

Effect of Prophylactic Use of Ciprofloxacin and Metronidazole in the Outcomes of Acute Pancreatitis`

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Abstract: ***Background:** One of the major causes of death in cases of severe acute pancreatitis is SIRS and MODS. Prophylactic antibiotics are known to reduce the septic complications in these cases. The aim of this study is to assess the efficacy of prophylactic use of Ciprofloxacin and metronidazole in reducing complications and mortality in severe acute pancreatitis. There are new concepts and developments in the diagnosis and management of acute pancreatitis. Current evidence suggests that there is no role of prophylactic antibiotics use in acute pancreatitis. However, it is very common to use prophylactic antibiotics in our setting. **Method:** This is a comparative two-armed study design done in the period between April 2021 to March 2022 in the department of General Surgery at RIMS Ranchi, involving 80 patients admitted with a diagnosis of acute pancreatitis in the inpatient ward of department of General Surgery at RIMS Ranchi. Patients were randomized into two groups ie, one receiving combination of iv Ciprofloxacin and metronidazole and other receiving normal saline as placebo; both started at the day of admission, and given for next 10 days. The occurrence of local and septic complications, mortality rate and length of stay were recorded and compared in both groups. **Result:** There were no significant differences between both the groups of patients of acute pancreatitis in the outcomes. **Conclusion:** The use of prophylactic ciprofloxacin and metronidazole is not associated with any significant clinical improvement, and thus its use can be avoided in routine clinical practice.*

Keywords: Acute pancreatitis, Ciprofloxacin-metronidazole, clinical outcome.

1. Background

Sepsis and related complications are the major cause of mortality in acute pancreatitis that can be as high up to 50%. Therefore, interest has been focused on the prophylactic administration of antibiotic ie, a combination of Ciprofloxacin and metronidazole to prevent these infections. Several studies conducted in the past 10 years proved that prophylactic antibiotics are helpful in decreasing the incidence of septic pancreatic complications. There are new concepts and developments in the diagnosis and management of acute pancreatitis. Since a couple of decades, it was reported that there is no role of prophylactic antibiotics based on the two landmark trials^[1]. The mortality rate due to organ failure has been recently reported between 36-50% in two different studies.^[2] So, this study had aimed to ascertain the efficacy of prophylactic antibiotics to prevent any local, systemic and septic as well as the effect of reduction in mortality in our setup where many clinicians still prefer to administer prophylactic antibiotics.

2. Material and Method

This comparative study was conducted during the period of April 2021 to March 2022 in RIMS Ranchi, in the selected groups of patients (n=80) who were admitted in the department of Surgery with the diagnosis of Acute pancreatitis.

The inclusion criteria –

- Patients older than 18 years,

- A clinical and radiological diagnosis of Acute pancreatitis,
- Admission within 72 hours of onset of symptoms
- No intake of antibiotics 3 days before admission.

Exclusion Criteria-

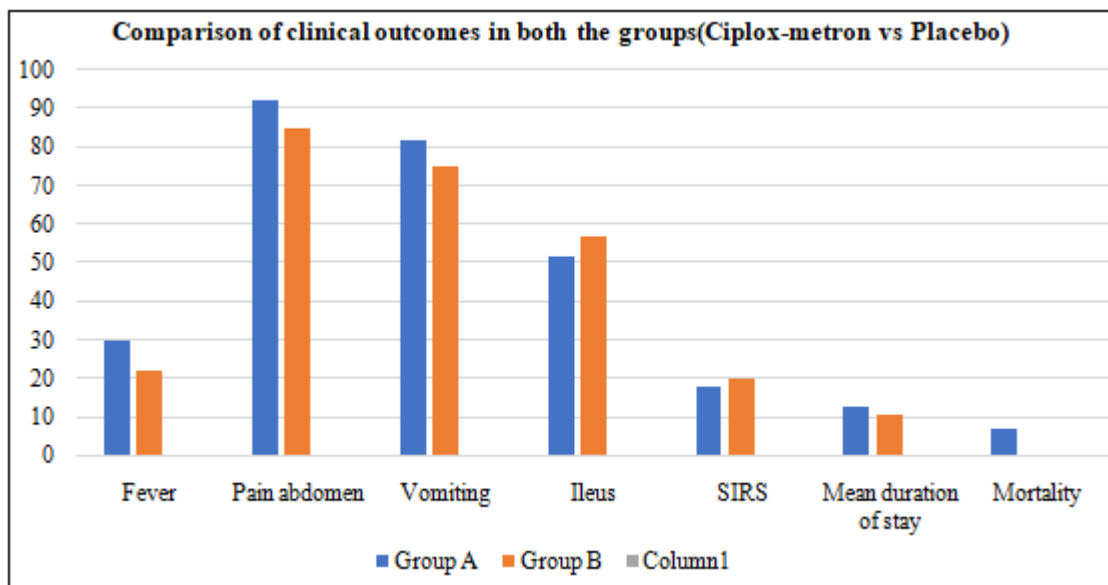
- Patients with Carcinoma related Pancreatitis,
- Incompliant patients,
- Presence of extensive comorbidities.

Informed written consent was obtained from all patients. Simple randomization was used to identify 2 groups of n=40 patients i.e.; The first group (Group A) were given combination of intravenous ciprofloxacin and metronidazole; while the other group (Group B) were given intravenous normal saline as placebo for 10 days.

