

## Original research article

## A double blind comparative assessment of omega 3 fatty acid infusion and octreotide infusion in acute pancreatitis

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### Abstract

**Background:** Over decades the treatment of acute pancreatitis remains debatable with no common consensus on treatment guidelines, with some workers using octreotide infusion and some workers only relying on fluid therapy and symptomatic management. This is the first of its kind double blinded comparative trial between omega 3 fatty acid infusion versus octreotide infusion and its response in cases of acute pancreatitis.

**Aim:** A double blinded comparative trial between omega 3 fatty acid infusion versus octreotide infusion and its response in cases of acute pancreatitis.

**Material and methods:** The was a double blinded randomised control trial study conducted in the Department of General Surgery, Vardhman Mahavir Medical College and safdarjung Hospital, New Delhi, India for one year. Omega 3 fatty acids infusion 60ml/hr over 4-5 hours (250 ml infusion) single dose on admission with 150 ml/hr IV fluid, pain relief with paracetamol/tramadol and H2 receptor antagonist and proton pump inhibitors. (60 patient Injection octreotide 100 mcg IV 8th hourly for 5 days with 150 ml/hr IV fluid (60 evaluation done, on admission and on day 5). Compared on the basis of biochemical values (serum lipase), clinical scoring system in pancreatitis (BISAP score), organ dysfunction score (Marshal scoring).

**Results:** The two groups were comparable in terms of age (omega 3 fatty acid mean age group, 38.6 years and octreotide mean age group 42.2 years). Sex wise 51male patients and 9 female patient in omega 3 fatty acid group and 53 male and 7 female patients in octreotide group. 7 patients in omega 3 fatty acid group had gall stone induced pancreatitis and 7 cases in octreotide group had gall stone induced pancreatitis.44 patients were alcoholic in Omega 3 fatty acid group and 47 patients were alcoholic in octreotide group. The two groups were comparable in terms of demographics, etiology, On admission mean lipase levels in Omega 3 fatty acid group was mean 281.34 and octreotide group was mean 321.11 (p=0.79, not significant) and day 5 lipase levels in omega 3 fatty acid group was mean 108.11 and octreotide group was 151.32 (p=0.05, highly significant). The two groups were comparable in terms of demographics, etiology, On admission mean Amylase levels in Omega 3 fatty acid group was mean 712.12 and octreotide group was mean 651.87 (p=0.66, not significant) and day 5 amylase levels in omega 3 fatty acid group was mean 229.66 and octreotide group was 367.85 (p=0.04, highly significant) . On admission mean BISAP score in omega 3 fatty acid group was 2.17 and octreotide 2.11 (p=0.67, not significant), day 5 mean BISAP score in Omega 3 fatty acid group was 1.19 and octreotide was 1.52 (p=0.0001, highly significant) . Mean Marshal score in omega 3 fatty acid group on admission was 2.71 and octreotide 2.59

( $p=0.645$ , non significant). Day 5 mean Marshal score in omega 3 fatty acid group was 1.11 and octreotide group 2.66 ( $p=0.0001$ , highly significant) (Table 7). Mean hospital stay in omega 3 fatty acid group was 3.39 days and octreotide was 5.51 days .

**Conclusion:** Omega 3 fatty acid infusion is the future in cases of acute pancreatitis which is cheap and easily available with no side effects and reduces the morbidity and mortality in acute pancreatitis with reduced hospital stay in turn resulting in overall reduced medical expenditure.

