



Original Research Article

A Double Blinded Comparative Study between Omega 3 Fatty Acid Infusion Versus Octreotide in Acute Pancreatitis

Authors

Dr Narayanaswamy T¹, Dr Supreeth K^{2*}, Dr Riya Rai³

¹Professor, Kempegowda Institute of Medical Sciences and Research Centre, Bangalore

^{2,3}Post Graduate, Kempegowda Institute of Medical Sciences and Research Centre, Bangalore

*Corresponding Author

Dr Supreeth K

Department of General Surgery, Kempegowda Institute of Medical Sciences and Research Centre, Bangalore 560004, India

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

Aim is to study the efficacy of omega 3 fatty acid infusion and set a new treatment protocol in cases of acute pancreatitis with the use of omega 3 fatty acid infusion in all admitted cases of acute pancreatitis unless otherwise contraindicated.

Methods: *This is a study where a double blinded randomised control trial was undertaken in proven cases of acute pancreatitis and patients were given omega 3 fatty acid infusion and octreotide infusion and the observations were documented and followed upon. 50 cases were given omega 3 fatty acid infusion and other 50 were given octreotide infusion and the clinical response, symptomatic improvement was assessed and compared using BISAP and Marshal scoring systems and lipase levels.*

Results: *Omega 3 fatty acid infusion was found to be highly significant as compared to octreotide in cases of acute pancreatitis in terms of clinical improvement, reduced hospital stay, and SIRS.*

Conclusions: *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, Octreotide, Omega 3 fatty acid infusion, ω-3 FA.*

Introduction

Acute pancreatitis is a life-threatening illness which is characterized by sudden inflammation of the pancreas.¹ The yearly incidence in the United States has been reported to be 70-80 new cases per 100,000 population and has increased over the last decade.² However, the true incidence and

prevalence of pancreatitis in India is unknown as establishing an accurate diagnosis is difficult and are under reported.³

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. 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. The omega-3 fatty acids (ω -3 FA) can alter production of cytokine, modulate inflammatory and immunological response and thus be expected to lower the rates of infectious complications.⁴ A Cochrane review has mentioned among majority of the interventions, octreotide was associated with fewer serious adverse events and a lower proportion of people with organ failure.¹ A lot of research into different medical treatments for the treatment of acute pancreatitis are happening, however, it is not clear about the benefits each treatment has, or indeed if any medical treatment is beneficial apart from supportive treatment.¹

Methods

Study Design: Double Blinded Randomised Control Trial

Study Period: 12 Months from November 2018 to October 2019

Study Area: Department of General Surgery, Kempegowda Institute of Medical Sciences and Research Centre (KIMS), Bangalore

Study Subjects: All 100 Proven Cases of Acute Pancreatitis Admitted to the Department of General Surgery, KIMS, Bangalore

Inclusion Criteria

- Aged 18 to 70 years
- Either sex satisfying Atlanta guidelines criteria- Any 2 out of 3 with
- Systolic BP < 90mm Hg,
- Serum Calcium - <7.5mg/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- >90bpm, Respiratory rate >20cpm, WBC >12000 or <4000 per mm³

Exclusion Criteria

- Patients with history of immunodeficiencies,
- 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 & amylase), USG → Diagnosed with acute pancreatitis

Two groups → Omega 3 fatty acids or octreotide by computer generated double envelop method
Inj. Omega 3 fatty acids infusion 60ml/hr

Over 4-5hours (250ml infusion) single dose on admission with 150ml/hr IV fluid, pain relief with paracetamol/ Tramadol and H2 receptor antagonist and Proton pump inhibitors. [50 patients]

Inj. Octreotide 100mcg iv 8th hourly for 5 days with 150ml/hr IV fluid, pain relief with paracetamol/Tramadol and H2 receptor antagonist and Proton pump inhibitors [50 patients]

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 (Marshall scoring)

Statistical Analysis

All the data were entered into Microsoft excel. The results were expressed using descriptive statistics (means, standard deviations, medians, range, proportions or percentages). The means or medians within the groups were compared using paired t test or wilcoxon signed rank test and between the groups by independent t-test and Mann Whitney U test. P-value of <0.05 is considered statistically significant.

