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STUDY OF ROLE OF PROPHYLACTIC ANTIBIOTICS USE IN PATIENTS WITH ACUTE PANCREATITIS IN SOUTH INDIANS

[1]Manoj Kumar Yatagiri, [2]Narendra, [3]Kalyan Seetharamaiah V*

[1]Assistant professor, Dept of General Surgery, Sri Lakshmi Narayana Institute of Medical sciences, Pondicherry, India
[2]Associate professor, Dept of General Surgery, Sri Balaji Medical college, Chennai, Tamilnadu, India
[3]Assistant professor, Dept of General Surgery, Sri Lakshmi Narayana Institute of Medical sciences, Pondicherry, India.

ABSTRACT
Prophylactic antibiotics are used frequently for acute pancreatitis (AP). Consensus guidelines do not recommend this currently, based on moderate quality evidence. The development of pancreatic infection is associated with the development of a deteriorating disease with subsequent high morbidity and mortality. The average length of stay was 13 days and 12 days in groups A and B respectively. MODS developed in 10 of 30 pts in grp A, whereas in 12 of 30 pts in grp B.IPN was diagnosed in 4 pts in grp A and 2 patient in grp B. 8 patients in grp A and 10 patients in grp B suffered mortality. 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.

Key words: Acute Pancreatitis, Pancreatic Infection, Antibiotics , Necrotising Pancreatitis, Therapeutic antibiotics.

INTRODUCTION

In spite of an increasing understanding of the pathophysiology of acute pancreatitis (AP) over the past few years, there is still no specific treatment for the ailment. Fifteen percent (range 4 % to 47 %) of patients with AP develop (peri)pancreatic necrosis, of which 33 % (range 16 % to 47 %) develop infected necrosis (IN) [1]. Furthermore, it has also been reported that extra-pancreatic hospital that acquired infections in patients with AP can adversely impact morbidity and mortality [2]. Even though use of prophylactic antibiotics appears plausible based on these premises, randomized controlled trials (RCTs) on the use of prophylactic antibiotics in AP have yielded heterogeneous results, and recent double-blinded placebo-controlled trials and meta-analyses have failed to show significant preventive benefit [3–6]. One of the earlier meta-analysis did demonstrate some benefit from carbapenems in subgroup analysis [7], but it was subsequently found that studies with the highest quality had the least effect of antibiotics on pancreatic infection [8, 9].

The course of necrotizing AP may include an early vasoactive and toxic phase and a late period dominated by infection of the pancreatic necrotic tissue. Once infection of pancreatic necrotic tissue occurs the prognosis does worsen and mortality increases. Patients with necrotizing AP are, however, prone to also develop other infections (urinary, respiratory, biliary, and systemic infections) during both the early and late phases of the disease . These infections complicate the clinical course of AP, may prolong hospitalization, and theoretically may also increase the risk for bacterial colonization of pancreatic necrosis.

In most patients, bacteria complicating acute necrotizing pancreatitis originate from the gastrointestinal tract and include Escherichia coli, Proteus mirabilis, Enterococcus faecalis, Pseudomonas aeruginosa, Bacteroides spp. and Clostridium spp.[10-11]

Corresponding Author :- Dr.Kalyan Seetharamaiah V Email:-drvrvkk@gmail.com

Some recent research has reported a rising incidence of fungal infection (Candida spp.) of up to 35%.12 Despite some clinical and experimental studies, the pathogenesis of secondary infection of the necrotic pancreas remains unclear; however, some evidence supports the hypothesis that such infection represents the translocation of a microorganism from the gastrointestinal tract.[10,13-14] Haematogenous dissemination, ascending infection caused by reflux into the pancreatic duct, the migration of microorganisms via the lymphatic system or a combination of these factors are the likely point of entry.[15-16]

The use and efficacy of prophylactic antibiotic therapy in acute pancreatitis has long been a point of controversy. The role of prophylactic antibiotics to prevent infection and reduce mortality in pancreatitis was first evaluated in the 1970s, where several randomised controlled trials (RCTs) had been conducted and concluded that prophylactic antibiotics were effective in preventing secondary pancreatic infections and therefore in reducing the related mortality.[17-19]

The use and efficacy of prophylactic antibiotic therapy in acute pancreatitis has long been a point of controversy. We review all 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.

Material and Methods:

A prospective study conducted at SLIMS hospital, Puducherry over a period of one year. 60 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 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)

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. Mild Acute Pancreatitis: no local or systemic complications and no organ failure. Moderate Acute Pancreatitis: AP with transient organ failure (<48hr). Severe Acute Pancreatitis AP with persistent organ failure (>48hr) or presence of local complications (necrosis,pseudocyst,abscess). Presence of systemic complications. Organ Failure: Presence of any of the following: Shock, pulmonar y insufficiency, Renal Failure, GI bleed. 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 10 of 30 pts in grp A, whereas in 12 of 30 pts in grp B.IPN was diagnosed in 4 pts in grp A and 2 patient in grp B. 8 patients in grp A and 10 patients in grp B suffered mortality. The results were compared and no significant difference in outcome was observed between two groups.

