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EFFICACY OF OCTREOTIDE IN INITIAL MANAGEMENT OF ACUTE VARICEAL BLEED

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ABSTRACT

OBJECTIVE *Aim of study was to see the efficacy of octreotide alone as initial therapy in controlling acute variceal bleeding.*
DESIGN : *It was randomized, prospective case control study.*
PLACE & DURATION : *Study was conducted in medical wards of Chandka Medical College Hospital from June 2003 to April 2004.*
PATIENTS & METHODS : *Ninety patients who were fulfilling inclusion criteria and had esophageal varices as cause of bleeding confirmed on endoscopy were included in the study. Among them 63 (70%) were male and 27 (30%) were females. Their average age was 30 years. Upper GI endoscopy was performed within 24 hours after hemodynamic stabilization. Patients were randomly allocated in A & B Groups. All patients of Group A and 22 patients of Group-B revealed esophageal varices with active bleeding from varices in different grades (I, II, III) and cherry red spots. Grades of hepatic encephalopathy were made on admission and child-Pugh scoring were made after investigation. Group-A (61) patients received octreotide on admission and Group – B patients received placebo treatment (blood transfusions, intravenous fluids and proton pump inhibitors) on admission. But 22 patients of Group-B were given octreotide after endoscopy after 24 hours in whom cause of bleeding was esophageal varices. Octreotide was started in dose of 50-microgram IV bolus then infusion of 50 microgram per hour for 48 hour and then 50 microgram subcutaneously 8 hourly for 5 days.*
RESULTS : *Bleeding was controlled in 49 (80.3%) patients of Group-A within 12 hours of start of octreotide and 13 (59%) patients of Group-B bleeding was controlled after 24 hours P = 0.007. 10 (16.3%) patients of Group-A and 06 (20.6%) patients of Group-B showed rebleeding after 72 hours after initial control, this difference was statically significant P<O.Ol. The rebleeding was remarkable in Child-Pugh's class B and C. 07 (11.4%) patients of Group-A and 08 (27.5%) patients of Group-B expired after 04 days of hospital stay.*
CONCLUSION : *It was concluded that octreotide is an effective initial therapy to stop the acute variceal bleeding specially at places where definitive endoscopic procedures like sclerotherapy and esophageal variceal ligation are not available.*

KEY WORDS : Cirrhosis, portal hypertension, Esophageal varices, acute bleeding, octreotide.

INTRODUCTION

The patients of cirrhosis present in many ways like upper gastrointestinal bleeding, ascites and coma. Up to 90% of patients with cirrhosis will develop esophageal varices at some time during their disease. The risk of initial variceal bleed in cirrhotic patients with varices is 25 to 35% and majority of these initial bleeds occur within first year after varices are diagnosed; survivors of an initial bleed have even higher risk of a recurrent bleed. Up to 70% usually re-bleed within 6 months. Risk of death from each episode is 30-50 %. [1, 2], variceal bleeding is one of the commonest medical emergencies and big public problem in poor countries. Hepatitis B and Hepatitis C viruses are leading causes of end stage liver disease with portal hypertension in this part of world. Bleeding stops on its own in 70% of patients before they reach the hospital, however early re-bleeding occurs within hours and days in at least 50%, of cases. [3,4] The risk of continued variceal bleeding or early re-bleed within first 6 hours is related to severity of liver

disease. [3,5,6] Factors that sustain bleeding and that cause re-bleeding in an individual are not fully understood. [7,8] However bleeding does not occur until the hepatic venous pressure gradient exceeds 12 mmHg. [1,9,10]

For the patients in whom varices seem to be probable cause of bleeding octreotide should be started empirically even before the cause is found before patients reaches to place like tertiary care centre where esophagogastro duodenoscopy (EGD) facilities are available and where definite procedures like esophageal variceal sclerotherapy (EVS), esophageal ligation could be under taken. So one important purpose of our study is to determine that octreotide, up to what extent it shall be of help, if given empirically as first line pharmacological therapy to stop the variceal bleed at the site of patient's first visit i.e. his home or at general practitioner clinic in remote area before he or she reaches the tertiary care hospital. This type of treatment is safe, readily available, does not need special equipment, does not need trained personnel, has very few side effects and almost as effective as sclerotherapy.

