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# Comparative Efficacy of Terlipressin and Octreotide along with Endoscopic Band Ligation in the Management of Esophageal Variceal Bleeding

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## Abstract

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Esophageal variceal bleeding is a medical emergency that carries a high mortality rate despite appropriate management. Terlipressin and Octreotide are two common agents used as adjuvant agents in the management of variceal bleeding. The objective of this study is to compare the effectiveness of Terlipressin with Octreotide along with endoscopic band ligation in the management of esophageal variceal bleeding in cirrhotic patients. This randomized control study was carried out at the Department of General Medicine, Fatima Memorial Hospital, Lahore, for six months extending from February 2019 to July 2019. A total of 100 cirrhotic patients were selected /based on predetermined inclusion and exclusion criteria. The patients were randomly divided into two groups of equal strength. Hence, 50 patients were included in Group A and 50 patients were included in Group B along with banding. Group A received Terlipressin whereas Group B received Octreotide. The two groups were monitored for variceal bleeding for 72 hours. The mean age of the patients in Group A was  $55.9 \pm 7.3$  years and for the patients in Group B it was  $56.8 \pm 7.4$  years. In Group A, 36 (72.0%) male and 14 (28.0%) female patients were included. In Group B, there were 34 (68.0%) male and 16 (32.0%) female patients. In Group A, the treatment was effective for 46 (92.0%) patients and in Group B, 36 (72.0%) patients had an effective treatment. It is concluded from this study that Terlipressin is statistically more effective than Octreotide in terms of preventing esophageal variceal bleeding.

**Keywords:** effectiveness, esophageal varices, liver cirrhosis, Terlipressin, Octreotide

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## 1. Introduction

Cirrhosis of liver is a combination of irreversible hepatic fibrosis and regenerative nodules formation due to constant hepatic injury. The most common cause of this injury worldwide is alcohol but hepatitis B and C are also major causes in the third world countries. The symptoms of liver cirrhosis range from being asymptomatic to jaundice, infertility, loss of hair, and pulmonary hypertension depending on the extent of the liver injury [1, 2]. The

disturbed architecture of liver due to fibrosis leads to increased vascular resistance, hyperdynamic circulation, and splanchnic vasodilation, ultimately causing the local complication of portal hypertension. Portal hypertension causes gastropathy and esophageal varices [1, 3]. Other complications due to hepatocellular failure include ascites, edema, hepatorenal syndrome, hepatic encephalopathy and hepatopulmonary syndrome [4].

Esophageal varices is a known complication due to portal hypertension in cirrhotic patients which occurs with a lifetime incidence of 80-90% [5]. The percentage occurrence of esophageal variceal bleeding (EVB) is 12% in the first year and 33% after three years [6, 7]. EVB is a medical emergency that carries a high mortality rate despite appropriate management. Endoscopic intervention along with pharmacological treatment achieves the control of bleeding in 70-80% of episodes [8, 9]. Endoscopic interventions used for EVB include endoscopic variceal band ligation (EVL) and if EVL proves unsuccessful, the other option is endoscopic injection sclerotherapy (EIS), [10].

Adjuvant pharmacological treatment is also a gold standard along with EVL. Terlipressin and Octreotide are two mainstays of pharmacotherapy. Treatment with EVL alone is inferior to the administration of EVL with Terlipressin [11]. The use of Terlipressin along with EVL not only increases the efficacy of the treatment but also reduces the chances of rebleeding from esophageal varices [11, 12, 13, 14, 15]. Terlipressin and Octreotide are not only meant for adjuvant treatment but they are also claimed as an equivalent to endoscopic therapy and are efficient enough to control variceal bleeding [16,17,18]. Although Terlipressin (95.4%) was reported to be more efficient than Octreotide (74.2%) [16].

The current study was designed to compare the effectiveness of Terlipressin with Octreotide in the management of esophageal variceal bleeding. Although both Terlipressin and Octreotide act as vasoconstrictors but Terlipressin has a prolonged biological activity with substantially less

side effects. The administration of Terlipressin and Octreotide along with EVBL was reported to be an effective drug choice with no side effects [17].

One of the two previous local studies had a smaller sample size of 57 subjects, whereas the other is more than 5 years old. Terlipressin and Octreotide both are safe and effective and can be used for treating patients [18].

