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Use and non-use of prophylactic antibiotics for severe acute pancreatitis- A comparative study

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***Abstract*---**Background: Acute pancreatitis is a frequent disease in Chile, with mortality rate of 10-30%. Prophylactic antibiotics administration has been part of severe acute pancreatitis treatment for theoretical prevention of infectious complications and mortality reduction. Yet the available evidence is controversial. Objective: To evaluate that prophylactic antibiotics do not reduce complications, need for intensive care unit bed or mortality in severe acute pancreatitis. Methods: A Randomized clinical trial with simple randomization was performed this was a preliminary report containing 53% of the total estimated sample. Patients with SAP evaluated and treated by the biliopancreatic surgery team at the hospital 01 April 2022 and 30 May 2022. Using a statistical significance level of 95% and a power of 80%, the sample size is 150 patients per group. The study was comprised of 150 patients divided into two randomized groups: group 1 (non-use of prophylactic antibiotics) contained 75 patients, and group 2 (use of antibiotic prophylaxis) contained 75 patients. Results: The average age of the total group (N=150) was 59.2±18 years; the average age in group 1 was 58±19.4 years and in group 2 it was 60±17.8 years (p=0.11). The distribution by gender showed a women predominance in the total group with 64% (N=123): group 1 had 64% (N=48) women, and group 2 had 63% (N=47) (p=0.27). The main etiology was lithiasis/stones being 84% of the total group with a similar distribution between the two groups (84% and 81%, respectively) but not significant. 22 patients needed a bed at the ICU (16%)- 10 patients from the group without antibiotics and 12

patients from the group with antibiotics (p=0.11). The average stay at the ICU of all the patients was 11±15.4 days. Conclusions: The prophylactic antibiotics use for severe acute pancreatitis was not shown to reduce complications, need for an intensive care unit bed or mortality.

***Keywords*---**Acute pancreatitis, Lithiasis, Antibiotic prophylaxis, randomized clinical trial, pain abdomen, mortality.

Introduction

Acute pancreatitis (AP) is a frequent pathology and one of the main hospitalizations causes of patients with abdominal pain.[1] Around 80% of patients recover fully in 1 week [2], since it mainly develops as an uncomplicated disease, without infectious events and without requiring intensive treatment. However, 20% of patients present local or systemic complications, with a mortality rate of 10-30%.[3,4] The Atlanta Consensus defines severe acute pancreatitis (SAP) as being morphologically related to extended necrosis of the pancreatic tissue (>30%), infection due to necrosis or abscess formation, and/or presence of retroperitoneal necrosis of extrapancreatic tissue. Even more important, SAP is identified by the presence of systemic organ complications (pulmonary, renal or hepatic failure) and cardiopulmonary dysfunction (shock).[5,6]

There are many systematic reviews of randomized clinical trials (RCT) that demonstrate the clinical effectiveness of prophylactic antibiotics in pancreatitis that reduce mortality and incidence of infection, whereas other reviews have not found a significant clinical benefit of the use of prophylactic antibiotics.[7]
In recent decades, the prophylactic administration of antibiotics has been part of the treatment of SAP in our environment for the theoretical prevention of infectious complications and mortality reduction[8]. The rationale behind the study was to demonstrate that prophylactic antibiotics do not reduce complications, need for intensive care unit bed or mortality in severe acute pancreatitis.

Materials and Methods-

A Randomized clinical trial with simple randomization was performed this was a preliminary report containing 53% of the total estimated sample. Patients with SAP evaluated and treated by the biliopancreatic surgery team at the hospital 01 April 2022 and 30 May 2022.

Sample size was calculated using the SPSS based on the Japanese meta-analysis of Ukai et al, which showed that the infection rate due to necrosis in the group that did not use antibiotics was 25%, demonstrating a reduction of 10% in the group that used antibiotics.[9] Using a statistical significance level of 95% and a power of 80%, the sample size is 150 patients per group. The study was comprised of 150 patients divided into two randomized groups: group 1 (non-use of prophylactic antibiotics) contained 75 patients, and group 2 (use of antibiotic

prophylaxis) contained 75 patients.

Inclusion criteria

All the patients with SAP admitted to the HHHA and treated by the hepatobiliary surgery team were included in the study.

Exclusion criteria

Patients with following criteria were excluded- (a) mild acute pancreatitis (MAP); (b) who began antibiotic for infection suspicion, since the concept of infection treatment is different from the concept of prophylaxis; (c) who had undergone another antibiotic therapy for another non-pancreatic infected site.

Methodology

Patients admitted with a diagnosis of AP were classified according to the APACHE II severity score and the CRP value. Patients with an APACHE II ≥8, or CRP ≥150 (normal value <10 mg/dl) or multiorganic dysfunction were classified as SAP. Once the SAP diagnosis was confirmed, randomization took place using a simple computational table by the study coordinators.

