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Research Article

Impact of Microbial Culture Analysis and Prophylactic use of Antibiotics in Acute Severe Pancreatitis

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ABSTRACT

Objective: The uses of prophylactic antibiotics are beneficiary in acute severe pancreatitis in reducing the infection. The main objective of this study is to compare the effects of antibiotics as prophylaxis and treatment in two groups with and without microbial cultural test, respectively. Methods: The study population consisted of 60 patients treated for acute severe pancreatitis. In group 1 (n=32) patients received prophylactic antibiotics according with the microbial test and were treated accordance with ultra-guided drainage and/or surgical debribment of infected necrosis were performed when the presence of pancreatitis was demonstrated. The primary endpoints were infectious complication rate, incidence of nosocomial infection and mortality rate. In group 2 (n=38), patients received prophylactic antibiotics (ciprofloxacin, metrodinazole) without microbial test. Results: In group 2, 38(54.28%) patients were administrated with prophylactic for >14 days than in group 1, 32(45.71%) the Fine Needle Aspiration and/Ultra Sound guided drainage fluid collections were urine sample 15.62%, blood sample 31.25%, Pus sample 9.37%, peritoneal fluid 12.50% and drain fluid 31.25%. In which 15.62% Escherichia.coli is most commonly grown gram negative bacteria. And carbapenems (meropenam, ertapenam) are most sensitive. We can observe significant difference between groups in mortality and duration of stay in the surgical ward or intensive care unit. Conclusion: In this study, with the microbial analysis the use of the prophylactic antibiotic can reduce the hospital stay, need of surgical management and reduce the frequent use of reoperation.

Key words: Acute severe pancreatitis, Antibiotic prophylaxis, Fine needle aspiration, Microbial cultural test, Nocsocomial infection, Ultra sound guided.

INTRODUCTION

Therapeutic use is an obvious and rational use for antimicrobials in patients with pancreatitis.[1] The two factors that are directly related to its morbidity and mortality are organ failure and infection. Organ failure may occur as early as the first week and can cause either early or delayed mortality[2,3] and also uncontrolled systemic inflammatory response syndrome is usually associated with high mortality rate.[4] Much of the morbidity and mortality accompanying this disease are due to pancreatic and peri-pancreatic infection with reported rates as high as 40% to 70 %.[5]

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Infected pancreatic necrosis is still assumed to indicate that surgical debridement is necessary. However, during recent years, several studies have reported that conservative treatment such as nonsurgical drainage was successful in some patients.[6-8] The clinical importance of pancreatic infection became significant to prevent the infected necrosis could be beneficial[9] and prophylactic antibiotics probably have positive effect on the course of the patient with necrotizing pancreatitis.[10,11] In most of the patients, bacteria complicating acute necrotizing pancreatitis originate from the gastrointestinal tract that includes Escherichiacoli, proteus mirabilis, Enterococcus faecalis, Pseudomonas aeruginosa bacteroides spp and Clostridium spp.[12,13]

The prophylactic use of antibiotics might be a beneficial treatment option at an early stage of the disease before necrotic areas become infected, since they are capable of penetrating pancreatic tissue and achieve M.I.C. (Maximum Inhibitory Concentrations) levels in serum and pancreatic juice.[14] Acute pancreatitis is a disease with extremely different clinical expressions and most of the patients suffer mild and limited disease, but one fifth of the patients develop multiple organ dysfunction syndrome (MODS), accompanied by high mortality rate.

MODS is not a predictive method but it is a best indicator of acute pancreatitis, its severity and mortality, mainly if it appears early, or persists for more than 48 hours or is multi organic.[15]

Reducing the complication of acute pancreatitis with the help of prophylactic antibiotics is still a controversy, but in this study the antibiotics plays a significant role, which reduces its complications and further hospital stay. Therefore, we initiated to investigate the effects of antibiotics in both group A and group B in-order to show the rational and knowledge concerning about the prophylactic use of antibiotics in acute pancreatitis. The primary aim of this prospective, randomized and observational study was to evaluate the effectiveness of the prophylactic antibiotics like carbapenams intravenously in delaying and preventing the pancreatic and peri-pancreatic infection in patients. And with this, the beneficiary of microbial test with respect to the patient samples makes wide difference and delaying in pancreatic infection and hospital stay. The main objective of study is to evaluate the effect of prophylactic administration of antibiotics in acute pancreatitis and rationale use of antibiotics can reduce the pancreatic and peri-pancreatic infection.