Results

The two groups were comparable in terms of age (Omega 3 fatty acid mean age group-39.7yrs and

octreotide mean age group 43.1yrs) (p value-0.15) not significant (Figure 1)
 Sex wise 43 male patients and 7 female patient in Omega 3 fatty acid group and 45 male and 5 female patients in octreotide group (p value- 0.54) not significant (Figure 2),
 6 patients in Omega 3 fatty acid group had gall stone induced pancreatitis and 6 cases in octreotide group had gall stone induced pancreatitis.35 patients were alcoholic in Omega 3 fatty acid group and 40 patients were alcoholic in octreotide group (Figure 3).
 The two groups were comparable in terms of demographics, etiology,
 On admission mean lipase levels in Omega 3 fatty acid group was mean 278.60 and octreotide group was mean 315.24 (p value-0.88) not significant and day 5 lipase levels in Omega 3 fatty acid

group was mean 105.24 and octreotide group was 149.06 (p value-0.06) highly significant (Table 2 Figure 4).
 On admission mean BISAP score in Omega 3 fatty acid group was 2.10 and octreotide 2.04 (p value-0.63) not significant and day 5 mean BISAP score in Omega 3 fatty acid group was1.20 and octreotide was 1.54(p value-0.0001) highly significant (Table 3 Figure 5).
 Mean MARSHALL score in Omega 3 fatty acid group on admission was 2.68 and octreotide 2.62 (p value-0.615) non significant. Day 5 mean MARSHALL score in Omega 3 fatty acid group was 1.14 and octreotide group 2.64 (p value0.0001) highly significant (Table 4 Figure 6).
 Mean hospital stay in Omega 3 fatty acid group was 3.32 days and octreotide was 5.40 days (p value- 0.0001) highly significant (Figure 7).

Table 1: Marshall Score Parameters and Calculations

Organ system	Score				
	0	1	2	3	4
Respiratory (PaO ₂ /FiO ₂)	>400	301-400	201-300	101-200	≤101
Renal*					
(serum creatinine, μmol/l)	≤134	134-169	170-310	311-439	>439
(serum creatinine, mg/dl)	<1.4	1.4-1.8	1.9-3.6	3.6-4.9	>4.9
Cardiovascular (systolic blood pressure, mm Hg)†	>90	<90, fluid responsive	<90, not fluid responsive	<90, pH<7.3	<90, pH<7.2
For non-ventilated patients, the FiO ₂ can be estimated from below:					
Supplemental oxygen (l/min)	FiO ₂ (%)				
Room air	21				
2	25				
4	30				
6-8	40				
9-10	50				

A score of 2 or more in any system defines the presence of organ failure.
 *A score for patients with pre-existing chronic renal failure depends on the extent of further deterioration of baseline renal function. No formal correction exists for a baseline serum creatinine ≥134 μmol/l or ≥1.4 mg/dl.
 †Off inotropic support.

Table 2: Comparison of mean values of Serum Amylase and Serum Lipase between 2 study groups on Day 1

Comparison of mean values of different parameters between 2 study groups on Day 1 using Mann Whitney Test						
Parameters	Groups	N	Mean	SD	Median	P-Value
Amylase	OMEGA 3 FA	50	709.14	631.03	440.00	0.59
	Octreotide	50	655.54	540.55	397.50	
Lipase	OMEGA 3 FA	50	278.60	178.44	211.50	0.88
	Octreotide	50	315.24	240.16	211.00	

Table 3: Comparison of mean values of BISAP score between 2 study groups on Day 1

BISAP	OMEGA 3 FA	50	2.10	0.86	2.00	0.63
	Octreotide	50	2.04	0.90	2.00	

Table 4: Comparison of mean values and P value of Serum Amylase, Serum Lipase and BISAP score between 2 study groups on Day 1 and Day 5

Comparison of mean values of different parameters between Day 1 & Day 5 in Octreotide group using Wilcoxon Signed Rank Test						
Parameters	Time	N	Mean	SD	Median	P-Value
Amylase	Day 1	50	655.54	540.55	397.50	<0.001*
	Day 5	50	375.02	342.35	232.50	
Lipase	Day 1	50	315.24	240.16	211.00	<0.001*
	Day 5	50	149.06	71.59	147.50	
BISAP	Day 1	50	2.04	0.90	2.00	<0.001*
	Day 5	50	1.54	0.68	1.00	