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.

However, even though guidelines do not recommend prophylactic antibiotics, based on the disparate data and moderate quality evidence, role of prophylactic antibiotics cannot be conclusively ruled out at present. At the same time, a “blanket cover” of prophylactic antibiotics for most patients with AP too does not appear justified. Assuming that antibiotic prophylaxis is useful in patients with severe AP, some controversial issues on this topic still remain. We refer to the selection of the most suitable antibiotic treatment the duration of treatment, the possible selection of resistant strains, and the possible usefulness of jejunal feeding.

Table.1: Results were compared and no significant difference in outcome was observed between two groups.

PATIENT CHARACTERISTICS	STUDY GROUP A (NO ANTIBIOTICS)	STUDY GROUP B (NO ANTIBIOTICS)
NUMBER OF PATIENTS	30	30
1. MALE	22	24
2. FEMALE	08	06
AGE		
18-54	24	26
>55	06	04
PRIMARY CAUSE OF PANCREATITIS		
BILIARY	10	08
ALCOHOL	14	16
ALCOHOL USE	24	24
% OF NECROSIS BY CECT		
<30%	08	06
>30%	16	20
NOT RECORDED	06	04
AVERAGE HOSPITAL STAY	13 Days	12 Days
MODS	10	12
IPN	4	2
MORTALITY	8	10

Imipenem, clindamycin, piperacillin, fluoroquinolones and metronidazole are known to have adequate tissue penetration and bactericidal properties in infected pancreatic necrosis, in contrast to penicillins, first-generation cephalosporins, aminoglycosides and tetracyclines, which are ineffective in acute pancreatitis.[20-21] Meropenem is shown to have as wide a spectrum as imipenem in preventing septic complications in acute pancreatitis.[22] The use of systemic antibiotics in pancreatic infections must be accompanied with drainage, either surgical or percutaneous. One of the main problems of prolonged administration of antibiotics in severe acute pancreatitis is the development of multidrug resistance bacterial and fungal infection, which is associated with long hospital stay and poor outcome. [23] Hence, each case should be individually evaluated, weighing the benefits of antibiotics against the significant adverse events associated with their use, including increased bacterial resistance and fungal infections. Microbiologists with a specific interest in pancreatitis should be involved in such decisions, and blood culture is highly suggested as this might detect bloodstream infections associated with 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.

Pulmonary, urinary, biliary, and other infections may frequently complicate the course of AP, prolong hospitalization, influence morbidity and mortality, and increase the need for adjunctive diagnostic and therapeutic measures [24]. In the present study, a lower incidence of extrapancreatic infections was observed in those patients who started antibiotic treatment earlier. Antibiotic treatment is thus likely to be more useful in the first h of disease when ileus, cholestasis, and application of central

venous and urinary catheters are like to favor bacterial penetration or translocation, and determine transient bacteremia and colonization of different organs and tissues. Appropriate use of antibiotic prophylaxis, especially in intensive care units, is a very debated topic, because indiscriminate use of antibiotics can result in the rapid emergence of resistant organisms [25].

A panel of experts recently provided a Level A recommendation regarding the use of prophylactic broad-spectrum antibiotics in CT-proven necrotizing pancreatitis. Nevertheless, these four could be potential rational indications for the use of prophylactic antibiotics and need to be evaluated further under randomized controlled settings. It would be important to be vigilant on the duration of antibiotic prophylaxis, and care should be taken to avoid prophylaxis for a prolonged period of time. Nevertheless, this study is important since, to our knowledge, it is first from the country that has evaluated the pattern of antibiotic use in patients with AP. It was performed in multiple high-volume tertiary care academic centers across the country. Furthermore, the data on the pattern of infections associated with AP in Indian patients is another strength of this multicenter study.

Conclusion:

Evidence is accumulating to suggest that prophylactic antibiotics in patients with acute pancreatitis is not associated with a significant decrease in secondary pancreatic infection and mortality. We do not therefore recommend routine prophylactic antibiotic therapy for all patients with acute pancreatitis. Conversely, the prompt use of prophylactic antibiotics once a physician detects early markers associated with high risk of pancreatic infection is mandatory.

Accurate selection of patients to be treated with antibiotics is crucial, because only necrotizing forms of the disease may benefit from the treatment. 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.

