International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Comparative Efficacy of Octreotide Andterlipressin in the Treatment of Esophageal Variceal Bleeding

Dr. R. K. Chaitanya Reddy[1], Dr. R. Selva Sekaran[2], Dr. R. Ramasubramanian[3], Dr. Shirish .N .D[4]

Department of Medical Gastroenterology, Thoothukudi Government Medical College Hospital, Thoothukudi, TamilNadu, India
Email: *rchaitanya13[at]yahoo.com*

Abstract: ***Background: To compare the efficacy of Terlipressin and Octreotide in control of acute esophageal variceal bleeding. Methods: In this comparative study 80 patients presenting with acute variceal bleed, during a period of one year(from August 2020 to July 2021), were selected. Patients were divided into two groups of 40 each by lottery method. Group A received Terlipressin, while Group B received Octreotide. Patients in these groups were matched for age, gender, grade of esophageal varices, and Childs-Pugh Class. The outcomes were recorded in terms of control of bleeding, rebleeding or death. Results: Out of 80 patients, 55% were male. Bleeding stopped within 48 hours in 78.75 % of patients (90% in group A vs 70 % in group B). Active bleeding continued in 5% vs 10% in group A and B respectively. Rebleeding after 48 hours was observed in 1.25% vs 3.75% patients in group A and B respectively. No death occurred in group A while one patient died in group B (0% vs 1.25%). The relative risk of continuous bleeding was 2.0 times more in group B as compared to group A, 95% confidence interval 0.867 to 10.014. Conclusions: Patients who were given Terlipressin had better control of bleeding, reduced risk of rebleeding, death as compared to those who were given Octreotide.***

Keywords: Octreotide, Terlipressin, Liver Cirrhosis, Portal hypertension, Esophageal Variceal bleed

1. Introduction

Variceal bleeding is a major cause of death in patients with cirrhosis and portal hypertension. Two types of drugs, namely, Terlipressin (vasopressin analogue) and Octreotide (somatostatin analogue) are being used for management of acute variceal bleed along with endoscopic therapy. It can be classified as Micro or macro-nodular on the basis of histopathology, but the etiological classification is more relevant in clinical scenario. In the order of prevalence, Viral hepatitis B and C,alcoholic liver disease are the common causes followed by autoimmune hepatitis, sclerosing cholangitis, primary biliary cirrhosis, hemochromatosis, and Wilson's disease.[1]Although themortality rate has decreased significantly during the past several decades due to remarkable improvements in diagnostic and therapeutic modalities for its management, acute variceal bleeding remains a leading cause of death in cirrhotic patients.[2,3]Three vasoactive drugs—terlipressin, somatostatin, and octreotide—play a role in the control of variceal bleeding by reducing portal blood flow and portal pressure.[4,5] Previous studies showed that the use of vasoactive drugs was associated with a significantly lower risk of mortality and transfusion requirements, and an improved control of bleeding.[6,7]Endoscopic variceal band ligation (EVL) has been the recommended preferred procedure for control of acute esophageal variceal bleeding, although endoscopic sclerotherapy (ES) can be used in this setting if EVL is technically not feasible.[8]Regarding the methods of endoscopic therapy, several studies suggested that the probability of rebleeding from esophageal varices (EVs) is significantly lower for endoscopic variceal ligation (EVL) than for endoscopic injection sclerotherapy (EIS).[9,10]Both Terlipressin and Octreotide when used for initial management of variceal bleed provide adequate time for endoscopic therapeutic measures which can be carried out within next 24 to 48 hours. Both these drugs have been compared in different studies on international level over the last two decades. Some studies showed that terlipressin is better in managing acute variceal bleed, while in other trials octreotide came out as a better option.[11-14] Still others reveal no statistically significant difference between the two treatment options.[15-19]

2. Patients and Methods

This comparative study was performed in in-patient wards of Medical Gastroenterology, General Medicine and emergency department of Thoothukudi Government Medical College and Hospital.

Eighty patients were divided into two groups of 40 each. Group A comprised patients who received Terlipressin 1mg 6 hourly for 48 hours. Group B comprised patients who received Octreotide 50 micrograms/ hour for 48 hours.