* - Statistically Significant

Table 5: Comparison of mean values of MODIFIED MARSHALL scoring between 2 study groups on Day 1 and Day 5

Comparison of mean Marshal Score between 2 study groups on Day 1 using Mann Whitney Test						
Paramet ers	Groups	N	Mean	SD	Median	P-Value
Marshal Score	OMEGA 3 FA	50	2.68	0.62	3.00	0.62
	Octreotide	50	2.62	0.57	3.00	

Comparison of mean Marshal Score between 2 study groups on Day 1 using Mann Whitney Test						
Parameters	Groups	N	Mean	SD	Median	P-Value
Marshal Score	OMEGA 3 FA	50	1.14	0.50	1.00	<0.001*
	Octreotide	50	2.46	0.56	3.00	

*** - Statistically Significant**

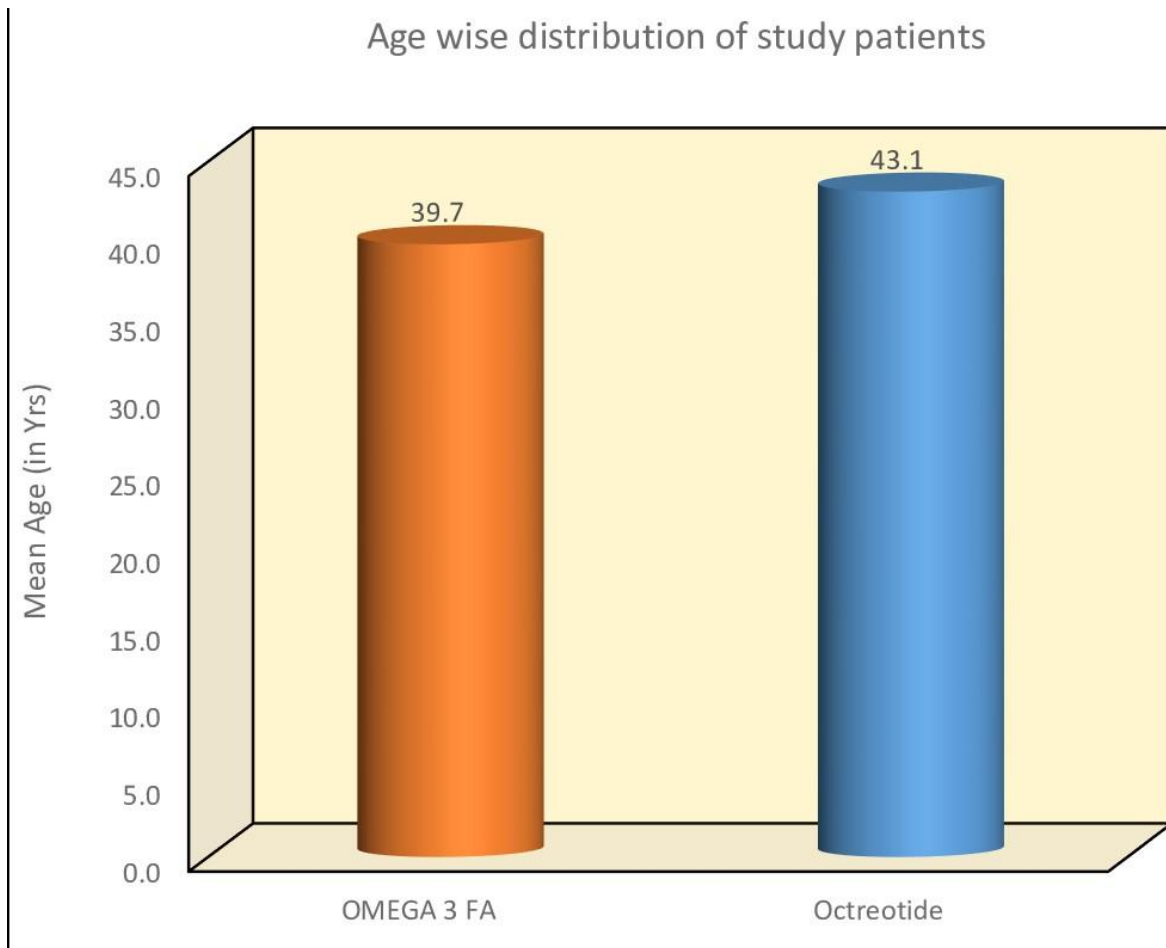


