
ORIGINAL ARTICLE

Outcome Comparison of Terlipressin and Octreotide in Patients Having Severe Gastrointestinal Bleed Due to Portal Hypertension

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ABSTRACT

Objective: The aim of the study is to compare hyponatremia as a complication of treatment with terlipressin and octreotide in patients having severe gastrointestinal bleed due to portal hypertension.

Materials and Methods: This randomized controlled trial was conducted at Department Of Medicine Mayo hospital, King Edward Medical University Lahore. 60 patients were divided into two groups randomly by taking 30 patients in **Group-A** who received Terlipressin 1 mg 6 hourly and same no. of patients in **Group-B** who received Octreotide 50 microgram per hour IV infusion both for 5 days. Daily electrolyte monitoring was done to see the Hyponatremia as the complication of the treatment.

Results: The mean age in group-A was 41.46 ± 8.58 years and in group-B the mean age was 44.20 ± 5.01 years. In group-A there were 17 (56.67%) male and 13 (43.33%) female patients while in group-B there were 12 (40%) male and 18 (60%) female patients. Hyponatremia was higher in group A, i.e. in 15(50%) patients as compared to group-B i.e. 4(13%) patients, p-value = 0.002.

Conclusion: In the light of these results it can be concluded that octreotide is a better treatment option than terlipressin in patients with upper gastrointestinal bleeding secondary to portal hypertension as far as hyponatremia is concerned because the acute decrease in serum concentration of sodium is more common in the later one.

Key words: Portal hypertension, gastrointestinal bleeding, Endoscopic findings

INTRODUCTION

Portal hypertension is defined as a pathological escalation of portal venous pressure leading to an increased portal pressure gradient above the upper normal value of 5 mm Hg. Portal hypertension has wide range of etiologies that mainly involve prehepatic, intrahepatic, and post hepatic sites.¹ Acute gastrointestinal (GI) bleeding continues to remain as the most detrimental and serious medical emergency with an incidence of (50–150)/100,000 each year.² It accounts for a mortality rate of 5%-15%.^{3,4} The etiology of upper gastrointestinal bleeding (UGB) can be divided into non-variceal bleeding (gastric ulcers, gastric erosions, duodenal ulcers, reflux esophagitis, malignancies, vascular ectasias, etc) and variceal bleeding (esophageal varices, fundal varices).⁴

Endoscopy is the first and most important diagnostic modality in patients with upper

gastrointestinal bleeding. Endoscopic diagnosis gives essential information which helps in the prediction of likely outcome and most crucially treatments can be delivered that can cease bleeding and simultaneously decrease the risk of re-bleeding.⁵

Both terlipressin and octreotide are the drugs that can be utilized to control the variceal bleeding in patients with upper GI bleed.⁶⁻⁸ Though their mechanism of action is different, both are equally effective in controlling the variceal bleed.⁹ Variceal bleeding is a complication that is frequently seen in cirrhotic patients with portal hypertension. Its frequency enhances with the increase in the duration of the liver cirrhosis.^{8,10}

Studies have revealed that hyponatremia is a common complication in the patients treated with terlipressin.¹¹ The exact pathophysiology though is not known. There has no clear documented proof

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of hyponatremia occurring as a complication of treatment with octreotide.^{9, 11, 12} The purpose of the study is to see hyponatremia as a complication of telipressin and to compare it with that of octreotide.

MATERIALS AND METHODS

Study design: Randomized controlled trial

Setting: Department Of Medicine Mayo hospital, King Edward Medical university Lahore

Sample size: Total 60 cases (30 in each group) were included in the study

Sampling technique:

Inclusion Criteria:

- Patient of any gender with proven cirrhosis and portal hypertension and varices in upper GI endoscopy.

Exclusion Criteria:

- Upper GI bleed other than variceal bleed.
- NSAIDs induced bleeding.
- Peptic ulcer disease.
- Gastric carcinoma.
- Malory Weiss tear.
- Vascular malformation.
- Patient of variceal bleed with ischemic heart disease.
- Pregnancy.

Data Collection Procedure:

60 patients presenting on medical floor meeting the inclusion criteria were selected. A written informed consent was obtained taken before the study. The demographic information like name, age, gender, address was collected through proforma. History and clinical examination findings were recorded. All the relevant investigations were performed including liver function tests and USG abdomen to document the cirrhosis of liver. Upper GI endoscopy was done to confirm the varices.

Once the varices are confirmed, patient was divided in two equal groups randomly using random number procedures. One group (Group-A) received terlipressin 1 mg 6 hourly and other group (Group-B) received Octreotide 50microgram per hour IV infusion both for 5 days. Daily electrolyte monitoring was done to see the hypomatremia as the complication of the treatment. All data was collected by researcher himself.

