not precisely define it (e.g. Robson 1903, Heuer 1934, Thompson et al 1940, Aird 1953, Williams et al 1960, Hadjis et al 1986). Presumably, this is at least partly because of the limited laboratory tests available to the authors of many of these papers.

To some extent it is a subjective term, for the simple reason that it describes the discolouration of the skin occurring in hyperbilirubinaemia, and the ease with which this discolouration can be seen varies between individuals. Jaundice is not usually visible until the serum bilirubin is about three times the normal level, or about 50 μmol/L (Gollan and Schmid 1979).

This problem of subjectivity is seldom encountered in more recent papers dealing with the subject, because most such papers use a biochemical definition based on serum bilirubin levels. However, it is replaced by a lesser problem, namely a lack of uniformity in this definition. Commonly, the (arbitrary) level of a total serum bilirubin of more than 100 micromoles per litre (μmol/L) is used (e.g. Armstrong et al 1984a, Thompson et al 1986 and 1989, Pain et al 1991, Parks et al 1994), but others have used different definitions, such as a total serum bilirubin of more than 50 μmol/L (Gillen and Peel 1986), more than 136 μmol/L (Semeraro et al 1989), or more than 200 μmol/L (Smith et al 1985). This lack of uniformity is clearly important when comparing results from different studies, because patients with higher pre-operative serum bilirubin levels may be at greater risk of post-operative complications (Hunt et al 1980, Greig et al 1988).