Patients with already known history or clinically suspected liver cirrhosis admitted to our hospital because of hematemesis and/or melena were included in the study after meeting the following criteria: (1) evidence of bleeding (hematemesis and/or melena) during the past 24 hours; (2) endoscopically proved hemorrhage from esophageal varices, with bleeding considered to be variceal when emergency endoscopy (within 6 hours of admission) showed active bleeding from a varix (oozing or spurting), stigmata of recent hemorrhage, or fresh bloodin the stomach and esophagogastric varices as the only potential source of bleeding; (3) age between 18 and 65 years; (4) no previous use of vasopressin and/or somatostatin to control the bleeding episode. Patients referred from other hospitals were included if they met the above-mentioned criteria and had not undergone EVL in the previous 5 days.

Variables in this study were age of patient, gender, Child-Pugh class, Grade of esophageal varices on endoscopy, Hemoglobin (Hb), Prothrombin time(PT), activated partial thromboplastin time (APTT), number of blood and fresh frozen plasma(FFP) units transfused, and Outcome. Patients

were continuously monitored for vitals, hematemesis and melena. The control of bleeding was established by stable pulse rate and blood pressure, and no fresh episode of hematemesis or melena at the end of 48 hours which was documented as 'bleeding stopped'. If hematemesis or melena continued after 48 hours despite treatment it was documented as "bleeding continued". If bleeding stopped initially with treatment, and then restarted after 48 hours as a fresh episode of hematemesis or melena during the same hospital admission, it was documented as 'rebleeding". Non responders or rebleeders underwent emergency variceal band ligation.

All patients underwent endoscopy after first 24-48 hours. If a patient was re-admitted after being discharged following successful control of bleeding a few weeks later, he or she was included in the study as a new case. 95% Confidence interval of relative risk was calculated by using confidence interval calculator available online at www.hutchon.net/confidRR.htm.2 x 2 table was drawn to calculate risk of continuous bleeding: 2 x 2 table: Formula for relative risk RR is: RR = a/ a+c ÷ b / b+d. Chi square test was used to compare the effect of treatment given, Child-Pugh Class and grade of varices on the outcome at 95% level of significance using SPSS version 10.0.

All patients gave written informed consent to participate in the study. The study protocol was approved by the ethical committee of our hospital.

3. Results

Out of 80 patients, 44 (55%) were male, 36(45%) were females. Mean age of the patients was 52.60 years (standard deviation 9.12) in group A. Mean age of patients in group B was 54.40 years (standard deviation 8.29). The age, Prothrombin time (PT), activated partial thromboplastin time (aPTT), and hemoglobin (Hb) were comparable in both groups (Table 1).

The variceal bleeding stopped in 63 patients (78.75%), of which 35 were in group A and 28 in group B. Bleeding continued in 12 patients(13.3%) ,4 in group A and 8 in group B. Rebleeding after 48 hours occurred in 4 patients (5%), 1 in group A and 3 in group B. One patient (1.25%) belonging to group B died in the study (Table 2). Chi square 4.068,degree of freedom 3 (p = 0.27).The Relative risk of continuous bleeding was 2.0 times more with treatment B as compared to those receiving treatment A. The 95% confidence interval for treatment B to treatment A risk of continuous bleeding RR calculated was 0.867 to 10.014 (Table 3). Majority had F2 grade of varices (Table 4). Bleeding stopped in all 7 patients with F1 varices.

In group A, 4 patients had F1 varices, 18 had F2 and 18 had F3 varices. In group B, 7 patients had F1, 17 had F2 and 16 had F3 varices (p = 0.45) (Table 4). 15 patients (18.75%) belonged to Child-Pugh class A, 45 (56.25%) to Child class B, and 20 (25%) belonged to class C. The outcome varied according to Child class as the severity of disease increased. Bleeding stopped in all 15 patients of Child class A, bleeding stopped in 40 patients with Child class B, but continued in 3 patients and rebleeding occurred in remaining 2 patients with Child class B. Among the 20 patients with Child class C, bleeding stopped in 11, continued in 7, rebleeding occurred in 2, while 1 patient belonging to Child class C died (p = 0.008). In group A, 6 patients belonged to Child class A, 26 to class B and 9 to class C. Whereas in group B, 9 patients had Child class A, 19 belonged to class B and 11 to Child class C (p = 0.50). (Table 5).

Patients in group A were given 1.89 +1.74 blood transfusions; while in group B 2.21+1.16 blood units were transfused. Number of FFPs transfused in both groups was also similar (3.34+ 2.62 versus 2.83+ 3.08). No cardiovascular side effects were observed in any of the patients during the study. No renal side effects were observed during the study.