Ciprofloxacin and metronidazole were used in the group that used prophylactic antibiotics. Their use was ideally orally or by nasogastric intubation: 500 mg of ciprofloxacin (ciprofloxacin, Ascend) every 12 hours and 500 mg of metronidazole (metropast, Pasteur) every 8 hours. Use of intravenous ciprofloxacin and metronidazole was reserved for patients unable to tolerate antibiotic use orally and/or by nasogastric intubation, for example in patients with ileus. The dose of intravenous antibiotics used was 400 mg ciprofloxacin (Ciprolife®, Aculife®) every 12 hours and 500 mg metronidazole (Apiroflex®, Biosano®) every 8 hours. The duration of the antibiotic prophylaxis was left up to the biliopancreatic surgery team, being set at 7 days. The rest of the treatment (nutritional support, transfer to ICU, check-up X-rays, surgery or procedures) did not vary between groups

Statistical Analysis

Analysis of data was done by using SPSS software ver. 22. Data were statistically described in terms of mean (±SD), frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using Student t test for independent samples if normally distributed. For comparing categorical data, Chi square test was performed. A probability value (p value) less than 0.05 was considered statistically significant.

Results

Table 1- Demographic profile and General characteristics of Both Groups

Variables	**Group 1 (N=75)**	**Group 2 (N=75)**	**p-value**
Age (Mean±SD)	58±19.4	60±17.8	0.11
Gender Males	27 (36)	28 (37)	0.27

Females	48 (64)	47 (63)	
Stones	63 (84)	60 (81)	0.17

As per table 1 the average age of the total group (N=150) was 59.2±18 years; the average age in group 1 was 58±19.4 years and in group 2 it was 60±17.8 years (p=0.11). The distribution by gender showed a women predominance in the total group with 64% (N=123): group 1 had 64% (N=48) women, and group 2 had 63% (N=47) (p=0.27). The main etiology was lithiasis/stones being 84% of the total group with a similar distribution between the two groups (84% and 81%, respectively) but not significant.

Table 2- Prognostic and Diagnostic indicators comparison in both groups

Indicators	**Group 1**	**Group 2**	**p-value**
APACHE II at admission	7.2±4.2	8.2±5.4	0.55
APACHE II at 48 hours	7.2±4.4	8±5.2	0.28
CRP at admission	194±110	150±106	0.18
CRP at 48 hours	162±109	194±109	0.11

As per table 2 The average CRP (mg/dl) on admission of all the patients was 176±118. In group 1 it was 194±110, and in group 2 it was 150±106 (p=0.18). The average CRP at 48 hours was 176±110. In group 1 it was 162±109, and in group 2 it was 194±109 (p=0.11) but it was not significant (p>0.05). The APACHE II average on admission of all the patients was 7.5±4.2. In group 1 it was 7.2±4.2, and in group 2 it was 8.2±5.4 (p= 0.55). The average APACHE II at 48 hours was 8±5. In group 1 7.2±4.4, and in group 2 it was 8±5.2 (p=0.28).

Table 3- Comparison of Outcome variables in both groups

Indicators	**Group 1**	**Group 2**	**p-value**
Days of Hospital stay	15.4±8	16.4±8.2	0.16
ICU stay	10	12	0.26
Complications	02	09	0.11
Mortality	00	02	0.71

As per table 3 22 patients needed a bed at the ICU (16%)- 10 patients from the group without antibiotics and 12 patients from the group with antibiotics (p=0.11). The average stay at the ICU of all the patients was 11±15.4 days. Eleven patients (6.6%) had some type of complication related to SAP, two patient in group 1 and nine in group 2 (p=0.11). The average hospital stay of all the patients was 16.2±14.2 days. In group 1 it was 15.4±8 days, and in group 2 it was 16.4±8.2 days (p=0.16). In mortality terms, two patients died (2% patients) during the study, two patients in the group 2 that died (p= 0.71).

Discussion

Mortality in severe acute pancreatitis is clearly associated with infectious

complications and thus the administration of prophylactic antibiotics has been part of SAP management for decades. However, the controversy continues due to insufficient evidence.[3,4]

The antibiotics used in SAP prophylaxis must have two conditions: cover the most common bacteria involved in the infected necrosis and local complications of patients with SAP, and adequately penetrate the pancreatic tissue. The most commonly involved germs are gram-negative and anaerobic bacteria, such as Escherichia coli, Klebsiella pneumoniae, Proteus and Bacteroides.[2,3]

A study published in 2018 used ciprofloxacin associated with metronidazole as antibiotic prophylaxis in acute pancreatitis and reported that there was no significant clinical improvement compared to the group that did not use antibiotic prophylaxis.[10]

Recent studies have reported that the use of antibiotic prophylaxis in SAP may be associated with the development of invasive pancreatic candidiasis; in addition, they did not demonstrate any reduction in related complications.[11]

Other studies have reported not only that the use of antibiotic prophylaxis has no significant clinical benefit, but also that it is associated with an increased intrahospital infection risk; therefore, the use of antibiotic treatment must be reserved only for patients with local infection or sepsis.[12,13] These numbers are consistent with our study, where we reported that the group that received antibiotic prophylaxis had more local complications than the group that did not use prophylaxis (p=0.01).