The aim of this article is to compare the effectiveness of Terlipressin and Octreotide along with endoscopic band ligation in the management of esophageal variceal bleeding in cirrhotic patients. The current study may help to decide the best pharmacological intervention and management plan in the future for patients with esophageal variceal bleeding.

## 2. Methodology

This randomized control study was conducted at the Department of General Medicine, Fatima Memorial Hospital, Lahore for a period of six months extending from February 2019 to July 2019. A sample of 100 patients (50 in each group) was selected using non-probability consecutive sampling and the sample size was calculated using WHO's sample size calculator for two proportions (2 sided) with 95% confidence level.

### 2.1. Inclusion Criteria

All cirrhotic patients within the age group of 40-65 years of both gender with upper GI bleed during the last 24 hours were included in this study.

### 2.2. Exclusion Criteria

Patients with the following characteristics were excluded from the current study.

1. Endoscopically proven non-variceal/bleeding (no varices seen).
2. Bleeding from gastric varices or due to portal hypertensive gastropathy on endoscopy.
3. Patients with peripheral arterial disease as per previous medical record.
4. Patients with a history of thrombocytopenia or other bleeding disorders (immune mediated thrombocytopenia, Von Willibrand disease, etc.).

### 2.3. Data Collection

A total of 100 cirrhotic patients fulfilling the inclusion criteria were selected from the medical wards of Fatima Memorial Hospital, Lahore. Approval from the Hospital Ethical Committee was obtained. The purpose of the study was explained to each participant and their informed consent was also obtained. The patients were enrolled in the study after their endoscopy was performed for diagnosing esophageal varices at presentation. The patients were randomly (by lottery method) divided into two groups. Terlipressin was administered to 50 patients included in Group A and Octreotide was administered to 50 patients included in Group B along with banding within 24 hours of upper GI bleed. Group A received Terlipressin 2mg (10ml) by IV bolus followed by 1mg (5ml) IV every 6 hours and then infusion by infusion pump at the rate of 50ml/h for 72 hours. Group B received 100ml bolus of 100µg IV Octreotide prepared as 1µg Octreotide in 1 ml of 0.45% dextrose saline. Group B was then continued on 50µg/h Octreotide as continuous infusion by infusion pump at the rate of 50µg/h for 72 hours. The two groups were monitored for variceal bleeding. The final outcome was efficacy in

preventing variceal bleeding within 72 hours. All this information was collected on a prescribed proforma.

### 2.4. Statistical Analysis

The collected data was analyzed using SPSS version 20. Chi square test was used to find out the significance of drug efficacy between the groups at p value of <0.05.

### 3. Results

The mean age of the patients in Group A was 55.9±7.3 years and the mean age of the patients in Group B was 56.8±7.4 years. In Group A, there were 16 (32.0%) patients in the age range of 40-50 years, 18 (36.0%) patients in the age range of 51-60 years and 16 (32.0%) patients in the age range of 61-65 years. In Group B, there were 12 (24.0%) patients in the age range of 40-50 years, 14 (28.0%) patients in the age range of 51-60 years and 24 (48.0%) patients in the age range of 61-65 years.

As far as the distribution of patients by sex is concerned, in Group A there were 36 (72.0%) male and 14 (28.0%) female patients, while in Group B there were 34 (68.0%) male and 16 (32.0%) female patients (Table 2).

The mean duration of cirrhosis in Group A was 7.2±3.4 years and in Group B, it was 5.0±2.7 years. In Group A, there were 12 (24.0%) patients in whom the duration of cirrhosis was 1-4 years, 20 (40.0%) patients in whom the duration of cirrhosis was 5-8 years and 18 (36.0%) patients in whom the duration of cirrhosis was 9-12 years. In Group B, there were 22 (44.0%) patients in whom the duration of cirrhosis was 1-4 years, 24 (48.0%) patients in whom the duration of cirrhosis was 5-8 years and 04 (08.0%) patients in whom the duration of cirrhosis was 9-12 years.

As far as the effectiveness of the treatment is concerned, in Group A there were 46 (92.0%) patients who exhibited the effectiveness of the treatment and 4 (8.0%) patients showed no effectiveness of the treatment. In Group B, there were 36 (72.0%) patients who exhibited the effectiveness of the treatment and 14 (28.0%) patients showed no signs of the effectiveness of the treatment. All these variables with their respective distributions are shown in Table 1.

The stratification of age with respect to the effectiveness of the treatment and the stratification of gender with respect to the effectiveness of the treatment are shown in Table 2 and Table 3, respectively.