Esophageal tamponade has been shown to be as effective mean to control the bleeding, however, at least 50% of the patients experience re-bleeding within 24 hours of intervention, procedure related complications (e.g. aspiration pneumonia, air way obstruction and perforation), tolerance of patients is poor and death occur in number of cases. [11,12] Vasopressin has serious cardiac side effects. (Myocardial Ischemia, cardiac failure and pulmonary edema) and along with vasopressin, vasodilators like nitroglycerides may be added to reduce side effects. [13] It has been shown that octreotide is as effective as vasopressin in acute variceal; hemorrhage without side effects. [14,15]

Endoscopic sclerotherapy has proved beneficial for control of active variceal bleeding. [16] It also prevent re-bleeding and improve survival of patients. [17]

However sclerotherapy is associated with re-bleeding in 25- 50% of patients and variceal obliteration requires 6-11 settings and procedure related complications[18] in 15-50% of patients, and requires endoscopic facility and expertise [19] which is not available every where every time.

PATIENTS & METHODS

This was randomized, prospective, case control study conducted in medical wards of Chandka Medical College, Hospital Larkana between June 2003 - April 2004. Patients presented with fresh upper gastrointestinal bleeding were included in study. Inclusion and Exclusion Criteria's are given in table no. 1.

TABLE NO. I

INCLUSION CRITERIA
i. Age 18 to 60 years
ii. Endoscopy reveals only varices as a sole cause of bleeding
iii. No bleeding from any upper GIT ulcer on endoscopy
iv. Chronic liver disease signs like palmar erythema, pallor, jaundice, spider nevi, loss of axillary hair, Gynecomastia, pedal edema, shrunken liver, enlarge spleen, Ascites
v. Ultrasound confirms the signs of portal hypertension due to cirrhosis of liver
EXCLUSION CRITERIA
1. Patient with known history of hypertension and High B.P. at the time of admission
2. Patient with renal failure
3. Patient with Ischaemic Heart Disease
4. Ulcer on upper G.I. endoscopy
5. Malignancies on upper G.I. endoscopy
6. Age above 60 years

Patients were divided in A & B Groups on the basis of base line characteristics of severity of disease. Patients were classified into groups A, B & C according to Child's Pugh criteria and scoring was done. Active variceal bleeding was endoscopically diagnosed when fresh blood was seen in esophagus and stomach with cherry red spots on large varices and no other source of bleeding was seen in stomach and duodenum. Varices were graded in Grade I (The varices can be depressed by the endoscope), Grade II (The varices cannot be depressed by the endoscope), Grade III (The varices are confluent around the circumference of oesophagus) Group-A patients consisted with past history of liver disease and peripheral signs of chronic liver disease with strong support of ultrasound. All Group - A patients were stared with octreotide 50 ug I/ V bolus followed by 50 ug I/V infusion per hour for 48 hours and 50 ug subcutaneously 8 hourly for 5 days, along with fresh blood transfusion. Group-B consisted of patients with haemetmesis and past history of jaundice but no any peripheral signs of chronic liver disease. They were kept on supportive medical therapy (Blood transfusion, Proton pump inhibitors and Vitamin-K) except octreotide. Endoscopy was done within 24 hours. In all those who had bleeding esophageal varices, octreotide started as in Group-A.

RESULTS

110 patients who presented with active upper gastrointestinal (UGI) bleeding in Medical wards of Chandka Medical College, Hospital were inducted in study. Out of them 20 cases not fulfilling inclusion criteria were excluded. The 90 cases with upper GI bleeding fulfilling inclusion criteria were selected for study. These included 63 (70%) males and 27 (30%) females. These patients were divided in to two groups Group-A patients consisted of 61 patients among them 44 (48.8%) were males and 17 (18.8%) were females. Group-B consisted of 29 (32.2%) patients among them 19 (21.1%) were males and 10 (11.1%) were females. Patients of both groups were divided into 04 age groups, majority of patients were in the range of 31 - 60 years. Grading of Hepatic encephalopathy was done at presentation in all cases of Group-A and B patients, which showed that 30 (33.3%) cases were in Grade-O, 26 (28.8%) cases were in Grade-I, 23 (25.5%) cases were in Grade-II, 6 (6.6%) cases were in Grade-III, 5 (5.5%) cases were in Grade-IV.

After admission and investigations child-pugh's grading for severity of liver disease was done. In Group-A patients 25 of 61 (40.9%) cases were in Class-A, 19 of 61 (31%) cases were in Class-B and 17 of 61 (27.8%) cases were in Class-C.

In Group-B patients 16 of 29 (55.1%) cases were in Class-A, 9 of 29 (31%) cases were in Class-B and 4 of 29 (13.7%) cases were in Class-C. The P value calculated by Mann-Whitney U test was 0.04; showing a significant difference between Child-Pugh's Grading in Group-A and Group-B. The mean of Child-pugh's score of group-A was

10.03±1.89 and that of group-B was 9.67±1.67. The P value was equal to 0.36, 95% C.I. This shows significant difference in Child-Pugh's score between Group-A and Group-B patients.

