

## ORIGINAL PAPER

# Effect of Octreotide in Reducing the Serum Amylase and Lipase Levels on Patients with Acute Pancreatitis

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## ABSTRACT

A randomized controlled trial has been conducted to evaluate the role of octreotide in reducing serum amylase and lipase in patients admitted with acute pancreatitis. 100 patients with acute pancreatitis were selected for the study and the effect of sub-cutaneous octreotide was looked into in reducing the serum levels of the enzymes, amylase and lipase. Out of these 100 cases, 56 patients had acute biliary pancreatitis, 33 patients had acute alcoholic pancreatitis and 8 patients had idiopathic pancreatitis. There were 2 patients with biliary helminthiasis presenting with acute pancreatitis and 1 patient presented with acute pancreatitis following trauma. Serum amylase and lipase was recorded in all patients on admission. Octreotide (100 micrograms x 3) was given subcutaneously to 50 patients selected randomly along with conventional treatment (Group A) and other 50 patients were given only conventional treatment (Group B) irrespective of their aetiology, age, sex and severity. Serum amylase and lipase was again measured after 48 hours of admission. The change in the level of serum amylase and lipase was calculated in both Group A and Group B and statistical significance was determined. In our study those patients who received octreotide, i.e., Group A had a reduction of serum amylase by 82% and serum lipase by 70% whereas those patients who did not receive octreotide, i.e., Group B had a reduction of serum amylase by 73% and serum lipase by 59%. This difference between Group A and Group B was found to be statistically significant for both serum amylase ( $p=0.0028$ ) and serum lipase ( $p=0.0437$ ) by *T*-test and ( $p=0.00798$  and  $p=0.0437$ ) by Mann-Whitney *U* test respectively.

**Keywords:** Octreotide, amylase, lipase, pancreatitis, Mann-Whitney test

## INTRODUCTION

Acute pancreatitis is an inflammation and autodigestion of glandular parenchyma of pancreas which lead to injury or destruction of acinar components. It can be initiated by factors, like gallstones, alcohol, trauma, and infections, etc. It can be hereditary too. Acute pancreatitis is classified into mild and severe forms. Majority of patients suffer from mild acute pancreatitis, a self limiting disease, which responds well to conservative treatment. In up to 20% of patients with acute pancreatitis, however, the disease progresses to a severe form involving both pancreatic and extrapancreatic necrosis. The generally prevalent belief today is that pancreatitis begins with the activation of digestive zymogens inside acinar cells, which cause acinar cell injury. The diagnosis of acute pancreatitis can be made when a patient presents with three fold elevated

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serum levels of amylase or lipase. If the patient presents within 24 hours after the onset of pain, the elevated serum pancreatic enzymes predict pancreatitis with a sensitivity of 98% and a specificity of 90%. Activated pancreatic enzymes seem to be involved in the generation and progression of this “autodigestive” acute inflammatory disease, and it was therefore hypothesized that the administration of somatostatin or its analogue octreotide might help prevent progression of the disease and its complications. This approach is somewhat controversial; however, as it is not clear whether pancreatic secretion continues to occur during the course of acute pancreatitis. Animal studies show an appreciable reduction of secretion in the inflamed pancreas, but studies in humans are not conclusive.

Octreotide is a synthetic, a long acting octapeptide analogue of the native hormone somatostatin, became available in 1982. It is a powerful inhibitor of basal and stimulated exocrine pancreatic secretion in healthy volunteers, and can be given subcutaneously. Octreotide have been shown to inhibit both pancreatic endocrine and exocrine function. This study is a prospective randomized controlled trial to assess whether octreotide reduces the elevated serum levels of amylase and lipase in patients admitted with diagnosis of acute pancreatitis.

## MATERIALS AND METHODS

A prospective randomized controlled study was carried out among the patients with the diagnosis of acute pancreatitis admitted in the department of general surgery and general medicine of Gauhati Medical College and Hospital, Guwahati, Assam for a period of one year from 1<sup>st</sup> August 2012 to 31<sup>st</sup> July 2013.

**Patients Selection:** Inclusion Criteria: The diagnosis of acute pancreatitis was confirmed by the presence of clinical signs and symptoms of acute pancreatitis along with:

- Raised levels of serum amylase and/or serum lipase more than 3 times the normal serum level and/or;
- Radiological evidence of acute pancreatitis either in ultra sound study, in CT scan or both.

**Exclusion Criteria:** Patients with acute pancreatitis along with hollow viscous perforation and generalised peritonitis was excluded from the study.

**Study Population:** 100 patients were randomized. Out of 100 patients, 50 patients were included in study group and 50 patients as control group. The study group was regarded as Group A and the control group as Group B. The study group received Octreotide 100 mcg injection subcutaneously 8 hourly in addition to the treatment protocol of acute pancreatitis whereas the control group did not receive Octreotide.