Table 1: Descriptive Statistics of the Two Groups

	Treatment given	N	Mean	SD
Age in years	Terlipressin	40	52.60	9.12
	Octreotide	40	54.40	8.29
PT at start (seconds)	Terlipressin	40	8.90	5.677
	Octreotide	40	10.52	10.51
PT after 48 hours(seconds)	Terlipressin	40	3.70	1.78
	Octreotide	40	4.10	4.24
APTT at start (seconds)	Terlipressin	40	9.30	5.95
	Octreotide	40	12.46	13.05
APTT after 48 hours(seconds)	Terlipressin	40	2.70	1.80
	Octreotide	40	3.50	2.80
Hb at start	Terlipressin	40	8.346	2.598
	Octreotide	40	8.435	2.231
Hb after 48 hours	Terlipressin	40	9.972	1.040
	Octreotide	40	9.858	1.190
Blood transfusion	Terlipressin	40	1.89	1.74
	Octreotide	40	2.21	1.16
FFP transfusion	Terlipressin	40	3.34	2.62
	Octreotide	40	2.83	3.08

PT= Prothrombin time, aPTT= activated partial thromboplastin time,
Hb= hemoglobin, FFPs = Fresh frozen plasma

Table 2: Comparison of Outcome between the two groups

Outcome / Given treatment	Bleeding Stopped	Bleeding Continued	Rebleeding	Death	Total
Group A Terlipressin	35(43.75%)	4 (5%)	1 (1.25%)	0	40 (50%)
Group B Octreotide	28(35%)	8 (10%)	3 (3.75%)	1 (1.25%)	40 (50%)
Total	63(78.75%)	12(15%)	4(5%)	1(1.25%)	80 (100%)

Table 3: Relative Risk of Continuous Bleeding

	GroupA (terlipressin)	GroupB (octreotide)
Bleeding continued	a=5	b=11
Bleeding stopped	c=29	d=24

Risk of continuous bleeding with Drug A = a/ a+c = 0.31; Risk of continuous bleeding with Drug B = b/ b+d = 0.15; Relative Risk = a / a+c ÷ b / b+d = 2.0;95 % Confidence interval = 0.867 to 10.014

Table 4: Comparison of Grades of Varices between groups

Grades of Varices / Treatment Given	F1	F2	F3	Total
Group A Terlipressin	4 (5%)	18(22.5%)	18(22.5%)	40(50%)
Group B Octreotide	7(8.75%)	17(21.25%)	16(20%)	40(50%)
Total	11(13.75%)	35(43.75%)	34(42.5%)	80(100%)

Table 5: Comparison of Child-Pugh Class between two Groups

Treatment given	Child Class A	Child Class B	Child Class C	Total
Terlipressin Group A	6 (7.5%)	26 (32.5%)	9 (11.25%)	40 (50%)
Octreotide Group B	9 (11.25%)	19 (23.75%)	11 (13.75%)	40 (50%)
Total	15 (18.75%)	45 (56.25%)	20 (25%)	80 (100%)

4. Discussion

Risk of variceal bleeding and the mortality associated with it increase with advanced Child-Pugh class as well as size of varices as seen on endoscopy. Hence, it was considered important to match the two groups for these confounding variables.[20] In a study from St.George University, USA, bleeding was controlled in all (100%) patients belonging to Child class A, 88.2%(30 out of 34) patients of Child class B, and only 46.6%(7 out of 15) among Child class C, thereby proving the fact that advanced Child class is associated with poor prognosis. Results showed that prognosis is worse with advanced variceal grade on endoscopy since bleeding was controlled in 100% patients having F1 varices, 88.8%(24 out of 27) patients with F2 varices and 61.5% (16 out of 26) patients with F3 varices.

The present study showed bleeding being controlled in 78.75% patients, active bleeding continuing in 15% and rebleeding after 48 hours occurring in 5%. The mortality rate was 1.25%. Patients who received Terlipressin showed a better control of bleeding when compared to those who received Octreotide. Patients who were on Terlipressin had a lower incidence of rebleed after 48 hours compared to Octreotide (1.25% versus 3.75%) and zero mortality compared to 1.25% in the Octreotide group (p = 0.35). The single patient who died in the Octreotide group had advanced liver disease as evident by Child class C and F3 varices on endoscopy. The cause of death was massive bleeding. The relative risk of continuous bleeding was 2.0 times more in the Octreotide group than in the Terlipressin group. This apparent difference between the two groups is marginal, and is not statistically significant as the 95% confidence interval for relative risk of continuous bleeding calculated above was 0.867 to10.014. The difference between the two groups is not statistically significant.