ENDOSCOPIC FINDINGS

Among 90 cases assessed on UGIE, in Group-A (61 of 90) patients all had esophageal varices of different grades. Among them 50 of 61 (81.9%) cases had grade-III varices, 6 of 61 (9.8%) cases had grade-II varices and 5 of 61 (8.1%) cases had Grade-I varices.

In Group-B (29 of 90) patients 22 of 29 (75.8%) cases had esophageal varices, were seen in different grades. 14 of 22 (63.6%) cases had grade- III varices 5 of 22 (22.7%) cases had grade-II varices, 3 of 22 (13.6%) cases had grade-I varices. All had cherry red spot; all had fresh blood seen in esophagus and stomach.

In 7 patients of Group-B the cause of haematemesis was non-variceal bleeding, 5 patients had peptic ulcer, 1 patient had gastric erosions and 1 patient had congestive gastropathy.

RESPONSE ON OCTREOTIDE THERAPY

In Group-A patients bleeding was controlled in 49 of 61 (80.3%) patients within 12 hours and 13 of 29 (44.8%) of Group-B patients after 24 hours. P=0.007, 10 (16.3%) patients of Group-A and 06 (20.6%) patients of Group-B developed rebleeding after 72 hours after initial control. This difference was statistical significant P<O.Ol. Average 06 to 08 pints of blood transfusions were needed for Group-A patients and 08 to 10 pints of blood transfusions were needed for Group-B patients. This difference was statistically significant P=0.009. 07 (11.4%) patients of Group-A and 08 (27.5%) patients of Group-B expired after 04 days of hospital stay. All expired patients of both groups were in Class-B and C of Child-pugh's score of liver disease. Nausea, pain in abdomen and hyperglycemia were observed in Group-A and Group-B who received bolus dose of octreotide. Average hospital stay of Group-A patients - was 08 days and 10 to 12 days of Group-B patients.

DISCUSSION

Esophageal variceal bleeding is a medical emergency when it occurs; we used octreotide empirically as first line pharmacological treatment to stop variceal bleeding. In our study mortality rate was 11.4% in octreotide group and 27.5% in Placebo and octreotide group patients. In our study incidence of oesophageal varices were 92.2%. Our figure correlates with figure reported from other studies conducted in Pakistan i.e. 90%. Oesophageal varices have three grades (I, II, III). In our study, the frequency of grade-II was 12.2% and grade-III was 80%. The findings of our study correlates with the findings of study of WM Shaikh et. al [20] of 2000 conducted at Larkana. In their study 84% patients were in grade-III. The diagnosis of oesophageal variceal bleeding was confirmed by UGI. In our study, we found haemtemesis, maleana and peripheral signs of liver disease in 80% of the patients and splenomegly in 100% of cases. Various studies from western countries have reported haemtemesis and maleana in 90% of cases. HBs Ag was found positive among 70 (77.7%) cases in our series while that of WM Shaikh et al. study and western countries studies 65% and 69% respectively. In our study infusion of octreotide showed significantly better control of bleeding in 49 / 61 (80.3%) then placebo octreotide group 13 / 29 (44.8%), our observation is consistent with reported studies. Besson et al. [21] reported control of bleeding in 85 / 89 (87%) of octreotide group and 72 / 101 (71 %) of placebo group. In Hwang et al, [22] study in which octreotide was compared with vasopressin in control of oesophageal variceal bleeding. They observed initial control of bleeding in octreotide group 21 / 24 (88%). Successful control of bleeding was observed in randomized trial by Sung et al. Besson et al. [23] in 84% of octreotide group.

In randomized study of Sivri et al. [24] control of bleeding was achieved within 6 hours in 73.3% of patients receiving octreotide. In McKee et al. [25] randomized trial initial control of bleeding was achieved within 48 hours in 18 / 20 (90%) patients receiving octreotide. In our study total 16 (17.7%) patients of both groups developed re-bleeding after 72 hours of initial control. Our observations are consistent with studies of WM Shaikh et al. [20], Sivri et al. [24] 22.7% and 13.3% respectively.

In our study total of 15 (16.6%) patients of both groups expired after 04 days of hospital stay. Our observations correlates with study of WM Shaikh et al.[20] and Sung et al i-e. [23] 04 patients and 03 patients respectively. In our study, serious side effects associated with octreotide therapy were nausea, abdominal pain and hyperglycemia, they were observed in 10 patients who received the bolus dose, which resolved with symptomatic treatment. Our finding correlates with the findings of reported western and local studies.

CONCLUSION AND RECOMMENDATIONS

In light of results of our study and its comparison with other studies, we concluded that octreotide is safe, cost effective; easily available does not need any special equipment, trained personnel and has very few side effects. We recommend that if any upper Gastrointestinal bleeding patient is encountered and history and examination suggest the variceal bleed then immediately start with octreotide whether in hospital or out side the hospital.

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