ORIGINAL RESEARCH PAPER

General Surgery

STUDY OF ROLE OF PROPHYLACTIC ANTIBIOTICS IN PATIENTS WITH ACUTE PANCREATITIS

KEY WORDS:

Dr. A. A. Ghasura Professor and Head of Department, BJMC and Civil Hospital Ahmedabad.

Dr. Aakash H. Patel* 3rd Year Resident, BJMC And Civil Hospital Ahmedabad.*Corresponding Author

Dr. Margi H. Hirpara 2nd Year Resident, BJMC And Civil Hospital Ahmedabad.

ABSTRACT

INTRODUCTION, AIMS AND OBJECTIVES: Acute pancreatitis is an inflammatory disorder of pancreas characterized by edema and when severe, Necrosis. It ranges from mild self-limiting disease to severe critical illness characterized by infected pancreatic necrosis and multiple organ failure and death. The mortality in acute pancreatitis is mostly due to MODS in first two weeks and infected necrosis in later period. Management is multidisciplinary and there is an ongoing debate over use of prophylactic antibiotics in patients with severe acute pancreatitis. The study aims to evaluate the current concept of avoiding use of prophylactic antibiotics in such patients. The study's objective is to compare the outcomes in patients randomly assigned to study group (no antibiotic use) and control group (antibiotic use). **METHODS:** A prospective study conducted at Civil Hospital Ahmedabad over a period of one year. 30 patients with Acute Pancreatitis randomized into two groups on odd-even basis; group A being study group not given prophylactic antibiotics, and group B being control group given routine prophylactic antibiotics. Inclusion and exclusion criteria were set. **RESULTS:** The outcomes were measured in terms of length of hospital stay, development of IPN/MODS and mortality. The average length of stay was 13 days and 12 days in groups A and B respectively . MODS developed in 5 of 15 patients in grp A, whereas in 6 of 15 patients in grp B. IPN was diagnosed in 2 patients in grp A and 1 patient in grp B. 4 patients in grp A and 5 patients in grp B suffered mortality. The results were compared and no significant difference in outcome was observed between two groups. **CONCLUSION:** The use of prophylactic antibiotics does not add to the benefit in the outcome of patients with acute pancreatitis unless infection of necrosis has developed when therapeutic antibiotics are given. Instead, antibiotic may add to the organ failure that is already present in these patients.

INTRODUCTION:

Acute pancreatitis is not an uncommon gastrointestinal emergency. Its incidence varies from 5 to 80 cases per 100,000 inhabitants per year, with an overall mortality rate of 10–15%. More than two-thirds of patients will recover within 1 week. The remaining one-third will experience multiple systemic and/or local complications, with a high mortality rate of 10–30%, 80% of deaths being due to infectious complications. The use and efficacy of prophylactic antibiotic therapy in acute pancreatitis has long been a point of controversy. We review cases and guidelines for the routine use of prophylactic antibiotics to prevent infectious complications and decrease the mortality from acute pancreatitis, and outline the situations where antibiotics may have a definite role and should be used.

MATERIALS AND METHODS:

A prospective study conducted at civil hospital Ahmedabad over a period of one year. 30 patients with moderate and severe Acute Pancreatitis were randomized into two groups; group A being study group not given prophylactic antibiotics, and group B being control group given routine prophylactic antibiotics. Inclusion and exclusion criteria were set as given below.

INCLUSION CRITERIA: All the patients diagnosed as having moderate and severe acute pancreatitis up to maximum of 30 days from symptom onset.

EXCLUSION CRITERIA:

1) Clinical evidence of sepsis (WBC> 16000/cu mm on admission or anytime thereafter during admission; fever >2 episodes over 24hr with axillary T>100°F)
2) Imaging or culture proven IPN
3) Evidence of infection at any other site in the body with elevated WBC count >16000/cu mm (pneumonia, UTI, Thrombophlebitis)

DEFINITIONS:

1) ACUTE PANCREATITIS- severe epigastric pain consistent with acute pancreatitis with elevation of amylase and lipase values above 3 times normal

Or

Imaging evidence (CT or USG) s/o acute pancreatitis.

