EFFECT OF OCTREOTIDE ON ACUTE PANCREATITIS PATIENTS IN KOLKATA, INDIA: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

BACKGROUND

Acute pancreatitis is the final result of premature pancreatic pro-enzyme activation leading to “auto digestion” of the parenchyma, thereby inducing a cascade of inflammatory response which further damages the organ. Theoretically inhibition of pancreatic secretion may prove useful in management of acute pancreatitis. There are evidences that somatostatin and octreotide apart from having inhibitory effect on pancreatic secretion also have some cytoprotective properties and that they counter the ileus and bacterial translocation in acute pancreatitis.

OBJECTIVE

The study was aimed at assessing the effect of octreotide on acute pancreatitis in the study area.

MATERIALS AND METHODS

Twenty six patients admitted with diagnosis of acute pancreatitis (n=26) were randomized into two groups. Group I acted as control, while Group II received 200 μg of subcutaneous octreotide thrice daily for a period of first 10 days post admission.

RESULTS

Positive treatment values with less complication rates were seen on treatment with octreotide in Group II.

CONCLUSION

Octreotide may be a useful addition in the otherwise conservative management of acute pancreatitis.

KEYWORDS

Acute Pancreatitis, Somatostatin, Octreotide.


INTRODUCTION

Acute pancreatitis is a potentially lethal disease with a spectrum of severity which may range from mild self-limiting course, responding well to conservative management, to severe illness with multi-organ failure and death. The pathophysiology of the disease is not fully understood and is believed to be the final result of premature pro-enzyme activation inside the pancreatic acinar cells. Co-localisation of zymogen granules and lysosomes occur within the acinar cells and is seen in minutes of pancreatic injury.1 This premature activation causes “auto-digestion” of the pancreas with the resultant release of pro-inflammatory, anti-inflammatory, reactive oxygen and chemotactic mediators. The net result is an inflammatory response which may lead to major systemic and metabolic complications if such mediators, toxins and vasoactive substances access the systemic circulation.2,3 and may lead to multi-organ dysfunction syndrome and death.4-8

At present the major problem is lack of a specific drug for the treatment of acute pancreatitis. The current standard of care is admission in an intensive care unit and symptomatic treatment.4-8

It is known that during the course of the disease, further endogenous induction of pancreatic secretion by enteral nutrition worsens the acute inflammation; hence, one of the basic principles of conservative management is avoidance of enteral feeding and nasogastric suctioning. Since the basic pathology behind acute pancreatitis is “auto-digestion,” it has been theorised that inhibition of pancreatic enzyme secretion may slow down the auto-digestion of the pancreatic parenchyma and hence may affect the prognosis.

Studies with somatostatin and analogues for pancreatic secretion inhibition began in the early 1980s for the treatment of acute pancreatitis.9-12 Limberg and Kommerell13 in 1980 used somatostatin for the treatment of acute pancreatitis and it stated “an impressive clinical improvement in all patients.” On the other hand other studies with somatostatin,10-12 and its analogues,14-16 showed contradictory results that they have no beneficial effect in the treatment. With a strong pathophysiological basis, yet conflicting results with somatostatin and its analogues in the management of acute pancreatitis, we set forth with the current study to see the effect of octreotide in acute pancreatitis patients of Kolkata, India.
MATERIALS AND METHODS

We evaluated the effect of octreotide on the course of acute pancreatitis. International guidelines were used as dictated by Tenner S et al17 and Banks PA et al18 for the diagnosis of acute pancreatitis. Adult patients having only moderate-to-severe pancreatitis with no co-morbidities were included in the study.

Twenty six patients with acute pancreatitis (n=26) were randomised into two groups of 13 each. Both the groups received the same treatment protocol. Group I acted as control, while Group II also received 200 μg of subcutaneous octreotide thrice daily for a period of 10 days post admission.

The effect of treatment was calculated using a standard scoring system (See Table 1).19,20 in which complications were scored on admission and within 30 days. A positive difference in scores indicates a positive treatment effect and reduced complication rate. The results were then put to statistical consideration using paired ‘t’ test.

The difference of the scores on admission and within thirty days was positive in the octreotide treated group (Group II), the value being +1.762, while that of the control group (Group I) was -2.0. These results were found to be statistically significant difference with p<0.05 (Table 3).


discussion

The complete pathophysiology behind acute pancreatitis is not fully understood, but the first step in the disease process is activation of the pancreatic enzymes within the parenchyma leading to “auto-digestion” and invoking an inflammatory response, which further damages the pancreas. Endogenous somatostatin is produced by the gastric and pancreatic islet D cells and is popularly known as “universal off” switch3 one of its actions being inhibition of secretion of pancreatic enzymes. Octreotide is a synthetic analogue of endogenous somatostatin. Upon the theory that inhibition of pancreatic secretion may be beneficial in acute pancreatitis, researches began in early 1980s with conflicting reports.10,11,14-16,21-23 Choi et al23 saw a “beneficial local effect” and remarked that “local inflammation was supressed by somatostatin treatment.” Even when better clinical outcomes were seen, the results failed to prove a statistical significance. A meta-analysis done by Carballo et al24 included some of these studies and proved a statistical significant outcome with somatostatin treatment.

For the optimum dose of octreotide, a study was conducted by Binder M et al20 with three different dosages of subcutaneous octreotide and results were interpreted according to the scoring system also used by us.19,20 Though the results had no statistical power, yet the lowest complication rate was seen lowest with 200 μg of subcutaneous octreotide thrice daily for 10 days (Table 4).


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effect of somatostatin was assumed to be the cause. Jenkins et al.\textsuperscript{27} showed the cyto-protective effects of somatostatin and octreotide, in that he recorded increased hepatic and splenic reticulo-endothelial system activity and significantly reduced endotoxin concentration in serum with somatostatin and octreotide treatment.

Octreotide has also been proposed to counter the ileus seen during acute pancreatitis. Hui Zhou et al concluded "The pathogenesis of ileus in the early stage of Acute Necrotising Pancreatitis may be related to the neuropathy of the enteric nervous system. Octreotide may reduce the severity of ileus by lessening the damage to enteric motor innervation."\textsuperscript{28} Another study by Guler O et al showed that in acute pancreatitis administering octreotide reduces bacterial translocation by preventing mucosal damage.\textsuperscript{29}

The ground for octreotide treatment in acute pancreatitis is strong with a logical physiological basis of mechanism by inhibition of secretion with studies showing its cytoprotective mechanisms and potential to reduce ileus and bacterial translocation; yet further studies with larger sample sizes are needed to solidify its efficacy.

**CONCLUSION**

Octreotide may be a useful addition in the management of acute pancreatitis, a disease with few other medical options. Further larger studies would be useful to better characterise the role of Octreotide in the management of acute pancreatitis.

**REFERENCES**