ROLE OF OCTREOTIDE ON OUTCOME OF PATIENTS WITH ACUTE PANCREATITIS

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ABSTRACT

BACKGROUND: acute pancreatitis is a multisystem disease carrying broad spectrum of clinical presentation and complications. The objective of this study was to determine the positive role of octreotide in the out come of patients suffering from acute pancreatitis.

OBJECTIVE: The objective of this study was to assess the role of octreotide in patients having acute pancreatitis.

PATIENTS AND METHODS: This is a descriptive, comparative, prospective study. The study was conducted in the department of surgery Saidu Group of Teaching hospital Saidu Sharif Swat from January 2011 to June 2014. Total of seventy consecutive patients having acute pancreatitis was randomized in a prospective trail for the treatment, at tertiary care hospital in Malakand division Swat KPK Pakistan. The data of patients were recorded on a purposely prepared proforma for this study. The diagnosis of patients was established on basis of biochemical (serum amylase, WCC, C-reactive protein) and radiological (USG, CT- scan) investigations. The patients were divided into two groups, A and B. Group A, had received octreotide along with fluids, omeprazole, analgesic. Group B received fluids, omeprazole, analgesic without octreotide. Ages of the Group A and B were matched (± 5 years). Data was analyzed using SPSS version 16 employing chi-square test (X^2 test). A p-value below 0.05 was considered statistically significant.

RESULTS: In this prospective, comparative study two groups, each of 35 consecutive patients were selected. The mean age in Group A was 37 ± 12.41 years and in Group B 40 ± 10.32 years ($p = 0.364$). There were 12 males and 23 females in group A, while 14 males and 21 females in group B. Both the groups were comparable. All the patients in octreotide group A and non-octreotide group B were survived. No major complications were noted in either group. As far as mean hospital stay was 7 ± 2.10 days in group A, while it was 9 ± 3.14 days in group B ($p < 0.032$). All the P- values for the criteria of study were calculated. P-values were significant when we consider pain control and hospital stay in two groups.

CONCLUSION: In our study we found that octreotide was more effective in the final outcome of patients with acute pancreatitis. There is clear cut beneficial effect of octreotide on hospital stay and reduced need of analgesics in patients having acute pancreatitis.

KEYWORDS: Acute Pancreatitis, Octreotide, Hospital Stay, pain control.

INTRODUCTION

Acute pancreatitis (AP) is a disease with a broad spectrum of clinical findings ranging from self-limiting mild disease to a very severe and lethal one. It has an incidence of approximately 40 cases per 100,000 adults in the United States¹. It has been observed that the incidence of acute pancreatitis is rising over the past several decades². It is a very lethal disease and the mortality due to pancreatitis ranges between 4%

and 15% for all cases and between 15% and 90% for more severe cases³.

Elevation of serum levels of pancreatic enzymes (amylase, lipase) > 3 -5 times of normal values and Ultrasonography (USG) or CT-scan abdomen offer a high degree of diagnostic specificity and sensitivity (> 80 -90%)^{4,5}.

Although the initiating pathophysiological processes are not known, the disease is caused by

the destruction of the gland and peripancreatic fatty tissue by digestive enzymes^{6,7}. These enzymes are produced in the acinar cells and activated in two possible ways (e.g. intra- and/or extra cellular). This 'auto digestion' process was suggested in 1901⁸.

Octreotide is an analogue of somatostatin which can reduce gastrointestinal, biliary, and pancreatic secretions, as well as decrease gastrointestinal motility. Octreotide has a longer half-life than somatostatin which allows for intermittent subcutaneous injections rather than a continuous intravenous infusion. Octreotide inhibits stimulated pancreatic secretion and so it is useful in pancreatic diseases and pancreatic injury⁹. It reduces secretion, release and activation of exocrine hormones. There is collection of pancreatic hormones in duct which in return causes irreversible destruction of exocrine and endocrine pancreatic parenchyma which leads to mal-digestion and diabetes¹⁰. It reduces the complications after elective pancreatic surgery⁹. It is reported that inhibitory effect of octreotide is last for 7 days of its administration. There is no target drug especially for pancreatitis in initial phase of disease to fight against systemic inflammatory response syndrome^{9,10}. There is lots of controversies about the role of octreotide in the treatment of acute pancreatitis, so we tried to evaluate whether there is a beneficial role of octreotide or not.