Figure 1: Age Distribution

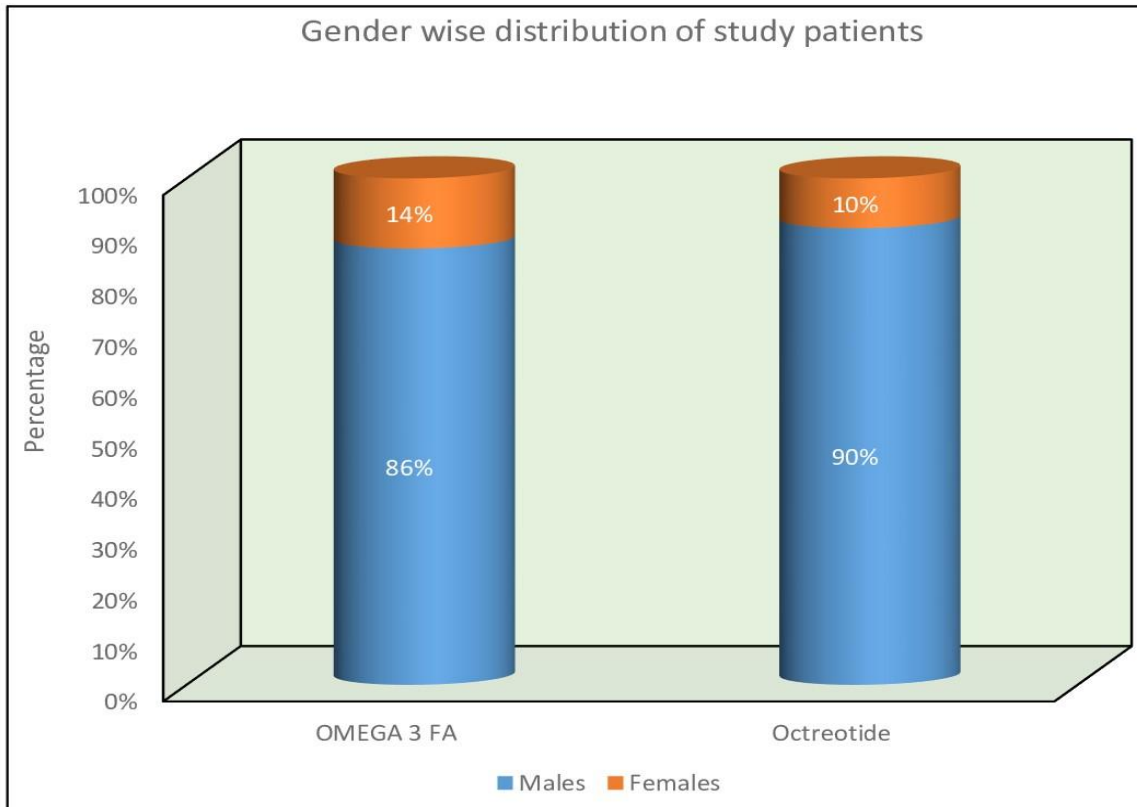


Figure 2: Sex Distribution

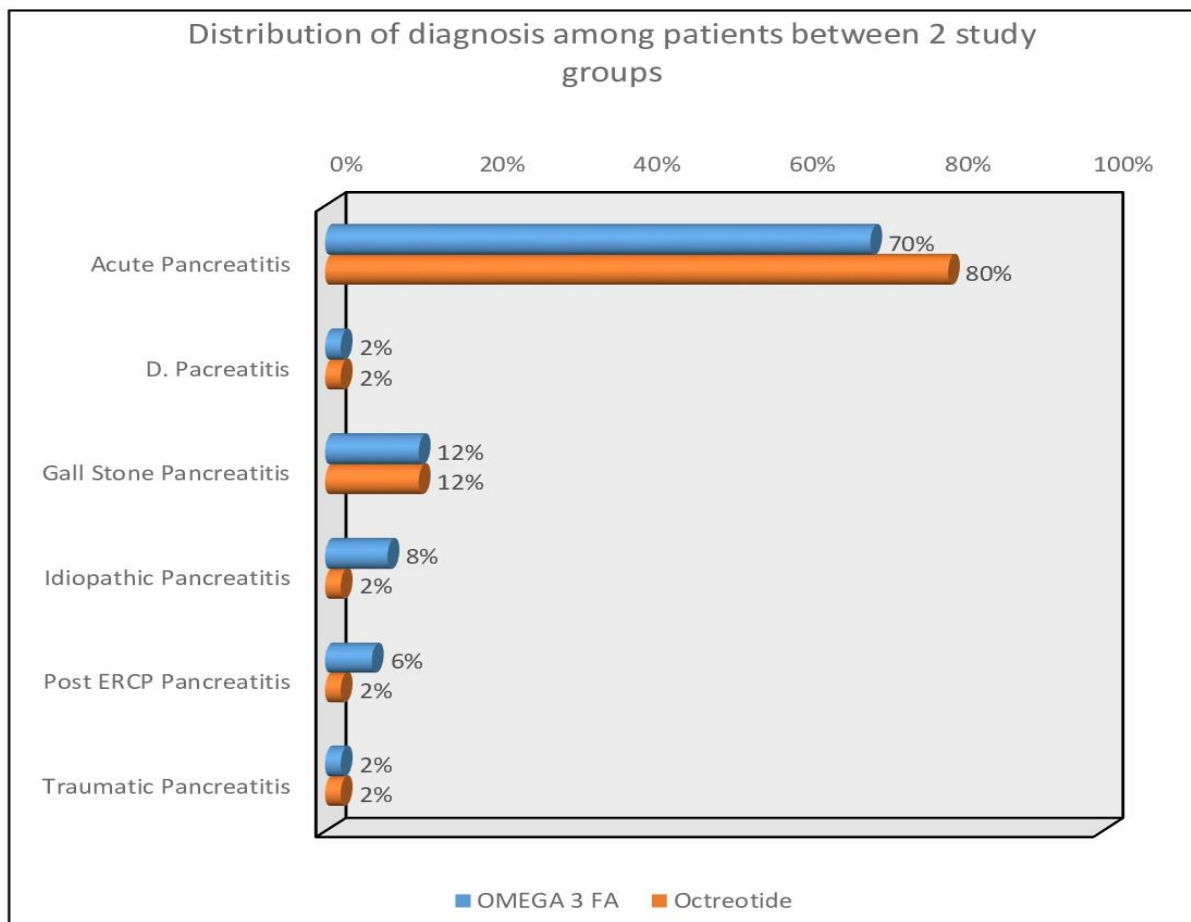


Figure 3: Etiological Distribution

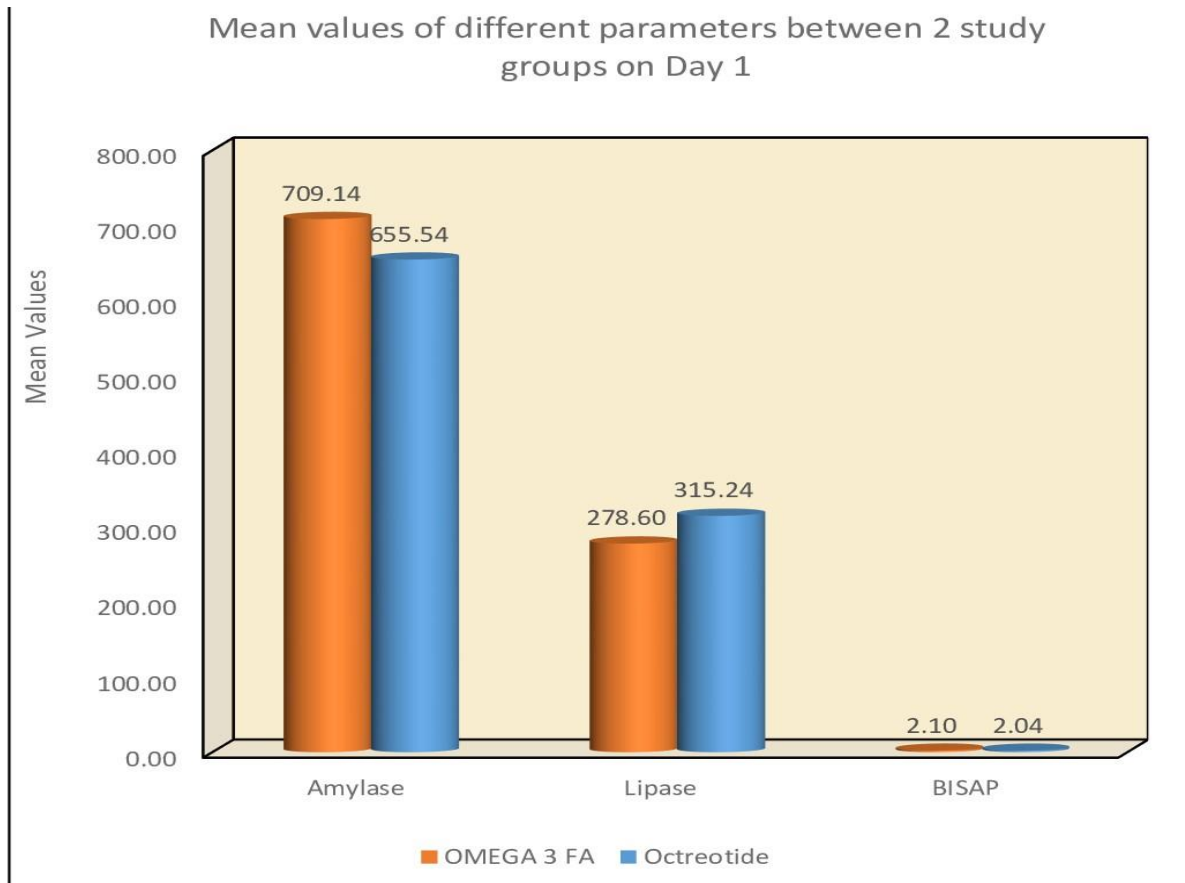


Figure 4: Comparison between Serum Amylase, Serum Lipase, and BISAP Score between 2 Study Groups on Day 1