METHOD

This was a prospective, randomized, single center, study from January 2014 to November 2014 for 10 months. Approval from the institutional ethics committee was obtained prior to the study. And all patients provided written informed consent form. The culture and sensitivity reports were collected from the records of department of microbiology for study period. A total of 70 patients were enrolled out of 32 patients was analyzed for culture and sensitivity. Prospective data is collected in the department of gastroenterology BGS Global hospital, diagnosed with severe and acute necrotizing pancreatitis for which the onset of disease occurred within the previous 72 hours.

Inclusion criteria: onset of disease occurred within 72 hours, clinical symptoms like abdominal pain, vomiting and nausea, elevation of serum alpha amylase greater than 3 times greater than the normal level and C-reactive protein >110 mg/l, CT-scan performed at 5-7 days after the onset of the disease inorder to assess the severity of acute pancreatitis on admission and during follow up and MODS >7 score. Already debribment of pancreatitis patients are excluded. The study categorize into two different group A and group B with different treatment strategies utilized in each.

In group 2, 38 patients are admitted to the hospital and were routinely given antibiotic prophylaxis, ciprofloxacin 800 mg/day and metrodinazole 1500 mg/day for 14 days. And patient present within the 72 hours from the onset of the disease CRP>110 mg/l, MODS >7 and necrosis of >35 to 40% as demonstrated on contrast enhanced CT-scan.In this, the only change to the former protocol other than that to antibiotic prophylaxis was that patients diagnosed with acute pancreatitis were routinely monitored Intra Abdominal Pressure (IAP) as well the growth of microorganism in the respective samples. However, in this group patients were not routinely monitor for the elevated intra abdominal pressure and no bacterial culture examination test were sent.

In group 1, 32 patients were admitted to the hospital with the same criteria, the only change to the former protocol other than that to antibiotic prophylaxis was that patients diagnosed with acute pancreatitis were routinely monitored Intra Abdominal Pressure (IAP) as well the growth of micro-organism in the respective samples. In this study, the feasibility and effectiveness of the subcutaneous fasciotomy of the anterior rectus abdominal sheath were assessed, as well as the regular check up with the Ultra sound (USG) guided drainage of intra-abdominal and peri-pancreatic fluid collections, as indications to obtain the bacterial cultures from peripancreatic fluid collection, urine, pus, blood, peritonel fluid and ultra guided fine needle aspiration cytology (FNAC) was performed in all patients in whom pancreatic necrosis had been confirmed by CT-scan and also in whom persisting symptoms of MODS score >7 or failure of at least one organ. When severe infection was observed, US-guided drainage or retro-peritonealscopic or surgical debribment (US guided drainage) of infected necrosis was performed.

Step 1: Percutaneous drainage was performed in all patients.

Step 2: Retro peritoneoscopic or surgical debribment depending on the size and accessibility of the infected collection is considered with patients in whom no improvement was seen after percutaneous drainage.

Step 3: Multi-resistant organism were derived as pathogens, predominantly bacteria, that were resistant to one or more classes of anti-microbial agents those includes Methacillin-Resistant Staphylococcus aureus (MRSA), Vancomycin-Resistant Enterococcus (VRE), gram negative bacteria producing ESBL (Extended spectrum beta-lactamase and remaining were resistant to multiple classes of anti-microbial agents.

RESULTS

Statistical analysis: Statistics are presented as the mean ± standard deviation and for comparisons between groups student t-test (for normally distributed data) were employed as appropriate. A p-value of <0.5 was considered to indicate statistical significance.