## STATISTICAL ANALYSIS

- a. The mean of the differences of serum amylase and lipase levels at the time of admission and after 48 hours were calculated in both the study (Group A) and control group (Group B).
- b. Test method: An unpaired T test was carried out between the mean values of Group A and Group B to find if the difference was statistically significant.
- c. Using the sample data, standard deviation, standard error of mean, degrees of freedom and P-value was calculated to test the significance between the study and the control group.

## RESULTS AND OBSERVATION

**Age Incidence:** In the present study, the age of the patients ranges from 15 to 74 years. The mean age was 36.9 years.

**Sex Incidence:** Out of 100 cases of acute pancreatitis, 63 were males and 37 were females. The male: female ratio was 1.7:1.

**Aetiology:** 56 patients had acute biliary pancreatitis, 33 patients had acute alcoholic pancreatitis, 2 patients were found to have worms in CBD, 1 patient had acute pancreatitis following trauma. In 8 patients, no cause could be determined and were termed as idiopathic pancreatitis.

**Assessment of Severity of Acute Pancreatitis:** All 100 cases were assessed and severity graded according to the Ranson’s Criteria. Ranson’s score  $\leq 3$  were graded as mild pancreatitis and Ranson’s score  $>3$  were graded as severe pancreatitis. In addition we maintained the severity scoring as per our own scoring system.

**Table 1** Types of Acute Pancreatitis on the basis of Severity

Grading	Gallstone Pancreatitis	Non-Gallstone Pancreatitis	Total no. of patients	Percentage (%)
Severe (Ranson's Score >3)	12	7	19	19%
Mild (Ranson's Score <3)	44	37	81	81%

**Table 1** represents the types of pancreatitis and their severity. We had severe gall stone pancreatitis (Ranson's >3) 12, and non-gall stone pancreatitis 7. This made it 19% of the total cases in the study. We had 81% Mild cases (Ranson's <3) out of which gall stone pancreatitis was 44 and non-gallstones cases were 37.

Role of Octreotide over Amylase and Lipase level in patients with acute pancreatitis and its statistical significance is given in the **Table 2**.

**Table 2** Effect of octreotide on serum amylase as well as lipase

	Serum Amylase (u/l)			Serum Lipase (u/l)		
	At Admission (mean)	At 48 hours (mean)	Mean Difference	At Admission (mean)	At 48 hours (mean)	Mean Difference
Group A (patients who received Octreotide)	1523.16	238.46	1239.70 (82%)	2468.72	728.36	1740.36 (70%)
Group B (patients who did not received Octreotide)	1521.04	430.86	1090.18 (73%)	2367.94	1069.26	1568.68 (59%)

**Table 2** shows the effect of octreotide in reducing the levels of serum amylase and lipase after 48 hours of treatment. Thus during the course of acute pancreatitis, amylase was inhibited by 82% in Group A patients receiving Octreotide with a mean reduction of 1239.70 u/L within 48 hours and 73% in Group B patients not receiving Octreotide with a mean reduction of 1090.18 u/L within 48 hours.

On the other hand, lipase was inhibited by 70% in Group A patients receiving Octreotide with a mean reduction of 1740.36 u/L within 48 hours and by 59% in Group B patients not receiving Octreotide with a mean reduction of 1568.68 u/L within 48 hours.

**Table 3** shows the statistical analysis of serum amylase reduction within 48 hours in Group A and Group B.

#### P-value and Statistical significance:

**Table 3** The Student's T-test was done between Group A and Group B to analyze the statistical significance

Results	Serum Amylase	Serum Lipase
t=	3.0623	2.0432
df=	98	98
Standard error of difference=	48.825	84.024.
CI= The mean of Group A- The mean of Group B=	149.5200	171.6800
95% CI of this difference=	52.6274 to 246.4126	4.9378 to 338.4222
P- value	0.0028.	0.0437

It is evident from the table above that the reduction of serum amylase and lipase in Octreotide treated group is found to be statistically significant by student's T-test.

**Table 4** Mann-Whitney U test was performed between the two groups

Results	Serum Amylase	Serum Lipase
Z- score	2.4128	1.8165
U- value	899.5	986
p- value	0.00798	0.03438

Similar to the earlier table the above-mentioned table shows the reduction of serum amylase and lipase in Octreotide treated group is found to be statistically significant by Mann-Whitney U test.

## DISCUSSION

The present study evaluates the role of octreotide in reducing the level of serum amylase and serum lipase in first 48 hours and its statistical significance. The study also compares the percentage of reduction of serum amylase and serum lipase between the study group (Group A) and control group (Group B) in relation to age, sex, aetiology and severity of the disease.

The age of the patients in the present study ranged from

15 to 74 years with mean age of 36.9 years (**Table 5**). Incidence of disease was highest in the age group 25-44 years (61%).