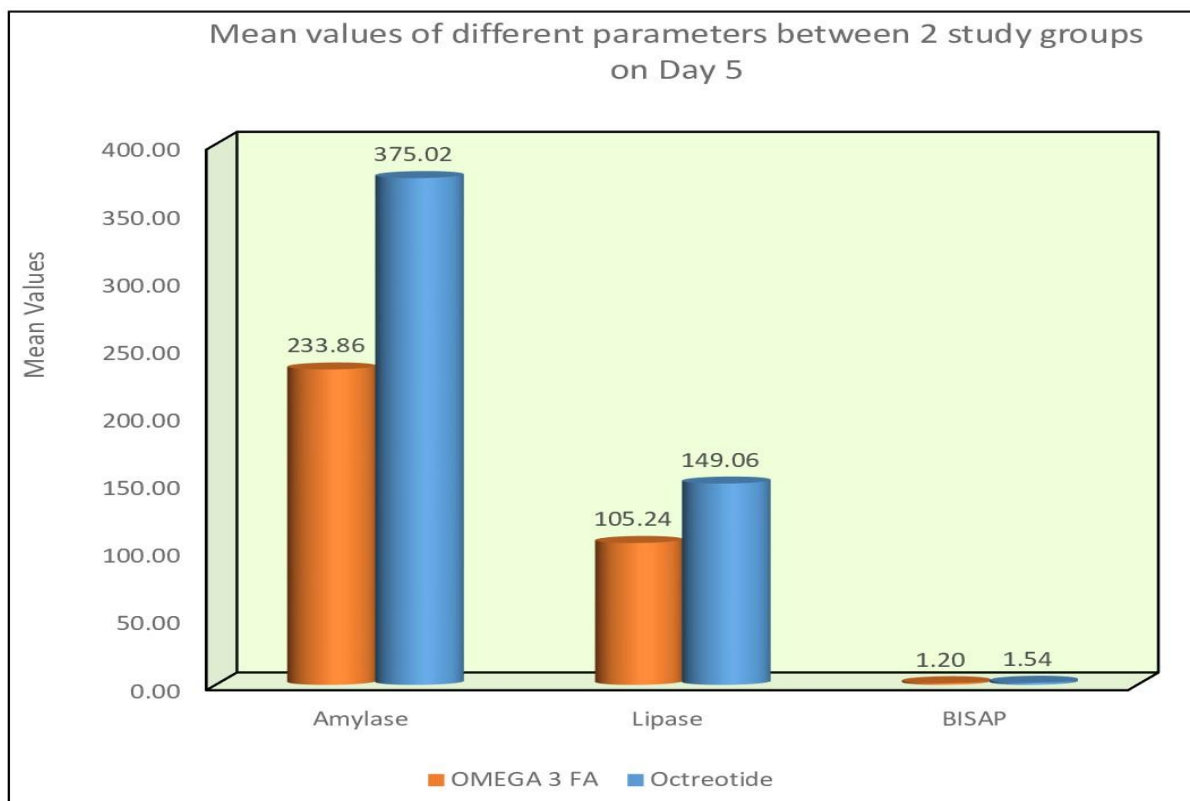


Figure 5: Comparison between Serum Amylase, Serum Lipase, and Bisap Score between 2 Study Groups on Day 5