2) MILD ACUTE PANCREATITIS- no local or systemic complications and no organ failure.

3) MODERATE ACUTE PANCREATITIS- AP with transient organ failure (<48hr)

4) SEVERE ACUTE PANCREATITIS-

AP with persistent organ failure (>48hr) or presence of local complications (necrosis, pseudocyst, abscess)

Presence of systemic complications (DIC, hypocalcaemia <7.5mg/dL)

5) ORGAN FAILURE- presence of any of the following:

Shock (SBP<90mmHg), pulmonary insufficiency (PaO2<60mmHg), Renal Failure (S. Creatinine > 2mg/dL)

GI bleed (>500mg/24 hr)

No antibiotic was administered in grp A patients. They were started on antibiotics only when they developed fever (at least three episodes >100 F), Infection of pancreatic necrosis or evidence of infection elsewere in the body.

Meropenem (1g iv BD) was administered to patients in group B. The protocol recommended stopping study drug when the patient was able to tolerate an oral diet and had a MOD score ≤2. Follow-up evaluations and procedures were performed after cessation of study treatment up to and including study day 30; however, for patients still in the hospital on day 45, follow-up continued. To be fully evaluable, a patient had to be followed for at least 30 days.

RESULTS:

The outcomes were measured in terms of length of hospital stay, development of IPN/MODS and mortality. The average length of stay was 13 days and 12 days in groups A and B respectively. MODS developed in 5 of 15 pts in grp A, whereas in 6 of 15 pts in grp B. IPN was diagnosed in 2 pts in grp A and 1 patient in grp B. 4 patients in grp A and 5 patients in grp B suffered mortality. The results were compared and no significant difference in outcome was observed between two groups.

PATIENT CHARACTERISTICS	STUDY GROUP A (NO ANTIBIOTICS)	CONTROL GROUP B (GIVEN ANTIBIOTICS)
NUMBER OF PATIENTS	15	15
1.MALE	11	12
2.FEMALE	04	03
AGE		
18-54	12	13
>55	03	02
PRIMARY CAUSE OF PANCREATITIS		
BILIARY	05	04
ALCOHOL	07	08
ALCOHOL USE	11	12
% OF NECROSIS BY CECT		
<30%	04	03
>30%	08	10
NOT RECORDED	03	02
AVERAGE HOSPITAL STAY	13 DAYS	12 DAYS
MODS	05	06
IPN	02	01
MORTALITY	04	05

DISCUSSION:

Acute Pancreatitis is clinically divided into two phases: 1) The early stage – the first 14 days from the onset of the disease – is characterised by a systemic inflammatory response syndrome (SIRS), which may be complicated by multiple organ dysfunction syndrome (MODS). 2) In 15–20% of cases, this may be followed by a stage of secondary bacterial infection within the inflamed pancreas, typically 2–3 weeks from the onset of pancreatitis.

Pathogenesis of secondary bacterial pancreatic infection is still debated. Pathogens can reach the pancreas through the haematogenous pathway, via the biliary system, ascending from the duodenum via the main pancreatic duct, or through transmural colonic migration via translocation of the colonic bacteria to the lymphatics. Most pathogens in pancreatic infection are gastrointestinal Gram-negative bacteria (*Escherichia coli*, *Pseudomonas*, *Proteus*, *Klebsiella*), which occur via disruption of the intestinal flora and damage to the bowel mucosa. Impaired body defences predispose to translocation of the gastrointestinal organisms and toxins with subsequent secondary pancreatic infection. But Gram-positive bacteria (*Staphylococcus aureus*, *Streptococcus faecalis*, *Enterococcus*), anaerobes and, occasionally, fungi have also been found. Infection of sterile necrosis is attributed to bacteria of gut origin in up to 70% of cases.