REFERENCE:

1. Banks PA, Freeman ML. Practice guidelines in acute pancreatitis. Am J Gastroenterol. 2006;101:2379–400.
2. Wu BU, Johannes RS, Kurtz S, Banks PA. The impact of hospital-acquired infection on outcome in acute pancreatitis. Gastroenterology. 2008;135:816–20.
3. Isenmann R, Runji M, Kron M, et al. Prophylactic antibiotic treatment in patients with predicted severe acute pancreatitis: a placebocontrolled, double-blind trial. Gasrtoenterology. 2004;126:997– 1004.
4. Dellinger EP, Tellado JM, Soto NE, et al. Early antibiotic treatment for severe acute necrotizing pancreatitis: a randomized doubleblinded, placebo-controlled study. Ann Surg. 2007;245:674–83.
5. Gascia-Barrasa A, Borobia FG, Pallares R, et al. A double-blind, placebo-controlled trial of ciprofloxacin prophylaxis in patients with acute necrotizing pancreatitis. J Gastrointest Surg. 2009;13:768–74.
6. Talukdar R, Vege SS. Recent developments in acute pancreatitis. Clin Gastroenterol Hepatol. 2009;7:S3–9.
7. Heinrich S, Schafer M, Rousson V, Clavien PA. Evidence-based treatment of acute pancreatitis: a look at established paradigms. Ann Surg. 2006;243:154–8.
8. Mazaki T, Ishii Y, Takayama T. Meta-analysis of prophylactic antibiotic use in acute necrotizing pancreatitis. Br J Surg. 2006;93:674– 84.
9. drVries AC, Besselink MG, Buskens E, et al. Randomized controlled trials of antibiotic prophylaxis in severe acute pancreatitis: relationship between methodology and outcome. Pancreatology. 2007;7:531–8.
10. Balzan S, de Almeida Quadros C, de Cleva R, Zilberstein B, Cecconello I. (2007) Bacterial translocation: overview of mechanisms and clinical impact. J Gastroenterol Hepatol 22:464–471.
11. Cicalese L, Sahai A, Sileri P, Rastellini C, Subbotin V, Ford H et al. (2001) Acute pancreatitis and bacterial translocation. Dig Dis Sci 46:1127–1132.
12. Beger HG, Rau B, Isenmann R, Schwarz M, Gansauge F, Poch B. (2005) Antibiotic prophylaxis in severe acute pancreatitis. Pancreatology 5:10– 19.
13. Olah A, Romics L Jr. (2010) Evidence-based use of enteral nutrition in acute pancreatitis. Langenbecks Arch Surg 395:309–316.
14. Dervenis C, Smailis D, Hatzitheoklitos E. (2003) Bacterial translocation and its prevention in acute pancreatitis. J Hepatobiliary Pancreat Surg 10:415–418.
15. Isenmann R, Beger HG. (2001) Bacterial infection of pancreatic necrosis: role of bacterial translocation, impact of antibiotic treatment. Pancreatology 1:79–89.

16. Widdison AL, Karanjia ND, Reber HA. (1994) Routes of spread of pathogens into the pancreas in a feline model of acute pancreatitis. Gut 35:1306–1310.
17. Dervenis C, Johnson CD, Bassi C et al. Diagnosis, objective assessment of severity, and management of acute pancreatitis. Santorini Consensus Conference. Int J Pancreatol 1999; 25(3): 195–210.
18. Dambrauskas Z, Gulbinas A, Pundzius J et al. Meta-analysis of prophylactic parenteral antibiotic use in acute necrotizing pancreatitis. Medicina (Kaunas) 2007; 43(4): 291–300.
19. UK Working Party on Pancreatitis. UK guidelines for the management of acute pancreatitis. Gut 2005; 54(Suppl III): iii1–iii9.
20. Demetri GD, von Mehren M, Antonescu CR et al. NCCN Task Force report: update on the management of patients with gastrointestinal stromal tumors. J Natl Compr Canc Netw 2010; 8 (Suppl 2): S1–41; quiz S42–S44.
21. Trudel JL, Wittnich C, Brown RA. Antibiotics bioavailability in acute experimental pancreatitis. J Am Coll Surg 1994; 178(5): 475–479.
22. Manes G, Rabitti PG, Menchise A et al. Prophylaxis with meropenem of septic complications in acute pancreatitis: a randomized, controlled trial versus imipenem. Pancreas 2003; 27(4): e79–e83.
23. Isenmann R, Schwarz M, Rau B et al. Characteristics of infection with Candida species in patients with necrotizing pancreatitis. World J Surg 2002; 26(3): 372–376
24. Uomo G, Visconti M, Manes G, et al. Nonsurgical treatment of acute necrotizing pancreatitis. Pancreas 1996;2:142–8.
25. Trilla A. Epidemiology of nosocomial infections in adult intensive care units. Intensive Care Med 1994;20:S1–4.