Digestive and Liver Disease 49 (2017) 585–594

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Review Article

Early management of acute pancreatitis: A review of the best evidence

Serena Stigliano[a], Hanna Sternby[b], Enrique de Madaria[c], Gabriele Capurso[a], Maxim S. Petrov[d,*]

[a] Digestive & Liver Disease Unit, S. Andrea Hospital, University "La Sapienza", Rome, Italy
[b] Department of Surgery, Institution of Clinical Sciences Malmö, Lund University, Malmö, Sweden
[c] Department of Gastroenterology, Alicante University General Hospital, Alicante Institute for Health and Biomedical Research (ISABIAL-FISABIO Foundation), Alicante, Spain
[d] Department of Surgery, University of Auckland, Auckland, New Zealand

ARTICLE INFO

Article history:
Received 10 October 2016
Accepted 27 January 2017
Available online 7 February 2017

Keywords:
Acute pancreatitis
Antibiotics
Enteral feeding
Endoscopic treatment
Fluid resuscitation
Pain management

ABSTRACT

In the 20th century early management of acute pancreatitis often included surgical intervention, despite overwhelming mortality. The emergence of high-quality evidence (randomized controlled trials and meta-analyses) over the past two decades has notably shifted the treatment paradigm towards predominantly non-surgical management early in the course of acute pancreatitis. The present evidence-based review focuses on contemporary aspects of early management (which include analgesia, fluid resuscitation, antibiotics, nutrition, and endoscopic retrograde cholangiopancreatography) with a view to providing clear and succinct guidelines on early management of patients with acute pancreatitis in 2017 and beyond.

1. Introduction

Despite more than 100 years of experience and thousands of experimental and clinical studies, the management of acute pancreatitis remains challenging. In the past the slow progress has reflected the paucity of high-level evidence and an undue emphasis on surgical management. This 20th century 'surgical odyssey' has been well described [1]. The more recent application of evidence-based medicine principles to the early non-surgical management of acute pancreatitis has yielded improved patient outcomes and is the subject of this review. While there have been numerous studies demonstrating no benefit for a range of pharmacological interventions in acute pancreatitis (including but not limited to aprotinin, atropine, calcitonin, fresh frozen plasma, glucagon, gabexate, glucocorticoids, lexipafant, non-steroidal anti-inflammatory drugs, octreotide), the focus of this article is on the best available evidence on the use of early treatments that are often considered by the modern day clinicians. A computerized literature cross-search of three databases (MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials) from January 1, 1990 to September 1, 2016 was performed. To provide the best quality evidence, the data from only randomized controlled trials (RCTs) and high-quality meta-analyses in patients with acute pancreatitis were presented, if available.

2. Pain management

Pain is the cardinal symptom of acute pancreatitis and its relief is a clinical priority. Different analgesics have been compared in patients with acute pancreatitis and the nine published RCTs are summarised in Table 1 [2–10]. These trials had different study designs, evaluated different analgesics, had small sample sizes, and only three of the trials were double-blind. From these studies, it appears that there is no credible clinical evidence to avoid the use of morphine in treating the pain associated with acute pancreatitis. There is no evidence to support the use of parenterally administered local anesthetics (Procaine) in the management of pain associated with acute pancreatitis. Patients with severe pain will require intravenous analgesia and patient-controlled analgesia should be considered. Epidural analgesia can be considered for those patients with severe and critical acute pancreatitis who require high doses of opioids for an extended period. Although it has been reported that analgesics could also be given transdermally or rectally, there are no RCTs comparing the different routes of administration of the same analgesic in patients with acute pan-

* Corresponding author at: Department of Surgery, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand. Fax: +64 9 377 9656.
E-mail address: max.petrov@gmail.com (M.S. Petrov).

http://dx.doi.org/10.1016/j.dld.2017.01.168
1590-8658/

Table 1
Randomized controlled trials of analgesics in patients with acute pancreatitis.

Study ID	Year	Setting	Intervention group	Control group	No. of patients			Allocation concealment	Reduction of pain score	Other important findings
					Intervention group	Control group				
Blamey et al. [2]	1984	UK	Buprenorphine (i.m.)	Pethidine (i.m.)	17	15		Single-blind	No difference	No difference in terms of adverse effects.
Ebbehoj et al. [3]	1985	Denmark	Indomethacin (rectal)	Placebo (rectal)	14	16		Double-blind	Significantly higher in the intervention group over the first 168 h	Number of opiate injections were significantly lower in the intervention group.
Jacobs et al. [4]	2000	Germany	Buprenorphine (i.v.)	Procaine (i.v.)	20	20		Open-label	Significantly higher in the intervention group over the first 48 h	Number of additional analgesics were significantly lower in the intervention group.
Stevens et al. [5]	2002	USA	Fentanyl (transdermal)	Placebo (transdermal)	16	16		Double-blind	Significantly higher in the intervention group between 36 and 60 h	A significantly reduced length of stay in the intervention group.
Kahl et al. [6]	2004	Germany	Pentazocine (i.v.)	Procaine (i.v.)	50	51		Open-label	Significantly higher in the intervention group over the first 72 h	Number of additional analgesics were significantly lower in the intervention group.
Peiro et al. [7]	2008	Spain	Metamizole (i.v.)	Morphine (s.c.)	8	8		Open-label	Non-significantly higher in the intervention group over the first 24 h	No difference in terms of adverse effects.
Layer et al. [8]	2011	Germany	Procaine hydrochloride (i.v)	Placebo	23	21		Double-blind	Significantly higher in the intervention group over the first 72 h	Number of additional analgesics were significantly lower in the intervention group.
Sadowski et al. [9]	2015	Switzerland	Epidural anesthesia w Bupivacaine + Fentanyl	Patient controlled anesthesia (Fentanyl i.v)	13	22		Open-label	Significantly higher in the intervention group on day 0 and 10, not on days 1 to 9	Significant improvement of pancreas perfusion in the intervention group.
			Tramadol (i.v.)	Dexketoprofen (i.v.) or Paracetamol (i.v.)	30	30	60			