#### 4. Discussion

Terlipressin and Octreotide are two common agents used as adjuvant agents in the management of variceal bleeding. Both of these agents were claimed as equivalent to endoscopic therapy in randomized studies [16, 18]. The combination of banding ligation and Terlipressin infusion for 2 days was reported superior to the sole infusion of Terlipressin for 5 days. It caused the reduction of very early rebleeding and treatment failure in patients with inactive variceal bleeding at endoscopy [11].

EVB occurs in 10–20% of cirrhotic patients every year and each bleeding episode can be associated with in-hospital mortality [7]. EVB remains the major cause of death in these patients, although the mortality rate has decreased substantially during the last 20 years [19, 20]. Currently, the keystone of the therapy of acute EVB is endoscopic variceal band ligation (EVBL).

Moreover, vasoactive agents such as Terlipressin, Octreotide, Vapreotide and

Somatostatin are recommended to be used as adjunctive therapy and were found to be highly effective in the management of these patients. Furthermore, these vasoactive drugs are recommended to be continued for 72–120 h (3–5 days) by various guidelines including Baveno IV, since the risk of rebleeding is considered to be the highest in the first 5 days of index bleed [21, 22]. The use of Terlipressin as adjunctive therapy has received attention recently and it was found to be associated with survival benefits as compared with the endoscopic intervention alone or when administered with other vasoactive agents [14, 15, 23].

Octreotide, a Somatostatin derivative, is equally effective as vasopressin in acute variceal bleeding when used in an infusion form [24, 25]. Recent studies showed that Terlipressin, a synthetic analogue of vasopressin, effectively controls variceal bleeding with/minimal side effects, even when used for an extended period of time [26].

In our study, the mean age of the patients included in Group A was  $55.9 \pm 7.3$  years and for Group B it was  $56.8 \pm 7.4$  years. In the study of Azam et al., 2012, the mean age of the patients included in the Terlipressin administered group was  $49.7 \pm 12.1$ , while for the Octreotide administered group it was  $49.8 \pm 11.2$  years. These figures are comparable to our study. In our study, Group A comprised 72% male and 28% female patients, while Group B comprised 68% male and 32% female patients. Similarly, in the study of Azam et al., 2012, there were 75.4% male and 24.6% female patients in the Terlipressin administered group and 73.8% male and 26.2% female patients in the Octreotide administered group, which is comparable with our study [12].

In Group A variceal bleeding was controlled in 92% patients within 72 hours, while in Group B variceal bleeding was controlled in 72% patients within 72 hours. In the study of Ansari et al., 2017, bleeding was controlled in 95.4% patients of the Terlipressin administered group and in 74.2% patients of the Octreotide administered group. These figures are comparable with our study [17]. In another study conducted by Cho et al., bleeding was controlled in 98% patients in the Terlipressin administered group and in 96% patients in the Octreotide administered group [27]. While in the study of Abid et al., the efficacy of Terlipressin vs. Octreotide in esophageal variceal bleeding was noted in 92.6% patients in the Terlipressin administered group and in 95.6% patients in the Octreotide administered group [16]. Furthermore, in a study by Azeem et al., the efficacy of Octreotide was reported as 87.69% and the efficacy of Terlipressin was reported as 96.92% in the prevention of early variceal rebleed [28]. A study by Fatima et al. also showed 90% efficacy in the case of Terlipressin and 70% efficacy in the case of Octreotide. Moreover, rebleed was seen only in 3.3% patients treated with Terlipressin and in 6.7% patients treated with Octreotide. The efficacy of Terlipressin for 24 hours vs. 72 hours was compared in a study. The efficacy of the treatment of Terlipressin for 24 hours was found to be 96.9% and for 72 hours, it was found to be 98.5% [28].

All the above mentioned studies are comparable with our study, so it can be concluded that Terlipressin is statistically more effective than Octreotide in terms of preventing esophageal variceal bleeding. Moreover, Terlipressin is also seen to be more effective than Octreotide in preventing

esophageal variceal rebleed at an early stage.

## 5. Ethics Approval and Consent

The study protocols and informed consent documents were approved by the Institutional Bioethics Review Committee (IBRC).

## 6. Availability of Data

The datasets used and/or analyzed during the study are available with the corresponding author and can be seen on a reasonable request.

## 7. Competing Interests

The authors declare no competing interests.

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