

## Original Research Article

# Comparative study between omega 3 fatty acid infusion versus octreotide in management of acute pancreatitis

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### ABSTRACT

**Background:** Acute pancreatitis is one of the commonest diseases. While some use octreotide infusion, some rely only on fluid therapy and symptomatic treatment. Ongoing research has commented about omega ( $\omega$ ) 3 fatty acid (FA) infusions being the future of acute pancreatitis treatment as it is cheap and has lesser side effects.

**Methods:** This prospective comparative study was done in patients with acute pancreatitis. Patients were divided into two groups, with group A receiving  $\omega$ -3 FA single-dose infusion of 60 ml/hour over 4-5 hours and the other group B were subjected to injection of octreotide 100 mcg IV 8th hourly for 5 days with IV fluids. The groups were compared based on improvement in biochemical markers, BISAP score and hospital stay.

**Results:** 132 patients were divided into 2 groups, on day 3 serum amylase levels in the  $\omega$ -3 FA group were  $268.54 \pm 65.84$ , and the octreotide group was  $299.18 \pm 94.31$  (p value=0.032). Day 3 serum lipase levels in the  $\omega$ -3 FA group were  $137.07 \pm 62.19$ , and the octreotide group was  $172.07 \pm 72.46$  (p value=0.002). Day 3 BISAP score in the  $\omega$ -3 FA group was  $1.21 \pm 0.41$ , and the octreotide group was  $1.39 \pm 0.49$  (p value=0.023). The duration of hospital stay in the  $\omega$ -3 FA group was  $8.03 \pm 1.09$  days and in the octreotide group was  $11.83 \pm 1.04$  days (p<0.0001).

**Conclusions:** Patients receiving  $\omega$ -3 FA reported lower amylase-lipase levels along with a lower BISAP score. Hence looking for a cheaper and safer alternative,  $\omega$ -3 FA infusion could reduce the problem on the patient and hospitalization concomitant expenses.

**Keywords:** Pancreatitis, Octreotide, Omega 3 FA

### INTRODUCTION

Acute pancreatitis (AP) is becoming one of the common diseases affecting the general population. It is known as “an inflammatory process of pancreas with possible peripancreatic tissue involvement and multi-organ dysfunction syndrome with increasing mortality rate”. Around 20% of cases have the potential to become severe. Pancreatic necrosis, pancreatic necrosis haemorrhage and pseudocyst are among them. This disease has fairly increased recently, leading to increased mortality and morbidity because of its clinical and weakening symptoms.<sup>1</sup> An increase in the frequency of AP may be attributed to various reasons, including multiple risk

factors that consolidated from damage to full-blown symptoms of AP in a matter of years.<sup>2</sup> The pathophysiology behind AP is still unclear. However, studies have shown the activation of pancreatic enzymes within the acinar cells. In addition, there is autodigestion of the pancreas because of the co-localization of zymogen granules and lysosomes. As the acinar cell gets injured, it releases pro-inflammatory cytokines including tumor necrosis factor-alpha (TNF-a), interleukins IL-1, 2, and 6 and anti-inflammatory mediators receptor antagonists.<sup>3</sup>

The investigation of different therapeutic strategies has been discovered to be beneficial in treating symptoms and slowing the course of illness. However, these treatment

methods don't offer permanent treatment. They may stop the pancreas from deteriorating further and enable the body to recover from systemic sickness because of pancreatic inflammation.<sup>4</sup> Newer approaches, such as omega-3-fatty acids ( $\omega$ -3 FA) and octreotide, are yielding encouraging outcomes in research. Accumulating evidence suggests that omega 3 fatty acids can change cytokine production, and initiated inflammatory responses. This should reduce the number of infectious complications and decrease hospital stays. Some patients get octreotide infusions, while others depend only on fluid therapy and symptomatic treatment. According to current studies, infusion of  $\omega$ -3 FA represents a promising alternative to AP therapy since it is inexpensive and has fewer adverse effects.<sup>5</sup>

With the advancement of technology, AP has become a treatable entity. There are many studies on  $\omega$ -3 FA and octreotide infusion. However, the treatment remains debatable over decades, with no common consensus on the treatment guidelines. There is a paucity of literature on whether octreotide or  $\omega$ -3 infusions have a superior response. Also, studies focusing on the safety and efficacy of  $\omega$ -3 FA and octreotide infusions in AP are lacking. Hence, we compare the effectiveness of  $\omega$ -3 FA infusion over octreotide in managing AP and their outcome.

