COMPARISON OF 1 DAY VERSUS 5 DAYS OF OCTREOTIDE INFUSION ALONG WITH ENDOSCOPIC THERAPY IN PREVENTING EARLY REBLEEDING AND MORTALITY FROM ESOPHAGEAL VARICES: A NATIONWIDE, MULTICENTER, NON-INFERIORITY, RANDOMIZED CONTROL TRIAL - PRELIMINARY RESULT

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Introduction

Baveno VII recommends vasoactive agents to achieve hemostasis and prevent rebleeding. However, an optimal shorter time frame limit for vasoactive drug therapy remains unclear. The aim of this study is to compare the efficacy of 1 day versus 5 days of octreotide infusion along with endoscopic therapy.

Method

This was a nationwide, multicenter, non-inferiority, randomized control trial including 151 patients with acute variceal bleeding who underwent endoscopic therapy; they were assigned randomly to 1 day (n=76) and 5 days (n=75) of continuous octreotide infusion (50 µg/hr). Rebleeding, transfusion requirement, and mortality were assessed.

Results

The study had predominantly male patients, with an average age of 55 years. The 5-day rebleeding (1.3% vs 1.3%, p = 0.99), 6-week rebleeding (9.2% vs 9.3%, p = 0.97), and 6-week all-cause mortality (7.8% vs 5.3%, p = 0.74) were similar in both groups. Patients in the 1-day group demonstrated fewer transfusion requirements, a significantly shorter time to initiate a solid diet, and a significantly reduced length of stay. The effect of proton pump inhibitor use was not associated with a decreased risk of variceal bleeding or adverse events in such patients. Hepatic encephalopathy grade 3/4 and no beta-blocker therapy at discharge were associated with increased mortality.

Conclusions

The 1-day regimen of octreotide infusion, following successful endoscopic therapy for variceal bleeding, demonstrates no inferiority compared to the standard 5-day regimen in preventing early rebleeding, 6-week rebleeding, and mortality.

Table 1. Baseline Characteristics and Clinical Outcomes			
	1-Day (N = 76)	5-Day (N = 75)	P Value
Demographic			
Age (year) *	55 ± 9.08	56 ± 9.08	0.823
Male (%)	65 (85.5)	62 (82.6)	0.631
Significant alcohol used (%)	63 (82.8)	57 (76)	0.294
HBV (%)	14 (18.4)	16 (21.3)	0.654
HCV (%)	8 (10.5)	11 (14.6)	0.443
History of esophageal varices bleeding (%)	29 (38.1)	28 (37.3)	0.917
History of endoscopic variceal ligation (%)	29 (38.1)	30 (40)	0.817
Child-Pugh score (point) **	7 (6 - 9)	7 (6 - 8)	0.402
Child-Pugh score (grade) (%)			0.650
A	26 (34.2)	23 (30.6)	
B	36 (47.3)	41 (54.6)	
C	14 (18.4)	11 (14.6)	
MELD score (point) **	14 (11 - 19)	12 (10 - 15)	0.082
At index of admission			
Systolic blood pressure (mmHg) *	114 ± 22.7	113 ± 22.74	0.792
SpO2 (%) **	99 (98 - 100)	99 (98 - 100)	0.707
Ascites (%)	23 (30.2)	24 (32)	0.818
Hepatic encephalopathy grade 3/4 (%)	4 (5.2)	5 (6.6)	0.745
Spontaneous bacterial peritonitis (%)	1 (1.3)	3 (4)	0.367
Hematocrit (%) *	23 ± 5.5	21 ± 5.5	0.051
Platelet count (cell/mm^3) **	108000 (79500 - 177000)	109000 (81000 - 153000)	0.632
INR **	1.39 (1.2 - 1.58)	1.35 (1.26 - 1.5)	0.609
Creatinine (mg/dl) **	0.93 (0.72 - 1.38)	0.9 (0.71 - 1.09)	0.537
Sodium (mmol/L) *	137 ± 4.6	136 ± 4.6	0.105
Aspartate aminotransferase (U/L) **	75 (37 - 141)	65 (38 - 113)	0.441
Alanine aminotransferase (U/L) **	36 (23 - 50)	39 (27 - 51)	0.500
Albumin (g/dl) *	2.8 ± 0.54	2.8 ± 0.54	0.448
Total bilirubin (mg/dl) **	1.5 (1 - 3.75)	1.2 (0.74 - 2.37)	0.025
Managements			
High volume center (>30 cases/year) (%)	46 (60.5)	46 (61.3)	0.919
Total packed red cell used (unit) **	2 (0 - 2)	2 (1 - 3)	0.002
Prior to endoscopy (unit) **	1 (0 - 2)	2 (0 - 2)	0.0501
Following endoscopy (unit) **	0 (0 - 1)	0 (0 - 1)	0.035
Active bleeding upon endoscopy (%)	12 (15.7)	19 (25.3)	0.147
Time to solid diet (hour) **	24 (20 - 24)	24 (16 - 48)	0.036
Beta-blocker prescription at discharge (%)	69 (90.7)	66 (88)	0.578
Type of Beta-blocker (%)			0.957
Carvedilol	17 (24.6)	16 (24.2)	
Propranolol	52 (75.3)	50 (75.7)	
Proton pump inhibitor therapy after endoscopy, (%)	60 (78.9)	59 (78.6)	0.966
Length of stay (day) **	5 (4 - 6)	6 (5 - 7)	<0.001
Outcomes			
5-day rebleeding (%)	1 (1.3)	1 (1.3)	0.999
6-week rebleeding (%)	7 (9.2)	7 (9.3)	0.979
6-week all-cause mortality (%)	6 (7.8)	4 (5.3)	0.745

Table 2 Multivariable Analysis for Predictors of 6-week rebleed and 6-week all-cause mortality			
	Adjusted Odds Ratio	**95% Confidence Interval**	**P Value**
6-week rebleed			
1-Day of Octreotide	1.09	0.31 - 3.75	0.886

High volume center (>30 cases/year)	0.45	0.12 - 1.65	0.230
HCV infection	2.02	0.43 - 9.36	0.368
SpO2 (%)	0.801	0.59 - 1.08	0.151
Ascites	1.40	0.39 - 5.041	0.604
Hepatic encephalopathy grade 3/4	4.75	0.83 - 27.22	0.080
AST (U/L)	0.99	0.97 - 1.004	0.187
6-week all-cause mortality			
1-Day of Octreotide	3.56	0.51 - 24.41	0.196
High volume center (>30 cases/year)	0.54	0.06 - 4.39	0.573
Hepatic encephalopathy grade 3/4	99.78	1.02 - 9743.06	0.049
Creatinine (mg/dl)	1.058	0.44 - 2.51	0.899
Sodium (mmol/L)	0.82	0.65 - 1.02	0.087
Albumin (g/dl)	0.48	0.05 - 4.203	0.513
Child-Pugh score (point)	0.39	0.13 - 1.15	0.090
MELD score (point)	1.08	0.84 - 1.38	0.532
Total packed red cell used (unit)	0.803	0.51 - 1.25	0.340
Active bleeding upon endoscopy	7.48	0.86 - 65.05	0.068
Without beta-blocker prescription at discharge	11.11	1.13 - 108.62	0.038