In mild pancreatitis, the mortality rate is less than 1%, in contrast to severe pancreatitis, which ranges from 10% in cases of sterile pancreatic necrosis to as high as 25% with infected necrosis. Consequently, interest has focused on the identification of pancreatic necrosis and the potential benefits of prophylactic antibiotics to prevent secondary infection of the necrotic pancreatic tissue.

Infection in acute pancreatitis has been encountered in 30–40% of patients. The most dangerous is necrotising pancreatitis, which constitutes around 30% of this group, with reported associated poor prognosis and high mortality. Furthermore, 80% of deaths from acute pancreatitis are due to secondary pancreatic infection. The use of antibiotic prophylactically in acute pancreatitis is still a matter of controversy, however. Many authors have advocated their use routinely, while others have condemned this practice.

Most guidelines have advocated the prompt and judicious use of antibiotic prophylaxis in the setting of severe acute pancreatitis. The role of prophylactic antibiotics in severe acute pancreatitis with associated necrosis remains unclear. Eighteen meta-analyses of RCTs were identified, between the years 1998 and 2015, which sought to determine whether prophylactic antibiotics reduce mortality and the incidence of infection in pancreatic necrosis in patients with severe acute pancreatitis and necrotising pancreatitis. 4 of them definitively concluded that prophylactic antibiotics are helpful in reducing mortality while 6 concluded no role in prevention of necrosis and development of complications.

CONCLUSION:

The use of prophylactic antibiotics does not add to the benefit in the outcome of patients with acute pancreatitis unless infection of necrosis has developed when therapeutic antibiotics are given. Instead, antibiotic may add to the organ failure that is frequently present in these patients.

Intravenous broad-spectrum antibiotics should be started when infected necrosis is suspected or proven, which can subsequently be narrowed down based on cultures of the infected collection. Some small case series show that treatment with antibiotics alone can be successful in obviating the need for surgical drainage in a small subset (approx. 5% to 10%) of patients, but in vast mast majority of patients, antibiotics should be regarded as supportive care in this phase of the disease, where drainage and/or Necrosectomy of (suspected) infected necrotic collections are regarded as the only option for effective treatment.

REFERENCES:

1. Baron TH, Morgan DE. Acute necrotizing pancreatitis. N Engl J Med. 1999;340:1412–1417. [PubMed] [Google Scholar]
2. Beger HG, Rau B, Isenmann R. Natural history of necrotizing pancreatitis. Pancreatology. 2003;3:93–101. [PubMed] [Google Scholar Beger HG, Rau B, Isenmann R, et al. Antibiotic prophylaxis in severe acute pancreatitis. Pancreatology. 2005;5:10–19. [PubMed] [Google Scholar]
3. Golub R, Siddiqi F, Pohl D. Role of antibiotics in acute pancreatitis: a meta-analysis. J Gastrointest Surg. 1998;2:496–503. [PubMed] [Google Scholar]
4. Sharma VK, Howden CW. Prophylactic antibiotic administration reduces sepsis and mortality in acute necrotizing pancreatitis: a meta-analysis. Pancreas. 2001;22:28–31. [PubMed] [plications in acute pancreatitis: a randomized, controlled trial versus imipenem. Pancreas. 2003;27:79–83. [PubMed] [Google Scholar]
5. Isenmann R, Runzi M, Kron M, et al. German Antibiotics in Severe Acute Pancreatitis Study Group. Prophylactic antibiotic treatment in patients with predicted severe acute pancreatitis: a placebo-controlled, double-blind trial. Gastroenterology. 2004;126:997–1004. [PubMed] [Google Scholar]
6. Shackelford's Surgery of The Alimentary Tract, 8th ed.
7. Blumgart's Surgery of The Liver, Biliary Tract and Pancreas, 6th ed.
8. Maingot's Abdominal Operations, 13th ed.
9. Sabiston Textbook of Surgery, 20th ed.
10. Schwartz Principles of Surgery, 11th ed.
11. Bailey and Love's Short Practice of Surgery, 27th ed.