METHOD AND MATERIALS

This comparative study was carried out on patients having acute pancreatitis at Saidu Group of Teaching Hospital (SGTH), a Tertiary Care hospital in Malakand division Swat KPK Pakistan. The diagnosis of patients was established after biochemical (serum amylase, White cell count (WCC), C-reactive protein) and radiological (USG, CT-scan) investigations. The data of patients were recorded on a specially prepared proforma for this study. Informed written consent was obtained from the patients after full explanation of the details of the disease process, options of treatment, possible side effects and complications and chances of

recurrences in either group. They were informed of their right to withdraw from the trial at any stage.

The protocol was approved by the Institutional Ethics Committee of SGTH, SMC. In our surgical department two group of patients were selected, to one Group A, octreotide in a dose of 0.1mg subcutaneously twice a day for 5 to 7 days, fluid and symptomatic management and to Group B, only fluid and symptomatic treatment were given. Known Cardiac, Pulmonary, Renal disease patients as well as pregnant women excluded from this study. For establishment of diagnosis, serum amylase (normal=0-180 somoegy u/dl), >3-5times normal, raised white cell count (normal= 4000-11000x10⁹/L), C-reactive protein (normal=<10mg/dl), > 100 mg/dl, Ultrasonography and Computed Tomographics scan were taken into consideration. Serum lipase is also an important diagnostic test in acute pancreatitis but the facility for that was not available here in our hospital and private laboratories. The patients were chosen with age matching (± 5 years) in both groups. Ringer lactate and/ or Dextrose saline were used and symptomatic management was done in both the groups.

Analgesic tramadol hydrochloride was used intramuscular in both groups. The use of analgesic more than three times a day was considered as patient not relieve of pain and the patient needed more analgesia.

The study parameter for both group were; pain, severity of pancreatitis by serum amylase, hospital stay and mortality in both the groups on admission.

RESULTS

The results of this prospective, comparative study were based on patient records from January 2011 to June 2014. Total of seventy consecutive patients were chosen. The patients were divided into 2 group's. Each group consisting of thirty five patients. One group received fluids, omeprazole and analgesia with

octreotide (Group A) and other received fluids, omeprazole, analgesia without octreotide (Group B).

STATISTICAL ANALYSIS: Data was analyzed using SPSS version 16 employing chi-square test (χ^2 test). A p-value below 0.05 was considered statistically significant.

The mean age in octreotide group Group A was 37 ± 12.41 years when compared with 40 ± 10.32 years in Group B ($p = 0.364$).

Gender wise comparison showed that, there were 12 males and 23 females' in octreotide group, while 14 males and 21 females in control group. Both the groups were comparable. There was no significant difference noted ($p < 0.622$). All the patients in both groups were survived. There was no major complication occurred in either group. As for as mean hospital stay was concerned it was 7 ± 2.10 days in octreotide group while it was 9 ± 3.14 days in control group ($p = 0.032$). The mean value of serum amylase in octreotide group (A) on admission was 746 ± 198 U/L and in non-octreotide group (B) it was 872 ± 147 U/L. The serum lipase facility was not available here in hospital and/or private laboratories therefore that were not performed.

The serum level of Amylase became normal in 2-3 days in group A while remain persistently raised for 5-7 days in group B. Similarly White cell count and C-reactive protein were rapidly decreases in Octreotide group (group A), as compare with non-octreotide group (group B).

The pain was present in all patients in both the groups, when the patients received three doses of analgesic (tramadol hydrochloride). The intensity of pain was decreases in group A, with the use of octreotide, while the non-octreotide group B needed more analgesia. So it can be said that there was greater relief of pain in group A which received octreotide. As far as hospital stay of the

patient is considered the hospital stay was longer in patients who did not received octreotide.

All the p-values for the criteria of study were calculated (Table 1).

TABLE 1: COMPARISON OF GROUPS. GROUP- A (OCTREOTIDE), GROUP- B (NON-OCTREOTIDE).