Patients demographic and the etiology of pancreatitis by groups are shown in Table 1. In group 2 38 (54.28%) patients were administrated with prophylactic antibiotics for >14 days as shown in Table 2. Where as in group 1 32 (45.71%) patients were administrated antibiotics according to bacterial culture test, multi-drug resistant micro-organism, requiring the administration of carbepanems were identified

Table 1: Patients Demographic details and its characteristics features of antibiotics (n=70)

	Group 1 (n=32) 45.71%		Group 2 (n=38) 54.28%	
	Male	Female	Male	Female
Age(Yrs) Mean ± SD	55 ± 1.03		55 ± 1.05	
Gender (Mean ± SD)	07.5 ± 04.79	0.5 ± 0.57	08.75 ± 04.11	0.75 ± 0.50
N (%)	30 (93.75)	02 (06.25)	35 (92.10)	03 (07.89)
Etiology n (%)				
Alcohol	10 (31.25)		13 (34.21)	
Biliary	18 (56.25)		20 (52.63)	
Idiopathic	04 (12.50)		05 (13.15)	
Severity Acute Pancreatitis				
MODS scale	1.25 ± 1.31		1.27 ± 1.32	
Necrosis ≥ 30%, n (%)	13 (40.62)		16 (42.10)	

more frequently in group 1 than group 2. of 05 (15.62%) urine samples were analyzed in group 1. Out of which 02 were negative with gram-negative micro-organism, and 03 were positive. Where as in Pus samples 03 (9.37%) were analyzed out of which 01 were negative with gram-negative micro-organism seen. and 02 were positive. Klebsiellla pneumonia is the common gram-negative micro-organism grown in urine and in pus sample.

In group 1, the FNAC and/USG guided drainage of large intra abdominal fluid collections were performed. In peritoneal fluid sample in group 1, 04 (12.50%) were analyzed out of 02 were negative with gram negative. Out of which 02 E.coli and 01 E.coli ESBL growth is seen. Out of which 01 was positive. Where as in drain fluid, 10 (31.25%) were analyzed and was negative with gram-negative micro-organism, 02 E.coli, 03 E.coli ESBL and Klebseilla pneumonia and 01 Pseudomonas and Proteus. In blood samples, 10 (31.25%) were analyzed out of which 03 (30%) were positive and 07 were negative with gram-negative micro-organism is seen. In which 01 of Pseudomonas ESBL, E.coli, Klebsiella and Klebsiella ESBL and 02 E.coli. Bacterial culture analysis shown in Table 3.

Overall, surgical interventions (open necrosectomy, repeated surgery and debridement) were more frequently performed in group 1 (p=0.741) and group 2 (p=0.382). The length of stay and clinical outcomes are shown in Table 4.

Table 2: Antibiotic Prophylaxis (group 2)

Class	No. of patients n (%)
Quinolones	
Ciprofloxacin	11 (28.94)
Penicillin	
Piperacillin	06 (15.78)
Cephalosporin's 3rd Generation	
Ceftriaxone	16 (42.10)
Amino glycosides	
Amikacin	02 (05.28)
Nitroimidazole	
Metrodinazole	03 (07.89)
Total	38 (100)

Table 3: Bacterial culture analysis

Growth of the Microorganism	No's Infected (N=32), n (%)
E.coli	05 (15.62)
E.coli ESBL	05 (15.62)
Klebseilla	03 (09.37)
Klebseilla ESBL	03 (09.37)
Pseudomonas	04 (12.50)
Pseudomonas ESBL	01 (03.12)
Proteus	02 (06.25)
No growth	09 (28.12)
Total	32

Antibiotic susceptibility Test

Escherichia coli and E.coli ESBL were highly sensitive to meropenam and ertapenam with MIC 0.5, moderate to imipenam and amkacin MIC 1.0. Klebsiella and klebsiella ESBL highly sensitivity to tigecycline MIC 1.0 and ertapenam MIC 0.5 and moderate to cephalosporin's and fluroquinoles 1.75 MIC. Pseudomonas is highly sensitivity to levofloxacin with MIC 0.25 and Pseudomonas ESBL is sensitivity to colistin with MIC 0.5. Proteus is highly sensitive to ciprofloxacin with MIC 0.5. The overall sensitivity pattern of antibiotics to bacterial culture analysis in acute pancreatitis was the highest to the carbapenams followed by good sensitivity towards quinolones, polypeptide antibiotic and glycycline antibiotic shown in Table 5.