## METHODS

This prospective comparative study was conducted in the Department of General Surgery, SRM Medical College Hospital and Research Centre in patients diagnosed and admitted with the clinical diagnosis of AP. The sample size for the present study was calculated by fixing the probability of type I error at 5% and that of type II error at 5%.

Hence the power of the study was maintained at 95%. The data required to estimate the sample size was imported from literature. The following formula was used for sample size calculation where pooled standard deviation=SDp, and difference of the mean= $\mu_1 - \mu_2$ . The sample size of 66 in each group.

$$N = 2 (Z\alpha + Z\beta)^2 (SDp)^2 \div (\mu_1 - \mu_2)^2$$

### Inclusion criteria

Patients between ages -18 to 70 years of either sex with Atlanta guidelines criteria-any 2 out of 3, serum amylase >3 times normal and lipase >3 times the normal were included in the study.

### Exclusion criteria

Patients with chronic pancreatitis, sensitive to  $\omega$ -3 FA, immunodeficiency -HIV reactive, primary hypertriglyceridemia, and other pre-existing comorbid conditions like cardiac failure, liver failure, renal failure or

lung pathology and received TPN in the last 2 weeks were excluded.

The study was begun after receiving approval from the institutional human ethics committee. The entry to the study was made after informed written consent was obtained from all the participants in the study group. After taking informed consent, a pre-structured performa was used to record the relevant information from individual cases selected for the study. A detailed clinical history and examination were conducted. Following an initial screening, each patient with AP confirmed by blood tests such as serum amylase and serum lipase and ultrasonography/computed tomography (USG/CT) were randomly assigned to two groups: group A – 66 patient are subjected to injection  $\omega$ -3 FA single-dose infusion 60 ml/hour over 4-5 hours (250 ml infusion) IV fluids, pain treatment with paracetamol or tramadol, H2 receptor antagonist, and proton pump inhibitor on admission; and group B - 66 patients are subjected to injection octreotide 100 mcg IV 8<sup>th</sup> hourly for 5 days with IV fluids, paracetamol/tramadol, as well as H2 receptor antagonists and proton pump inhibitors, provide pain relief. Antibiotics were not provided to either group until haematological confirmed infection. Biochemical values serum amylase and serum lipase) were used to make the comparison, BISAP score, hospital stay. The continuous variables will be analyzed and presented as mean SD. The significance of continuous scale data between two groups shall be determined using the student t-test. The Chi-square will be used to evaluate the significance of the categorical data analyzed, a p value of less than 0.05 would be taken as significant. Statistical package for the social sciences (SPSS) statistical package and Microsoft excel were used to compute the data.

## RESULTS

In this study, 132 patients with proven AP were included. Patients were divided into 2 groups, group A, which was treated with  $\omega$ -3 FA infusion and group B was treated with octreotide infusion. The mean age of group A patients was 38.96 years, and in group B, patients were 39.62 years. There is no statistically significant difference in age and gender between groups. All patients in both groups presented with abdominal pain on admission. in the  $\omega$ -2 FA group, 55 patients (83.3%) had vomiting, in the octreotide group, 57 patients (86.4%) had vomiting. In the  $\omega$ -2 FA group, 11 patients (16.7%) had smoking habits, in the octreotide group, 6 patients (9.1%) had a smoking habit. in the  $\omega$ -2 FA group, 20 patients (30.3%) were alcoholics, in the octreotide group, 24 patients (36.4%) were alcoholic. 7 patients (10.6%) in the  $\omega$ -3 FA group had gall stone induced pancreatitis, and 8 patients (12.1%) in the octreotide group had gall stone induced pancreatitis. There is a statistically insignificant difference in diagnosis between groups. There is a statistically insignificant difference in the total count, lactate dehydrogenase (LDH), serum calcium, procalcitonin and serum creatinine between groups. On admission assessment, serum

amylase, serum lipase and BISAP score showed no statistically significant difference between groups. On day 3 assessment, there is a statistically significant difference in serum amylase, serum lipase and BISAP score between

groups. The duration of hospital stay in the ω-3 FA group was 8.03±1.09 days and in the octreotide group was 11.83±1.04 days. There is a statistically significant difference in duration of stay between groups.