**Table 5** Age incidence of different studies

Study	Number of Patients	Range	Median (in years)
OzkanKarakoyunlar et al, 1999 <sup>1</sup>	43	24-86	57.03
Uhl et al, 1999 <sup>2</sup>	302	18-93	50
Paran et al, 2000 <sup>3</sup>	50	43-67	55
Garg et al. 2001 <sup>4</sup>	169	15-80	41.3
Nippon R et al.2004 <sup>5</sup>	1688	13-79	62
Yeung YP et al. 2006 <sup>6</sup>	101	20-96	64
Papachirstou et al.2009 <sup>7</sup>	185	15-90	52
Peter J et al.2012 <sup>8</sup>	242	20-83	47
Present study	100	15-74	36.9

In the present study male preponderance was seen with M:F ratio 1.7:1. The different studies having the similarities with the present studies are narrated in **Table 6**.

**Table 6** Sex incidence of different studies

Study	Total cases	Males	Females	M:F
OzkanKarakoyunlar et al <sup>1</sup>	43	14(32%)	29(68%)	0.48:1
Uhl et al <sup>2</sup>	302	198(65.6%)	104(34.4%)	1.9:1
Paran et al <sup>3</sup>	50	22(44%)	28(56%)	0.78:1
Garg et al <sup>4</sup>	169	116(68.63%)	53(31.3%)	2.1:1
Nippon R et al <sup>5</sup>	1688	1047(62%)	641(48%)	1.6:1
Yeung YP et al <sup>6</sup>	101	43(42.6%)	58(57.4%)	0.74:1
Papachirstou et al <sup>7</sup>	185	94(51%)	91(49%)	1.03:1
Peter J et al <sup>8</sup>	242	159(65%)	83(35%)	1.8:1
Present study	100	63(63%)	37(37%)	1.7:1

In the present study the most common aetiology of acute pancreatitis was biliary in origin consisting of 56% of cases. Alcohol abuse was the second most common cause with 32% of the cases. In 8% of the cases no cause could be determined. Helminthiasis was found in 2% of cases and trauma was found in 1% of cases. This findings were supported by Uhl et al<sup>2</sup>, Paran et al<sup>3</sup>, Papachirstou et al<sup>7</sup> and Peter J et al.<sup>8</sup>

We calculated the Ranson's score of the 100 cases and found that 19 patients suffered from severe acute

pancreatitis with Ranson's score >3 and 81 patients had mild disease with Ranson's score <3.

This study closely resembles the study of Kemmer TP et al. 1992<sup>9</sup>, where the influence of octreotide was seen on human pancreatic secretion. The study showed that during secretin and ceruletide stimulation, amylase was significantly inhibited by 84%, 78%, and 81% with 5, 20, and 80 micrograms/h octreotide, respectively. All decreases p value less than 0.05. and thus were statistically significant.

Friess H et al, (1994)<sup>10</sup>, analyzed the effect of octreotide (3 x 100 micrograms, daily) given over a time period of 7 days on hormone-stimulated exocrine pancreatic secretion in 6 healthy volunteers using a secretin-ceruletide test. Following the first injection of octreotide and following 7 days of octreotide treatment secretin/ceruletide-stimulated amylase, trypsin and chymotrypsin secretion was significantly inhibited by 84%, 76%, and 77%.

R. Arcidiacono et al<sup>11</sup> evaluated the potential of octreotide to prevent acute pancreatitis in patients who underwent endoscopic sphincterotomy (EST).

OzkanKarakoyunlar et al<sup>1</sup>, studied 43 patients with a diagnosis of acute pancreatitis treated with high dose octreotide 0.5 mcg/kg/hr by continued intravenous infusion and found that the decrease in serum amylase was significantly more pronounced in the octreotide treated group (p< 0.000 with t-test for paired samples; p=0.0004 with Mann-Whitney U test).

Most of the studies dwelling on the subject has mentioned the use of sub-cutaneous injection of octreotide to prevent as well as the treatment of acute pancreatitis<sup>11,12,13,14,15</sup>. In the present study we could produce evidence that octreotide reduces the level of serum amylase and serum lipase in patients suffering from acute pancreatitis.

## CONCLUSION

This study was undertaken to see the effect of sub-cutaneous octreotide on the serum levels of amylase and lipase in patients with acute pancreatitis. The idea was to see if octreotide can significantly reduce the high levels of serum amylase and lipase in patients with acute pancreatitis. The finding was striking. Subcutaneous octreotide reduced the levels of both the enzymes within 48 hours significantly in all cases. In fact although not statistically significant, it reduced hospital stay in these patients.

So it can be suggested that sub cutaneous octreotide in acute pancreatitis cases may be used with the other standard management strategy. It may help the enzyme related damages to the pancreas as well as the surrounding organs to reduce.

**Conflict of interest:** None declared.

**Ethical clearance:** Taken.

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**Declarations:**

- (1) The article is original with the author(s) and does not infringe any copyright or violate any other right of any third parties;
- (2) The article has not been published (whole or in part) elsewhere and is not being considered for publication elsewhere in any form, except as provided herein;
- (3) All author (s) have contributed sufficiently in the article to take public responsibility for it and
- (4) All author (s) have reviewed the final version of the above manuscript and approve it for publication.

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