Characteristics	Octreotide (Group A)	Non-Octreotide (Group B)	Significance
Age			P=0.364
Mean	37	40	
SD	12.41	10.32	
Sex			P=0.622
M	12	14	
F	23	21	
Outcome			P=0.00
Recover	35	35	
Mortality	00	00	
Hospital stay			P=0.032
Mean	7	9	
SD	2.10	3.14	
S.Amylase			P=0.631
Mean	746	872	
SD	198	147	
S- Amylase became normal (in Days)	2-3	5-7	P=0.026
Analgesic Doses/24 hrs	3doses/24hrs	>3 doses/24hrs	P=0.041

DISCUSSION

This study showed that octreotide play a positive role in the treatment of acute pancreatitis, as taking into account pain relief, hospital stay, recovery of pancreatic enzymes and morbidity, while in literature the role of octreotide in acute pancreatitis (AP) is controversial.

Xu et al in a recent meta-analysis concluded that there are no added benefits of using octreotide in moderate to severe acute pancreatitis¹¹. A similar finding was noted in a local study conducted by Rafi et al¹².

In contrast, Wang et al in a recent randomized controlled trial concluded that high dose octreotide within 48 hours of onset of AP may

reduce the risk of severe acute pancreatitis as it raises plasma somatostatin levels to normal and decreases plasma levels of IL-6 and TNF- α ¹³. In a local study by Zubair and colleague, excellent result were noted in their patients treated with octreotide¹⁴.

No major complication like, shock, respiratory problems, renal failure etc, were noted in either group of our study. The chances of shock and ARDS (acute respiratory distress syndrome) increased in non-octreotide group. There is clear cut change in pain intensity, its duration, hospital stay and mortality¹⁵. In a study conducted by Paran et al reveals that there are high chances of sepsis and ARDS in patients not receiving octreotide, along with prolong hospital stay and high mortality. The hospital stay is shorter in patients receiving octreotide, while patients not receiving Octreotide show higher mortality. There is definitely great role of octreotide in severe acute pancreatitis. The chances of sepsis and ARDS are low in patient receiving octreotide^{16,17}. Furthermore there is positive role of Octreotide in reducing post endoscopic retro grade cholangio-pancreato graphy induced pancreatitis¹⁸.

Benefits of octreotide observed clinically in experimental models are, Less hypoglycemia, less acidosis, reduction in pancreatic edema, little damage to pancreas and there is reduction in mortality^{15,19,20}.

Pleural effusion, ascites, pancreatic edema and retroperitoneal edema is reduced in octreotide group. It is considered that if oral intake is started early then serum amylase levels and pancreatic edema are evident to reduce fast²¹.

We observed in our study that serum Amylase and white cell count (wcc) level were fell down rapidly in octreotide group as compared with non-octreotide group, similar observation of rapid fall in amylase secretion in patients of pancreatitis when they received octreotide were noted^{18, 22,23}.

Many studies concluded that along with bedside index for severity in acute pancreatitis, serial urea and creatinine guidelines can be used to manage the disease²⁴. There are 30-50% chances of mortality in cases of severe acute pancreatitis²⁰. One of the studies says that there is same mortality in both the groups and other study says that there is no difference in mortality or complications. These are again inconclusive evidences. They are nor favoring neither discouraging the use of octreotide in cases of pancreatitis^{15,16,17}.

It is a fact that less amount of analgesia is needed to control pain in octreotide group. It is controversial that, whether there is any change in duration of pain and intensity in octreotide and non octreotide group²⁵.

Role of intravenous fluids especially Ringer lactate can't be denied as there is reduction in systemic inflammatory response syndrome with its use^{26,27}. Previously it was thought that fluid resuscitation improves the prognosis of acute pancreatitis.

CONCLUSION

In our study we had found that octreotide has a beneficial role as for as intensity of pain, its duration and hospital stay is taken in to account. There is also rapid decrease in the serum level of pancreatic enzymes. The statistical results were significant regarding pain control and hospital stay. When we read literature of recent days, many studies reveal that the use of octreotide has a beneficial role in the treatment of pancreatitis.

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