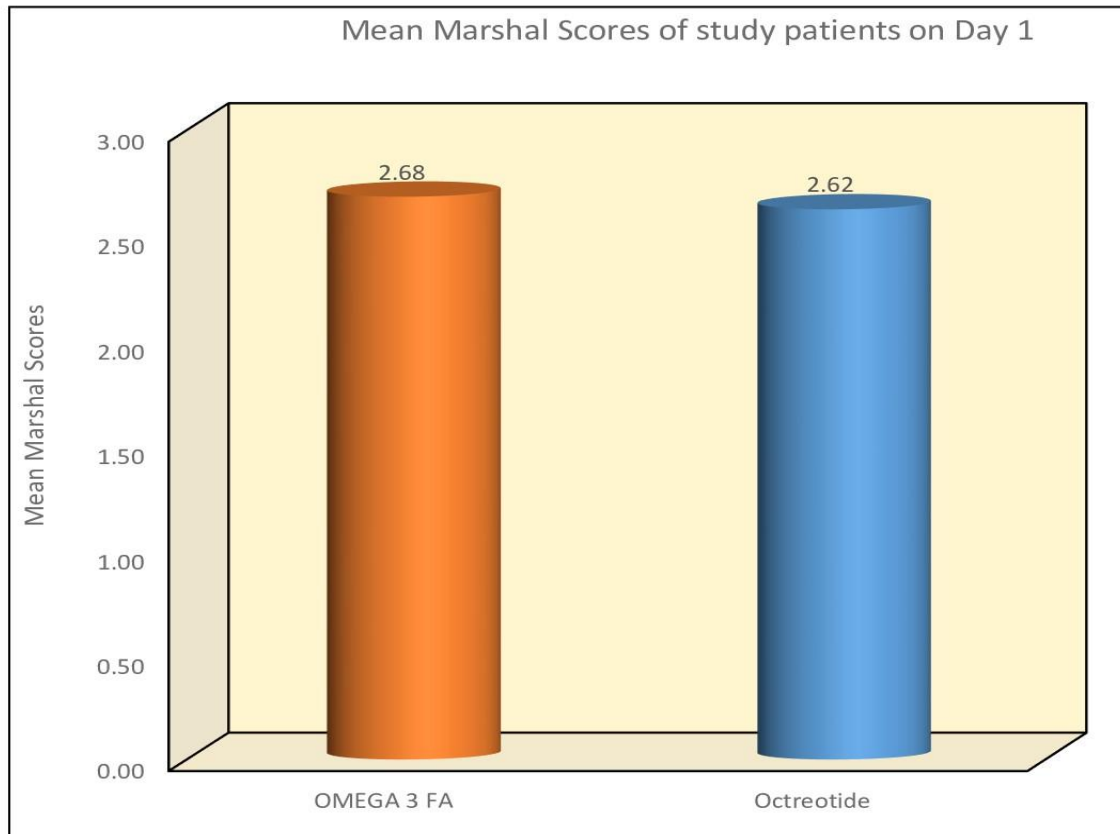


Figure 6: Modified Marshall Scoring Between Study Groups on Day 1

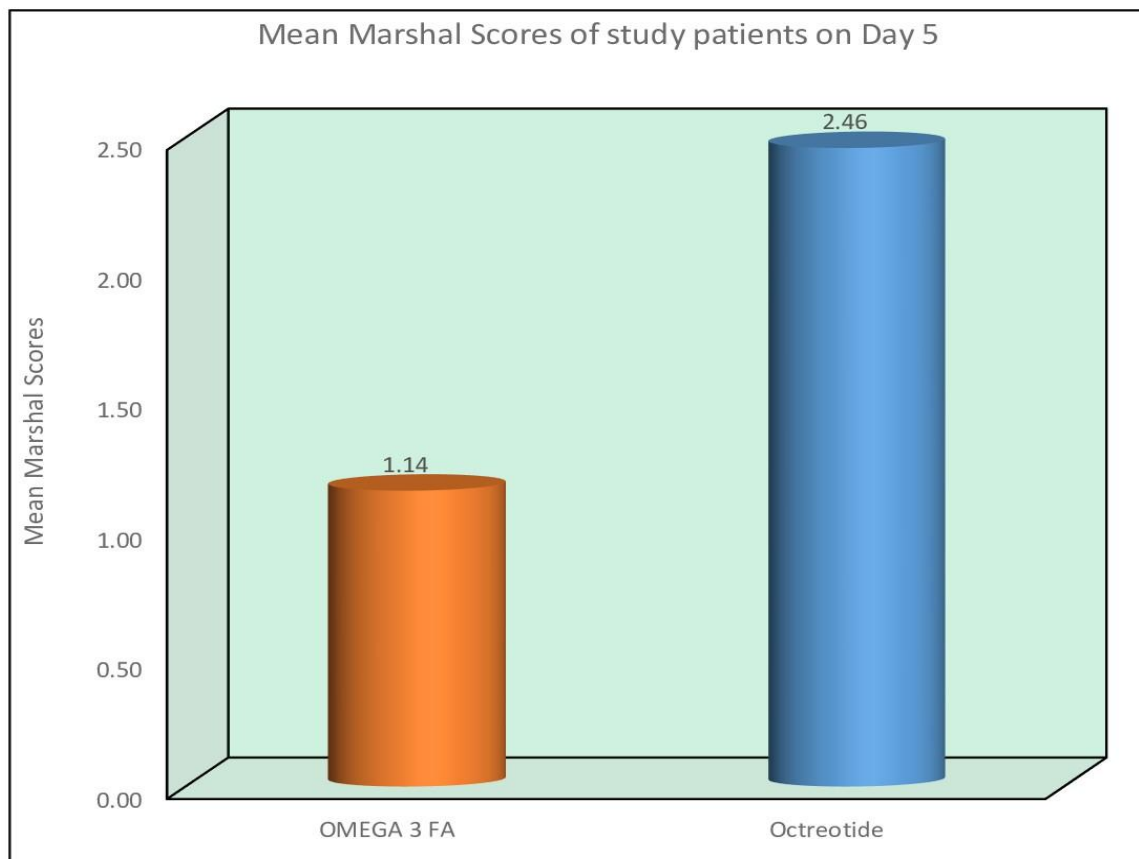


Figure 7: Modified Marshall Scoring Between Study Groups on Day 5

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 MARSHALL 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.

Our trial proves that in adwerant 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. ω -3 FA suppresses the inflammation and improves the course of infection by reducing proinflammatory eicosanoid and cytokine production. The ability of ω -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 ω -3 FA improves outcomes in patients with AP, definitive conclusions have been lacking. Therefore, perspectives on the use of ω -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.

ω -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.

Declarations

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Conflict of Interest: None declared

Ethical Approval: Not Required

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