Data Analysis

All data was entered and analyzed using SPSS version 20. Qualitative data was presented in form of frequency (%) and quantitative data was presented in form of mean ± S.D. Chi-square test / Fisher’s Exact test was applied to compare categorical data such as gender and Hyponatremia in both study groups. Mann Whitney U test was applied to compare age and Na+ level in both study groups. P-value ≤ 0.05 was considered as significant value.

RESULTS

In this study, the mean age in group-A was 41.46 ± 8.58 years and in group-B the mean age was 44.20 ± 5.01 years. In group-A there were 17 (56.67%) male and 13 (43.33%) female patients while in group-B there were 12 (40%) male and 18 (60%) female patients. The mean Sodium Level in group –A and group-B was 128.00±10.66 and 137.80±5.40 respectively, the mean Na+ level in group B was statically higher in group-B as compared to group-A, p-value < 0.001. Moreover, Hyponatremia was seen among 15(50%) patients in group-A and in 4(13%) patients of group-B. Hyponatremia was statistically higher in group-A as compared to group-B, p-value = 0.002.

Table 1: Comparison of Age, Gender, Na+ Levels and Hyponatremia in Both Study Groups.

		Group-A (n=30)	Group-B (n=30)	p-value
		Terlipressin	Octreotide	
Age(Years)		41.46±8.58	44.20±5.01	0.136
Gender	Male	17 (56.67%)	12 (40%)	0.196
	Female	13 (43.33%)	18 (60%)	
Na+ Level		128.00±10.66	137.80±5.40	< 0.001
Hyponatremia	Yes	15(50%)	4(13.3%)	0.002
	No	15(50%)	26(86.7%)	

DISCUSSION

Gastroesophageal varcies can ensue due to portal hypertension in cirrhotic patients, when there is an

enhancement in the resistance to the portal blood flow and also because of an increased pressure of venous blood in the portal veins .Increased

resistance can be structural (due to alteration of liver vascular architecture by a process of fibrosis and formation of regenerative nodules) and dynamic (increased hepatic vascular tone due to dysfunctional endothelial lining and decrease in bioavailability of nitric oxide).¹³

Terlipressin or octreotide are both being used to control variceal bleeding. In portal hypertensive animals, pre-infusion of octreotide followed by the addition of terlipressin has an additive or complementary effect on splanchnic hemodynamics.¹⁴ Terlipressin is itself a prodrug that in turn helps to release vasopressin into circulation which is very effective in the treatment of patients with variceal bleeding as a consequence of portal hypertension.^{7, 15} Its efficacy is attributed by the virtue of its extensive agonistic action on V1 vasopressin receptors that are found in great abundance inside splanchnic circulation. When V1 receptors are activated, they lead to splanchnic vasoconstriction and ultimately cause decrease in portal and variceal pressure.¹⁶

Octreotide is a synthetic analogue of somatostatin that has a longer half life. The half-life, however has nothing to do with its prolonged hemodynamic effects, what might be caused by rapid desensitization or tachyphylaxis.^{17, 18} Studies also suggest the effectiveness of terlipressin as monotherapy is much greater than combination of octreotide and telipressin.¹⁴

Sola E, et al reported that 1.72% of patients presenting with variceal bleed as a result of portal hypertension developed severe hyponatremia with standard doses of terlipressin.¹¹ This emphasized upon the researchers to observe the effects of terlipressin on serum sodium concentration in patients who are treated with it for gastrointestinal bleeding. They concluded that treatment with terlipressin for gastrointestinal bleeding quite often leads to an abrupt reduction in serum sodium levels, which can prove fatal in affected patients.¹¹

Another study reported that octreotide and terlipressin in combination did not have any cumulative effect in reduction of hepatic venous pressure gradient in cirrhotic patients. In addition, the systemic hemodynamic changes were comparable between the two groups.¹⁴

Comparison of Hyponatremia as a complication of Terlipressin and Octreotide has not been discussed widely in a single trial. A study conducted Aga Khan Hospital compared both these drugs and reported that terlipressin wasn't inferior to Octreotide in terms of efficacy when

used as an adjuvant therapy in the treatment of variceal bleeding. In terlipressin group, duration of hospital stay was much shorter as compared to octreotide group but at the same time it didn't have any clinical significance.¹⁹ In our study we found that Hyponatremia was seen among 15(50%) patients in group-A and in 4(13%) patients of group-B. Hyponatremia was statistically higher in group-A as compared to group-B, p-value = 0.002. The complication of hyponatremia was higher in our study when compared with previous studies reported above.

So, it is very essential that clinicians should be vigilant while using terlipressin as it has hazardous neurological complications of acute hyponatremia that can have detrimental effects on the patients.¹¹

CONCLUSION

Hyponatremia is a common complication that can occur as a side effect of both octreotide and terlipressin. But according to this study greater no. of patients developed hyponatremia as a result of terlipressin use. So one need to be cautious regarding the possible effects of hyponatremia on the patients and therefore the use of Octreotide in such a scenario is more attractive and a safer option.

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