In a multi-center randomized trial conducted in five centers in France, comparing Terlipressin with Octreotide, bleeding was controlled in 59% of those receiving Terlipressin and 78 % of patients receiving Octreotide.[21-26]

The dose of Terlipressin used in the French study was 2 mg and then 1 mg 4 hourly for 24 hours.[40]In present study 1mg Terlipressin was given 6 hourly for 48 hours. The dose of Octreotide in present study was 50 µg/ hour IV infusion for 48 hours. In the French study, octreotide was given as continuous intravenous infusion of 25 µg/hr over 12 hours and then 100 µg at hour 12 and hour 18 subcutaneously. These minor differences in the dose and duration of drugs did not have a significant impact on the results. Even the comparatively lower doses used in our study were able to effectively control the bleeding and showed similar or lower mortality in both groups.

In a Cochrane review, Terlipressin was compared with Placebo in seven studies, in which the former showed significant reduction in mortality. In various small studies where Terlipressin was compared with Octreotide, no difference was demonstrated in any major outcome.[27-34] Similarly in present study, there is no statistically significant difference between the two groups. In a study reported by Baik SK et al, 2mg IV bolus of Terlipressin was compared with 100µg IV bolus of Octreotide followed by 250µg/hr Octreotide infusion.[9] They compared the hemodynamic effects of the two drugs documented by Hepatic venous pressure gradient (HVPG) and portal venous flow (PVF). However these measurements are beyond the scope of present study due to lack of facilities for measuring HVPG in our hospitals. In one study by Badaruddin AH et al26, hemodynamic effects of Terlipressin were measured as increase in blood pressure and decrease in pulse rate after administration of 2mg bolus followed by 2mg 6 hourly in patients with bleeding esophageal varices. However they did not compare Terlipressin with Octreotide. Haemostasis was achieved more frequently with Octreotide compared to Terlipressin (RR 1.62). [35]

When patients came with acute variceal bleed, apart from Terlipressin or Octreotide, Blood and Fresh frozen plasma(FFP) was also transfused to achieve immediate hemodynamic stability and correct coagulopathy. This did not differ significantly in the two groups, with 1.97 + 1.71 units of blood , and 3.10 + 2.67 FFPs being transfused in the Terlipressin group, and 2.17 + 1.12 units of cross matched blood and 2.63 + 3.11 FFPs in the Octreotide group. In the Aga Khan study, 3.7 + 2.2 versus 4.0 + 2.6 packed cell units were transfused in the Terlipressin and Octreotide groups

respectively.13 In the study in France, mean transfusion requirement was 3 blood units in the Terlipressin group and 1 blood unit in the Octreotide group34. The number of blood transfusions required is an indirect estimate of severity of variceal hemorrhage, which is almost same in both the groups.

After the initial 24-48 hours, patients in both groups were offered endoscopic therapy. The choice between sclerotherapy and band ligation was based on the expertise of the operator available. In 3 patients of the Terlipressin group, balloon tamponade was done using Sengstaken Blakemore tube after failure to control the bleeding in first 48 hours. In all of these patients bleeding was controlled after tamponade or endoscopy. In the Aga Khan study, all patients underwent variceal band ligation within 24 hours of admission.[20] In another local study, Octreotide was compared with sclerotherapy. 12 The results showed better outcome where octreotide was used in combination with endoscopy.[36-40] Endoscopic therapy in combination with a vaso-active drug should be offered to all patients with variceal bleed as it is the gold standard of treatment.

As it is known that Vasopressin causes coronary vasoconstriction, it can cause coronary ischemia in some patients. Terlipressin, though a synthetic analogue of Vasopressin has minimal systemic side effects. In the French study, Terlipressin was used in combination with transdermal nitroglycerine, but still 2 patients developed bradycardia and one of them died.[41] No cardiovascular side effects were observed in the present study even with Terlipressin.

The financially deprived patients were provided free of cost treatment through the hospital department fund. Administration of Terlipressin is much easier than Octreotide as the latter requires continuous infusion. The advantages of terlipressin over octreotide include better efficacy, low cost and easy administration of terlipressin.