DISCUSSION

Antibiotic prophylaxis in acute severe pancreatitis (with pancreatic necrosis,organ failure and or/sepsis) has been a controversy over last two decades and various clinical trials have been performed and results were contradictory.[16-23] The aim of the current study was to impact and effect of antibiotic prophylaxis and treatment in two different groups. The use of prophylactic antibiotics in group 2 had no significant effect on acute severe pancreatitis such as incidence of infectious and mortality rate compared with group 1.

According to the bacterial cultured isolated and antibiotic susceptibility test, the antibiotics had a signigicant role in group 1, in which it reduces the infection and length of stay as compared to group 2, this phenomenon should be examined in further treatment prospective. However, surgical interventions and, the absence of nosocomial infection is supported by the use of antibiotic prophylactic in acute severe pancreatitis, which is in accord with expert panel on the management of the acute pancreatitis.[24]

E.coli was the most common organism in the acute severe pancreatitis after analyzing bacteriology in acute severe pancreatitis,[25] The antibiotic sensitivity pattern showed that most of the bacteria were sensitivity to carbapenams and quinolones. In multi center study[22] showed that combination of ciprofloxacin and metrodinazole did not show significant reduction of infected pancreatitis necrosis were determined as 15.75% in group 2 than in group 1 12.56% (p>0.05).

Table 4: Clinical Outcomes

Outcomes	Group 1 (n=32)		Group 2 (n=38)		p-value
Sepsis	02 (06.25)		03 (07.89)		0.217*, 0.072[1]
Infected Pancreatitis	04 (12.56)		06 (15.78)		
Severe Acute Pancreatitis	20 (62.50)		18 (47.36)		
Major Organ Failure	04 (12.50)		06 (15.78)		
Length of stay	**ICU Ward**	**Surgery Ward**	**ICU Ward**	**Surgery Ward**	0.741*, 0.382[1]
≤ 2 weeks	02	01	00	03	
≤ 4 weeks	01	03	02	04	
≤ 6 weeks	00	00	01	00	
Deaths					
Overall deaths (n),%	03 (09.37)	05 (13.15)			

*Group-1, [1]Group-2

Table 5: Sensitivity towards the antibiotics (group 1)

Growth of the microorganism	Sensitivity of the drug	MIC (Minimum Inhibitory Concentration)
E.coli	Meropenam*	0.5
E.coli ESBL	Ertapenam*	0.5
Klebseilla	Tigecycline[1]	1.0
Klebseilla ESBL	Ertapenam*	0.5
Pseudomonas	Levofloxacin[3]	0.25
Pseudomonas ESBL	Colistin[2]	0.5
Proteus	Ciprofloxacin[3]	0.5

*Carbapenams, [1]Glycylcycline antibiotic, [2]polypeptide antibiotic, [3]Quinolones.

In 2009[26] Showed that prophylactic use of ciprofloxacin reduce the secondary risk for pancreatitic infection nor the mortality rate, but in this study it is considered as beneficiary as well as less impact result in group 2. In another study, meta-analysis of eight trails,[17] shows significant reduction in pancreatic and non-pancreatitic infection and in length of stay but not beneficiary towards the mortality rate and need for surgical intervention, similar results can be observed in the current study. In Cochrane review of seven studies,[27] found benefit of carbapenams was considered in isolation and significant decrease in pancreatitic infection. Better designed studies are needed, if the use of antibiotic prophylaxis is to be recommended.

The overall resistance pattern of antibiotic are cephalosporins, ampicillin, amoxicillin, co-trimazole. This may be due to the wide use of these antibiotics as empirical therapy and not recommended for bacterial cultural analysis.

CONCLUSION

The prospective study shows the details of pathogen and their sensitivity towards antibiotics pattern. It is clear that E.coli is still most common gram-negative micro-organism grown and carbapenams are the sensitive. The beneficiary of bacterial culture analysis in acute severe pancreatitis makes wide differences and delay in pancreatitic infection decrease the need for interventional and surgical management. And also prevent the further development of antimicrobial resistance and it does not affect the mortality rate. Routine monitoring of susceptibility patterns is necessary. This will help in the rational and prophylactic preparation to clinical and also the preparation of antibiotic policy of the individual institute.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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