**Keywords:** Acute pancreatitis, Celepid, Octreotide, Omega 3 fatty acid infusion,  $\omega$ -3 FA

## Introduction

Worldwide, over the last decade, yearly incidence of pancreatitis and related hospitalizations has increased. Acute pancreatitis is the most common cause of GI related hospitalizations in the world, with more than 274,000 hospitalizations in 2012. <sup>1</sup> The yearly incidence of AP in the United States is approximately 70-80 new cases per 100,000 populations and has increased over the last decade.<sup>2</sup> True incidence and prevalence of pancreatitis in India is unknown since, it being difficult to establish an accurate diagnosis, a number of cases are misdiagnosed or are not recorded or reported. Nevertheless, in 2004, a high prevalence of chronic pancreatitis in Southern India (114-200/100,000 population) was registered in a study of chronic pancreatitis in the Asia-Pacific region.<sup>3</sup> 20% of acute pancreatitis evolve into severe acute pancreatitis at a given point of time in the world resulting in an average mortality of 20%.<sup>4</sup> Aggravated acinar cell injury causing heightened immune response, resulting in pancreatic necrosis and generation of free radicals causing; SIRS and distant organ damage resulting in MODS.<sup>5</sup> Hence, attempts to enhance immune function, suppress the hyper inflammatory responses and re-establish tissue and organ homeostasis in AP patients have been made in clinical practice.<sup>6</sup> Accumulating evidence has suggested that omega-3 fatty acids ( $\omega$ -3 FA) can alter cytokine production, modulate inflammatory and immunological response and thus be expected to lower the rates of infectious complications, shorten the hospital stay in the intensive care unit (ICU) or on regular medical wards as well.<sup>7,8</sup> Anti-inflammatory and immune-modulatory effects of  $\omega$ -3 FA may provide an important therapeutic option for the patients with AP. Aim of this double blinded randomised controlled trial first of its kind it to prove that omega 3 fatty acid infusion in acute pancreatitis have magical response which is highly significant as compared to other treatment modalities like octreotide infusion. Omega 3 fatty acid infusion is the future in cases of acute pancreatitis and can reduce overall mortality and morbidity. This double blinded comparative trial between omega 3 fatty acid infusion versus octreotide infusion and its response in cases of acute pancreatitis.

## Material and methods

The was a double blinded randomised control trial study conducted in the Department of General Surgery, Vardhman Mahavir Medical College and safdarjung Hospital, New Delhi, India for one year. after taking the approval of the protocol review committee and institutional ethics committee.

### Methodology

All 120 proven cases of acute pancreatitis were included in this study.

### Inclusion criteria

patients age of 18 to 65 years, either sex satisfying Atlanta guidelines criteria any 2 out of 3 with systolic BP <90 mmHg, serum calcium <7.5 mg/dl, Usg/CT showing acute pancreatitis, serum amylase and lipase >3 times the normal, fitting to SIRS criteria (systemic

inflammatory response syndrome) i.e., temp>100.4°F, heart rate >90 bpm, respiratory rate >20 cpm, WBC >12000 or <4000 per mm<sup>3</sup>.

### Exclusion criteria

patients with history of immunodeficiency's, retro positive cases with primary hypertriglyceridemia, severe cardiac disease like acute myocardial infarction, congestive cardiac failure, with serum creatinine->2.0mg/dl with unavailable dialysis facility or received TPN in last 2weeks were excluded from the study.

### Study procedure

Initial screening with blood inv (S. lipase and amylase), USG. Diagnosed with acute pancreatitis. Divided into two groups omega 3 fatty acids or octreotide by computer generated double envelop method injection. Omega 3 fatty acids infusion 60ml/hr over 4-5 hours (250 ml infusion) single dose on admission with 150 ml/hr IV fluid, pain relief with paracetamol/tramadol and H2 receptor antagonist and proton pump inhibitors. (60 patient Injection octreotide 100 mcg IV 8th hourly for 5 days with 150 ml/hr IV fluid (60 evaluation done, on admission and on day 5). Compared on the basis of biochemical values (serum lipase), clinical scoring system in pancreatitis (BISAP score), organ dysfunction score (Marshal scoring).

### Results

The two groups were comparable in terms of age (omega 3 fatty acid mean age group, 38.6 years and octreotide mean age group 42.2 years) (p=0.15, not significant) (table 1).