5. Conclusions

1) In those with esophageal variceal bleeding, the patients who were treated with Terlipressin had comparatively better control of bleeding, less incidence of rebleeding, and lower mortality compared to those who were treated with Octreotide.
2) Esophageal variceal bleeding is one of the commonest and life threatening medical emergencies in patients with portal hypertension due to advanced liver cirrhosis. We should know which is the best drug available for management of acute variceal bleed in emergency department, before the patient is referred for endoscopy. The drug should be effective as well as safe.
3) Further workup to study and compare the efficacy of vasoactive drugs to endoscopic therapy should be done.
4) In efficacy, cost and ease of administration, terlipressin is superior to octreotide in patients with esophageal variceal bleeding.

References

[1] Chung RT, Podolsky DK. Cirrhosis and its complications. In: Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, editors. Harrison's Principles of Internal Medicine.20th ed.New York: McGraw Hill, 2018
[2] D'Amico G, De Franchis R. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. Hepatology 2003; 38: 599-612.
[3] McCormick PA, O'Keefe C. Improving prognosis following a first variceal haemorrhage over four decades. Gut 2001; 49:682-685.
[4] Baik SK, Jeong PH, Ji SW, Yoo BS, Kim HS, Lee DK, Kwon SO, et al. Acute hemodynamic effects of octreotide and terlipressin in patients with cirrhosis: a randomized comparison. Am J Gastroenterol 2005;100:631-635.
[5] Bosch J, Kravetz D, Rodes J. Effects of somatostatin on hepatic and systemic hemodynamics in patients with cirrhosis of the liver: comparison with vasopressin. Gastroenterology 1981;80:518-525.
[6] D'Amico G, Pagliaro L, Bosch J. The treatment of portal hypertension: a meta-analytic review. Hepatology 1995;22:332-354.
[7] Wells M, Chande N, Adams P, Beaton M, Levstik M, Boyce E, Mrkobrada M. Meta-analysis: vasoactive medications for the management of acute variceal bleeds. Aliment Pharmacol Ther 2012;35:1267-1278.
[8] . e dFranc his R .Evolving cons ens us in portal hypertens ion report of the Baveno IV consensus workshop on methodology of diagnosis and therapy in portal hypertension . JHepatol 2005 ; 43 : 167 – 67 .
[9] Lo GH, Lai KH, Cheng JS, Lin CK, Huang JS, Hsu PI, Chiang HT. Emergency banding ligation versus sclerotherapy for the control of active bleeding from esophageal varices. Hepatology 1997;25:1101-1104.
[10] Villanueva C, Piqueras M, Aracil C, Gomez C, Lopez-Balaguer JM, Gonzalez B, Gallego A, et al. A randomized controlled trial comparing ligation and sclerotherapy as emergency endoscopic treatment added to somatostatin in acute variceal bleeding. J Hepatol 2006;45:560-567.
[11] Walker S, Kreichgauer HP, Bode JC. Terlipressin vs. somatostatin in bleeding esophageal varices: a controlled, double-blind study. Hepatology 1992;15:1023-30.
[12] Pedretti G, Elia G, Calzetti C,Magnani G,Fiacadorri F. Octreotide versus terlipressin in acute variceal hemorrhage in liver cirrhosis. Emergency control and prevention of early rebleeding. Clin Investig 1994;72:653-59.
[13] Feu F, Ruiz del Arbol L, Banares R, Planas R, Bosch J. Double-blind randomized controlled trial comparing terlipressin and somatostatin for acute variceal hemorrhage. Gastroenterology 1996;111:1291-99.
[14] Walker S, Kreichgauer HP, Bode JC. Terlipressin (glypressin) versus somatostatin in the treatment of bleeding esophageal varices--final report of a placebo-controlled, double-blind study.Zeitschrift fur Gastroenterologie 1996;34:692-98. .
[15] Baik SK,Jeong PH,Ji SW,Yoo BS,Kim HS,Lee DK, et al.Acute hemodynamic effects of octreotide and