**Table 1: Distribution of patients' characteristics between groups.**

Patients' characteristics	Group				P value
	Omega-3 FA N (%)		Octreotide N (%)		
<b>Age group (in years)</b>					
<20	6	9.1	7	10.6	0.243
21-30	15	22.7	15	22.7	
31-40	15	22.7	16	24.2	
41-50	12	18.2	10	15.2	
51-60	16	24.2	9	13.6	
>61	2	3.0	9	13.6	
<b>Gender</b>					
Female	3	4.5	4	6.1	0.689
Male	63	95.5	62	93.9	
<b>Smoking</b>					
No	55	83.3	60	90.9	0.194
Yes	11	16.7	6	9.1	
<b>Alcohol</b>					
No	46	69.7	42	63.6	0.460
Yes	20	30.3	24	36.4	
<b>Diagnosis</b>					
AP	52	78.8	54	81.8	0.894
Gall stone pancreatitis	7	10.6	8	12.1	
Idiopathic pancreatitis	4	6.1	2	3.0	
Post ERCP pancreatitis	2	3.0	1	1.5	
Traumatic pancreatitis	1	1.5	1	1.5	

**Table 2: Comparison of lab parameters between groups on admission.**

Lab parameters on admission	Group				P value
	Omega 3 FA		Octreotide		
	Mean	Standard deviation	Mean	Standard deviation	
<b>Total count</b>	12892.65	3089.75	12930.06	3384.86	0.947
<b>LDH</b>	289.12	103.57	272.18	105.32	0.353
<b>Serum calcium</b>	8.26	1.28	8.25	1.26	0.951
<b>Procalcitonin</b>	1.49	0.34	1.47	0.35	0.746
<b>Serum creatinine</b>	0.82	0.15	0.83	0.21	0.715

**Table 3: Comparison of outcome variables between groups.**

Outcome variables	Group				P value
	Omega 3 FA		Octreotide		
	Mean	Standard deviation	Mean	Standard deviation	
<b>Serum amylase</b>					
On admission	706.27	121.75	680.77	156.91	0.299
Day 3	268.55	65.84	299.18	94.31	0.032
<b>Serum lipase</b>					
On admission	319.02	82.04	306.53	70.57	0.350
Day 3	137.08	62.19	172.08	62.19	0.002
<b>BISAP score</b>					
On admission	2.21	0.71	2.14	0.68	0.532

Continued.

Outcome variables	Group				P value
	Omega 3 FA		Octreotide		
	Mean	Standard deviation	Mean	Standard deviation	
Day 3	1.21	0.41	1.39	0.49	0.023
Duration of hospital stay	8.03	1.10	11.83	1.05	<0.0001

## DISCUSSION

AP is a potentially fatal illness characterised by a sudden inflammation of the pancreas. AP is the leading cause of GI-related hospitalizations worldwide. While the prevalence of AP has been predicted to rise, data on the prevalence of AP in India is unavailable due to clinical restrictions such as improper diagnosis besides under-reporting.<sup>6</sup> During the initial phases of AP, a pro-inflammatory retort occurs, characterised by large cytokine releases resulting in SIRS and then organ failure that is accounted for a significant rate of mortality.<sup>7</sup> Henceforth, clinical practices intended to manage AP involve the strategies related to suppressing hyperinflammatory responses and thereby collectively re-establish tissue and organ homeostasis. Among the major intervention AP treatment substances,  $\omega$ -3 FA and octreotide were reported with positive influences in modulating the cytokine storm.<sup>8</sup> Thus, the study compared the effects of  $\omega$ -3 FA and octreotide infusions on AP patients.