There is only one RCT that has shown the usefulness of prophylactic antibiotics with carbapenems in patients with SAP (5). Among the controversies surrounding the use of prophylactic antibiotics in SAP are the economic cost and the prolonged exposure effect to a certain antibiotic therapy, which can put pressure on the ecosystem and increase bacteria resistant to these antibiotics. We do not know if it is cause or effect, or only coincidence, but we have noted and reported an increase in the multidrug-resistant bacteria number in recent years in the cultures of pancreatic infections in patients with SAP.[14]

Conclusion

The use of prophylactic antibiotics in SAP does not reduce the local and/or systemic infectious complications, need for a bed in the ICU or mortality. More studies on this aspect must be done to avoid crucial use of antibiotics.

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Conflict of Interest- None declared

References

1. Bansal SS, Hodson J, Sutcliffe RS, Marudanayagam R, Muiesan P, Mirza DF, et al. Performance of the revised Atlanta and determinant-based classifications for severity in acute pancreatitis. Br J Surg. 2016;103(4):427-33.
2. Bai Y, Gao J, Zou DW, Li ZS. Prophylactic antibiotics cannot reduce infected pancreatic necrosis and mortality in acute necrotizing pancreatitis: evidence from a meta-analysis of randomized controlled trials. Am J Gastroenterol. 2008;103(1):104-10.
3. Jiang K, Huang W, Yang XN, Xia Q. Present and future of prophylactic antibiotics for severe acute pancreatitis. World J Gastroenterol. 2012;18(3):279-84.
4. Rinninella E, Annetta MG, Serricchio ML, Lago AA, Miggiano GA, Mele MC. Nutritional support in acute pancreatitis: from physiopathology to practice. An evidence-based approach. Eur Rev Med Pharmacol Sci. 2017;21(2):421-32.
5. Beger HG, Gansauge F, Poch B, Schwarz M. The use of antibiotics for acute pancreatitis: is there a role?. Curr Infect Dis Rep. 2009;11(2):101-7.
6. Kylanpaa L, Rakonczay Z, Reilly DA. The clinical course of acute pancreatitis and the inflammatory mediators that drive it. Int J Inflam. 2012;360685.
7. Sharma VK, Howden CW. Prophylactic antibiotic administration reduces sepsis and mortality in acute necrotizing pancreatitis: a meta-analysis. Pancreas. 2001;22(1):28-31.
8. Villatoro E, Mulla M, Larvin M. Antibiotic therapy for prophylaxis against infection of pancreatic necrosis in acute pancreatitis. Cochrane Database Syst Rev. 2010;2010(5):2941.
9. Ukai T, Shikata S, Inoue M, Noguchi Y, Igarashi H, Isaji S, et al. Early prophylactic antibiotics administration for acute necrotizing pancreatitis: a meta-analysis of randomized controlled trials. J Hepatobiliary Pancreat Sci. 2015;22(4):316-21.
10. Mandal AK, Chaudhary S, Shrestha B, Paudel MS, Poudyal NS, Paudel BN, et al. Efficacy of Prophylactic use of Ciprofloxacin and Metronidazole in Mild and Moderately Severe Acute Pancreatitis. JNMA J Nepal Med Assoc. 2017;56(206):207-10.
11. Horibe M, Sanui M, Sasaki M, Honda H, Ogura Y, Namiki S, et al. Impact of Antimicrobial Prophylaxis for Severe Acute Pancreatitis on the Development of Invasive Candidiasis: A Large Retrospective Multicenter Cohort Study. Pancreas. 2019;48(4):537-43.
12. Nakaharai K, Morita K, Jo T, Matsui H, Fushimi K, Yasunaga H. Early prophylactic antibiotics for severe acute pancreatitis: A population-based cohort study using a nationwide database in Japan. J Infect Chemother. 2018;24(9):753-8.
13. Mourad MM, Evans R, Kalidindi V, Navaratnam R, Dvorkin L, Bramhall SR. Prophylactic antibiotics in acute pancreatitis: endless debate. Ann R Coll Surg Engl. 2017;99(2):107-12.
14. Losada HM, Curitol SS, Andres TT, Portillo NL. Comparison of use and non-use of prophylactic antibiotics for severe acute pancreatitis. Int Surg J 2021;8:2281-5.