All patients were treated with standard protocol. The clinical course of the disease was monitored using routine laboratory tests and sepsis indices like WBC <4000 or >12000 cells/cumm, pyrexia, Respiratory rate <20, heart rate >90 bpm. Also, other systemic parameters were noted in order to exclude Systemic Inflammatory Response Syndrome - Multiple Organ Dysfunction Syndrome. Contrast-enhanced CT and ultrasonography were repeated when requested on the grounds of clinical outcome. The primary comparable outcome was incidence of fever, Pain abdomen, vomiting, ileus (>3 days), SIRS, mean duration of stay and mortality. These were noted and compared in both the groups.

3. Result

- In Group A cases, the incidence of fever after admission was 30% (12/40), while in Group B was 22.5% (9/40)
- Pain abdomen was a seen in 37/40 i.e.; 92.5% in Group A cases, while that in Group B cases was seen in 34/40 ie; 85% cases.
- Vomiting was seen in 33/40 i.e.; 82.5% of the Group A cases, while in Group B cases it was seen in 30/40 i.e.; 75% of the cases.
- The incidence of prolonged ileus (>3 days) was seen in 21/40 i.e.; 52.5% of the cases of Group A, while it is seen in 23/40 i.e.; 57.5% of the cases in Group B cases.
- SIRS was seen in 7/40 i.e.; 17.5% of the Group A cases while that in Group B cases was 8/40 i.e.; 20% cases.
- Mean duration of stay in Group A cases were 13 days, while in Group B cases were 11 days
- Mortality was seen in 3/40 i.e.; 7.5% of Group A cases while that in Group B cases were 2/40 i.e.; 5% of Group B cases



4. Discussion

Acute pancreatitis remains a common clinical condition requiring frequent admissions in surgical emergency. The use of prophylactic antibiotics has been commonly seen in our settings. The possible reason to prefer prophylactic antibiotics could be unhygienic or contaminated working place, fear of hospital acquired infections and to prevent local and septic complications. In general, infectious complications from acute pancreatitis account for high morbidity and mortality with 80% of death related to infectious complication itself.^[3] The antibiotics which have found to achieve the highest inhibitory concentrations in pancreatic tissue are Carbapenems, Fluoroquinolones, Metronidazole and high dose Cefuroxime^[4].

In this study, the incidence of fever, Pain abdomen, vomiting, ileus and SIRS in Group A were 30%, 92%, 82%, 52% and 17.5% respectively; while that of Group B were 22.5%, 85%, 75%, 57.5%, and 20% respectively. The mean length of hospital stay in Group A was 14 days while that of Group B was 11 days. The mortality rate in Group A was 7.5%, while that in Group B was 5%. These data were not significantly comparable in both the groups in this study. A recent meta-analysis of published randomized controlled trials concluded that prophylactic antibiotic treatment of patients with acute pancreatitis is effective in reducing both the infection rate and the mortality rate. In this study, we tested a combination of Ciprofloxacin and metronidazole, in comparison with placebo in order to compare different clinical outcomes including the mortality rate. Ciprofloxacin

and metronidazole were generally well tolerated with fewer serious adverse events than the placebo. A previous comparison study of imipenem-colistin to non treatment in patients with necrotizing pancreatitis demonstrated a significant reduction in the incidence of pancreatic infection with treatment but no difference for operations or mortality. The only published double-blind study (n = 114) in acute necrotizing pancreatitis, which had a greatly improved design compared with previous studies, demonstrated no advantage of early antimicrobial (ciprofloxacin and metronidazole) prophylaxis when compared with placebo. In this study, 35 of 76 patients with necrotizing pancreatitis received additional, non-study antibiotics (half in the first week) for increasing SIRS or MODS with no significant difference between the antibiotic and the placebo group^[5]. A study from Isenmann et al and this report are added to the data in the Cochrane review, then the comparisons between antibiotic and placebo lose statistical significance both for pancreatic infection and mortality.^[5]

5. Conclusion

Prophylactic use of Ciprofloxacin and metronidazole in acute pancreatitis is not associated with reduction in clinical symptoms, incidence of SIRS, ileus, duration of hospital stays and mortality rate; than placebo. Thus, routine use of prophylactic antibiotics is not found to associate with any significant clinical improvement.

References

- [1] Dellinger EP, Tellado JM, Soto NE, et al. Early antibiotic treatment for severe acute necrotizing pancreatitis: a randomized, double-blind, placebo-controlled study. *Annals of surgery*. 2007;245(5):674-83
- [2] Wu BU, Johannes RS, Sun X, Tabak Y, Conwell DL, Banks PA. The early prediction of mortality in acute pancreatitis: a large population-based study. *Gut*. 2008;57(12):1698-703.
- [3] Mourad M, Evans R, Kalidindi V, Navaratnam R, Dvorkin L, Bramhall S. Prophylactic antibiotics in acute pancreatitis: endless debate. *Ann R Coll Surg Engl*. 2017;99(2):107-12.
- [4] Büchler M, Malfertheiner P, Frieß H, et al. Human pancreatic tissue concentration of bactericidal antibiotics. *Gastroenterology*. 1992;103(6):1902-8
- [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; 126:997–1008