In a previously conducted analysis, Choudari et al have also designated smoking and alcohol consumption as threat aspects for both incidence and recurrence of AP.<sup>9</sup> The treatment policy for AP relies upon the etiological conclusion of whether the development of AP is gall bladder induced or not. These are usually confirmed through a blood test or an ultra-sonographic method.<sup>10</sup> The current study revealed gall stone-induced pancreatitis in both groups at a significant rate yet with no statistical significance. Higher levels of LDH are regarded as an indication of persistent organ failure in the case of AP. As LDH secretion is associated with conditions involving lower oxygen supply, elevated levels of the enzyme signal necrosis of pancreatic cells and infection and eventually mortality.<sup>11</sup>

The current study revealed the levels of LDH in patients of groups A and B to be statistically insignificant ( $p=0.353$ ). However, the levels were higher than normal (245 U/L). In the earlier study conducted to evaluate the relationship of elevated LDH levels to organ failure in AP, it was found that serum LDH levels in patients at the time of hospitalization are autonomously connected with organ failure in AP.<sup>11</sup> Procalcitonin is an early concomitant marker with a systemic inflammatory response that would eventually lead to organ failure.<sup>12</sup> Measurement of procalcitonin levels at the time of admission in both groups was revealed to be higher than the normal range (0.05 ng/ml) yet was statistically insignificant among both the groups ( $p=0.746$ ). Analyzing the levels of total calcium in

relation to the severity of AP has been reported earlier by Pokharelet al.<sup>13</sup> They estimated the calcium value for mild AP to be 8.22. The total serum calcium values in the patients of AP at the onset of hospitalization were reported as 8.26 and 8.25 in both groups ( $p=0.951$ ; statistically insignificant). Serum creatinine is also regarded as a reliable biomarker for diagnosing AP as higher biochemical levels indicate pancreatic necrosis. While the AP patients displayed elevated levels of serum creatinine at the time of admission ( $>1.3$  mg/dl) in both groups that were statistically insignificant ( $p=0.718$ ), it is hence definitive of the fact that pancreatic necrosis is being instigated within the system. Enzymes derivative of pancreatic acinar cells such as amylase and lipase are utilized as markers for diagnosing AP.<sup>12</sup> Amylase is the most common enzyme being tested for the confirmation of AP. While amylase levels spike within 12 hours of AP incidence, returning to normal within 5 days, lipase levels stay at their peak for a prolonged period of 8-14 days.<sup>12</sup> BISAP at the time of hospitalization in both groups were statistically insignificant ( $p=0.532$ ), which decreased to  $1.21\pm 0.41$  and  $1.39\pm 0.49$  from  $2.21\pm 0.71$  and  $2.14\pm 0.68$  in groups  $\omega$ -3 FA and octreotide respectively. BISAP score eventually reduced more in groups treated with  $\omega$ -3 FA, differing significantly from octreotide. Treatment with  $\omega$ -3 FA also reduced in-hospital days to 8.03 days than those who received octreotide for treatment, whose hospitalization days extended to 11.83 days. Patients receiving  $\omega$ -3 FA tend to report lower amylase-lipase levels along with a lower BISAP score. It is likely that  $\omega$ -3 FA averted the advancement of the pancreas's organ dysfunction and re-treated it, evident from the reduced BISAP scores. Many researchers reported the application of  $\omega$ -3 FA in the management of AP in terms of reducing the progression of the disease along with cessation of organ failure by minimizing the necrosis rate had been reported by many researchers.<sup>6,8,14</sup> The management of AP using octreotide was known to produce adverse side effects and is said to be an expensive drug. Hence, to seek a better economic and effective management strategy for AP, studies involving the utilization of  $\omega$ -3 FA were carried out.  $\omega$ -3 FA infusion could reduce the inclusive problem on the patient and hospitalization concomitant expenses.

### Limitations

The cases in the study group had heterogeneous morphology with varying clinical presentations and underlying etiology. Hence one need to be cautious while drawing conclusions from this group to particular individuals. For further study in the future, a potential avenue would be to recruit specific AP due to each cause

at the time of diagnosis and follow these more homogenous groups over the course of the disease.

## CONCLUSION

The present study shows a great benefit of  $\omega$ -3 infusions in AP over octreotide infusion. Serum amylase and lipase were significant markers of AP with high values in both groups at admission. These values after treatment can be used as a prognostic marker and showed a significant reduction on day 3 in  $\omega$ -3 FA group infusions compared to the octreotide infusion. A statistically significant decrease in BISAP score and duration of hospital stay was also noticed in the  $\omega$ -3 FA group on day 3 compared to octreotide. In the future,  $\omega$ -3 FA infusion can be used in AP because cheap and readily accessible with minimal adverse effects noted that could reduce morbidity and mortality in AP with a minimal hospital stay, which in turn reduces the overall hospital expenditure.

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