terlipressin in patients with cirrhosis: a randomised comparison.Am J Gastroenterol 2005;100:631-35.
[16] Umar M, Khar HB, Anwar F, Zahid M, Jilani RA. The management of acute variceal bleed by Octreotide. J Rawalpindi Med Coll 2000;4(1&2):14-16.
[17] Ahmed SI,Jamil M,Mahmud MR, Naseemullah M,Hanif M. Non-selective beta blockers versus endoscopic sclerotherapy for the prevention of variceal haemorrhage in decompensated chronic liver disease. J Rawalpindi Med Coll. 2004;8:61-64.
[18] Cheema TM, Sohail M, Anjum M,Arif M. Octreotide and endoscopic sclerotherapy in acute variceal hemorrhage. J Rawalpindi Med Coll 2004;8:93-95.
[19] Salih M, Abid S, Mumtaz K, Jafri N, Hamid SS, Shah H et al.Efficacy and cost effectiveness of Terlipressin versus Octreotide in bleeding esophageal varices in combination with endoscopic band ligation. Hepatology. 2005;42:211A.
[20] Salih M, Abid S, Mumtaz K, Jafri N, Hamid SS, Shah H et al.Efficacy and cost effectiveness of Terlipressin versus Octreotide in bleeding esophageal varices in combination with endoscopic band ligation. Hepatology. 2005;42:211A.
[21] Sherlock S, Dooley J. Diseases of the liver and biliary system.11th ed. Oxford: Blackwell Science, 2002.
[22] Khan AN, Macdonald S, Ali M, Sherlock D. Portal hypertension. emedicine [online] last updated 2007April 18.
[23] Abraldes JG, Dell'Era A, Bosch J. Medical management of variceal bleeding in patients with cirrhosis. Can J Gastroenterol 2004;18(2):109-13.
[24] Buencamino C. Esophageal varices. Emedicine [online] last updated 2005 September 1 [cited 2007 April 22].
[25] Gow PJ, Chapman RW.Modern management of oesophageal varices. Postgrad Med J 2001;77:75-81.
[26] Carale J, Mukherjee S. Portal hypertension. [serial online]last updated on 2006 March 10[cited 2007 March 15].
[27] Portal venous system. Image. [online][cited 2007April 23].
[28] Garcia-Tsao G. Portal hypertension. Curr Opin Gastroenterol 2003; 19(3):250-58
[29] Freytag A, Deist T. Atlas of Gastroenterological Endoscopy. [online]2003[last updated 2003 Dec 30][cited 2007April23].
[30] D'Amico G, Pagliaro L, Bosch J, Pharmacological treatment of portal hypertension: An evidence-based approach. Semin Liver Dis 1999; 19(4):475-505.
[31] Therapeutic options for esophageal variceal bleed management. Image[online][cited2007April20].Availablefrom:URL: http://www.omge.org/globalguidelines/guide08/g_data8_fr.php.
[32] Shah HA, Mumtaz K, Jaferi W, Abid S, Hamid S. Sclerotherapy plus octreotide versus sclerotherapy alone in the management of gastro-oesophageal variceal hemorrhage. J Ayub Med Coll .2005;17(1):10-14.
[33] Badruddin AH, Rasool G, Chaudry MA.Hemodynamic effects of Terlipressin in patients with bleeding esophageal varices secondary to cirrhosis of liver. J Coll Physicians Surg Pak. Dec 2006:16(12):755-59
[34] Ioannou G, Doust J, Rockey DC. Terlipressin for acute esophageal variceal hemorrhage (Cochrane review). In: The Cochrane Library, Issue 4, 2003
[35] Iannou GN, Doust J, Rockey DC. Systemic review: terlipressin in acute oesophageal variceal haemorrhage. Ailment Pharmacol Ther.2003 Jan;17(1):53-64.
[36] Lebrec D. A discussion of how terlipressin limits mortality in cases of bleeding oesophageal varices. Eur J Gastroenterol Hepatol. 1998; 10:549-52.
[37] Hirschowitz fiberoptic endoscope. 1960[online image] [cited 2007April20]. Available from: URL: http://www.case.edu/artsci/dittrick/site2/museum/artifacts/group-d/fiberscope.htm.
[38] Sengstaken-Blakemore tube[online image] [cited 2007April 21]. Available from: URL: http://www.thoracic.org/sections/clinical-information/critical-care/critical-care-cases/cases/variceal-hemorrhage-updated%20management.html.
[39] Sengstaken-Blakemore tube for esophageal tamponade. [online image][Cited 2007April21]. Available from:URL:http://www.medical-dictionary.thefreedictionary.com/esophageal+tube.
[40] Shah NH, Umar M, Anwar F, Ishtiaq O, Bashir K. Association of Child-Pugh class with patterns of mortality in hepatitis C virus related chronic liver disease.J Rawalpindi Med Coll. 2001; 5(2):65-67.
[41] Silvian C, Carpentier S, Sautereau D, Czernichow B, Metreau JM, Fort E et al. Terlipressin plus transdermal nitroglycerine vs. Octreotide in the control of acute bleeding from esophageal varices: A multicenter randomized trial. Hepatology 1993;18:61-65.