Original Research Article

A Double Blinded Comparative Study between Omega 3 Fatty Acid Infusion Versus Octreotide 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 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 hyperinflammatory 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. 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. 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.

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 (Marshal 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 (PaO2/FiO2) |      | >400| 301–400         | 201–300      | 101–200      | ≤101         |
| ResT*                |       | ≤134| 134–169         | 170–310      | 211–439      | >439         |
| Serum creatinine (μmol/l) |    | ≤1.4| 1.4–1.8         | 1.9–3.6      | 3.6–4.9      | >4.9        |
| Cardiotoxic (systolic blood pressure, mm Hg) |  >90 | <90, fluid responsive | <90, not fluid responsive | <90, pH<7.3 | <90, pH<7.2 |

A score of 2 or more in any system defines the presence of organ failure.

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

| 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 | Octreotide |
|-----------|------------|------------|
|           | 50         | 2.10       | 0.86       | 2.00       | 0.63       |

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

| 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

| Parameters | 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 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. 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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