**Table 1: Age wise distribution of study patients**

Age	OMEGA 3 FA	Octreotide
Mean age	38.6	42.2

Sex wise 51male patients and 9 female patient in omega 3 fatty acid group and 53 male and 7 female patients in octreotide group (p=0.54, not significant) (table 2)

**Table 2: Gender wise distribution of study patients**

Gender	OMEGA 3 FA=60	Octreotide=60
Male	51	53
Female	9	7

7 patients in omega 3 fatty acid group had gall stone induced pancreatitis and 7 cases in octreotide group had gall stone induced pancreatitis.44 patients were alcoholic in Omega 3 fatty acid group and 47 patients were alcoholic in octreotide group (table 3).

**Table 3: Distribution of diagnosis among patients between 2 study groups**

Parameter	OMEGA 3 FA=60	Octreotide=60
Acute Pancreatitis	44	47
D. Pancreatitis	2	2
Gall Stone Pancreatitis	7	7
Idiopathic Pancreatitis	4	2
Post ERCP Pancreatitis	2	1
Traumatic Pancreatitis	1	1

The two groups were comparable in terms of demographics, etiology, On admission mean lipase levels in Omega 3 fatty acid group was mean 281.34 and octreotide group was mean 321.11 ( $p=0.79$ , not significant) and day 5 lipase levels in omega 3 fatty acid group was mean 108.11 and octreotide group was 151.32 ( $p=0.05$ , highly significant) (Table 4 and table 6 ).

The two groups were comparable in terms of demographics, etiology, On admission mean Amylase levels in Omega 3 fatty acid group was mean 712.12 and octreotide group was mean 651.87 ( $p=0.66$ , not significant) and day 5 amylase levels in omega 3 fatty acid group was mean 229.66 and octreotide group was 367.85 ( $p=0.04$ , highly significant) (Table 4 and table 6 ).

**Table 4: Comparison of mean values of serum amylase and serum lipase between 2 study groups one day.**

Parameters	Groups n=60	Mean	SD	Median	P value
Amylase	OMEGA 3 FA	712.12	638.17	444.00	0.66
	Octreotide	651.87	549.15	399.00	
Lipase	OMEGA 3 FA	281.34	182.55	213.00	0.79
	Octreotide	321.11	244.74	212.50	

On admission mean BISAP score in omega 3 fatty acid group was 2.17 and octreotide 2.11 ( $p=0.67$ , not significant), day 5 mean BISAP score in Omega 3 fatty acid group was 1.19 and octreotide was 1.52 ( $p=0.0001$ , highly significant) (Table 5 and table 6).

**Table 5: Comparison of mean values of BISAP score between 2 study groups on Day 1**

BISAP score					
Groups, n=60	Mean	SD	Median	P value	
Omega 3 FA	2.17	0.86	2.00	0.67	
Octreotide	2.11	0.90	2.00		

**Table 6: Comparison of mean values and p value of serum amylase, serum lipase and BISAP score between 2 study groups on day 5.**

Parameters	Groups, n=60	Mean	SD	Median	P value
Amylase	Omega 3 FA	229.66	148.45	190.00	0.03*
	Octreotide	369.85	345.39	233.50	
Lipase	Omega 3 FA	108.11	57.21	98.50	0.005*
	Octreotide	151.32	73.21	148.00	
BISAP	Omega 3 FA	1.19	0.47	1.50	0.006*
	Octreotide	1.52	0.64	1.50	

\* Statistically Significant

Mean Marshal score in omega 3 fatty acid group on admission was 2.71 and octreotide 2.59 ( $p=0.645$ , non significant). Day 5 mean Marshal score in omega 3 fatty acid group was 1.11 and octreotide group 2.66 ( $p=0.0001$ , highly significant) (Table 7). Mean hospital stay in omega 3 fatty acid group was 3.39 days and octreotide was 5.51days ( $p=0.0001$ , highly significant)

**Table 7: Comparison of mean values of modified Marshal scoring between 2 study groups on day 1 and day 5.**

	Groups, n=60	Mean	SD	Median	P value
Marshal score	Omega 3 FA	2.71	0.58	3.50	
	Octreotide	2.59	0.59	3.50	0.645

Marshal score	Omega 3 FA	1.11	0.53	1.00	<0.001*
day 5	Octreotide	2.46	0.54	3.50	

\* Statistically Significant

### Discussion

As per statistical analysis the use of omega 3 fatty acid turned out to be highly significant in terms of cases of acute pancreatitis where a dramatic reduction in lipase levels was noted with a single 250ml infusion of omega 3 Fatty Acid and reduction in the overall mortality and morbidity by reduced BISAP scores. Omega 3 Fatty Acid stopped the progression of organ dysfunction and mostly reversed it which was proved by reduction in the Marshal scores. Overall omega 3 Fatty Acid infusion reduces the early conversion of cases of acute pancreatitis to severe acute pancreatitis and halts organ dysfunction, allows early enteral nutrition thus reducing the incidence of conversion of sterile necrosis into infected one.

Fish oil derived omega-3 polyunsaturated fatty acids ( $\omega$ -3 PUFA) when administered along with adequate nutritional support has been reported to have a beneficial effect on the immune response; enhancing immunity, reducing inflammatory response, altering cytokine production and hence improving outcomes in AP.

Accumulating evidence has suggested that omega-3 fatty acids ( $\omega$ -3 FA) can alter cytokine production, modulate inflammatory and immunological response and thus be expected to lower the rates of infectious complications, shorten the hospital stay in the intensive care unit (ICU) or on regular medical wards as well. 7-9 Anti-inflammatory and Immunomodulatory effects of  $\omega$ -3 FA may provide an important therapeutic option for the patients with AP.

Our trial proves that in adverant use of antibiotics in acute pancreatitis is not justified (as proved by Dutch pancreatitis study group 2011). Omega 3 fatty Acid overall reduces the hospital stay, ICU stay, reverses SIRS and MODS thus reducing the no of DALY's. On 6 and 12 weekly follow up patients in omega 3 fatty acid group had no complaints or relapses in terms of symptomatology.

The treatment of acute pancreatitis at present is largely supportive. However, a therapeutic window for intervention with modulators of inflammation exists between the onset of clinical symptoms and peak proinflammatory cytokine expression. Polyunsaturated fatty acids (omega-3) are the precursors of the lipid mediators and play an important role in regulation of inflammation.  $\omega$ -3 FA suppresses the inflammation and improves the course of infection by reducing proinflammatory eicosanoid and cytokine production. The ability of  $\omega$ -3 FA to regulate these immune processes has been well described in many experimental and clinical studies

### Conclusion

Although several meta-analyses have been conducted recently in an effort to clarify whether the administration of  $\omega$ -3 FA improves outcomes in patients with AP, definitive conclusions have been lacking. Therefore, perspectives on the use of  $\omega$ -3 FA treatment in critically ill patients remained conflicting. This is the first of its kind comparative analysis between octreotide which proved ineffective by multiple trials in acute pancreatitis but still remains the go to drug for many workers versus omega 3 fatty acids infusion which showed promising results in our trial. Octreotide has its own side effects and is a costly drug which needs to be given 3 times a day for 5 days. A single infusion of omega 3 fatty acid infusion reduces the overall burden on the patient and hospitalisation associated costs. As omega 3 fatty acid infusion had no side effects noted it can be safely tagged as the go to drug therapy in acute pancreatitis hypersensitivity ruled out per se.  $\omega$ -3 PUFA improves the early clinical outcomes of the patients of moderate to severe AP and due consideration should be given to

making IV omega- 3 PUFA supplementation part of the standard management protocols for moderate to severe acute pancreatitis.

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