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Severe Bradycardia caused by Octreotide in an Adolescent: A Case Report

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ABSTRACT

Background and Objective: Octreotide is a somatostatin analogue used to control upper gastrointestinal (GI) bleeding. Adverse effects observed include hyperglycemia, growth hormone deficiency, hypertension, Q-T interval prolongation, and ventricular fibrillation. In rare cases, mild bradycardia has been reported.

Case Report: A 16-year-old boy was admitted with shock due to hematemesis and melena a bleeding duodenal ulcer. He was treated with an intravenous venous octreotide infusion at a dose of 1 microgram/kg/hour, and bleeding was controlled with coagulation forceps and adrenaline injection. Because of rebleeding, octreotide was increased to 2 micrograms/kg/hour because of bleeding again. After 24 hours, he developed severe bradycardia (pulse rate (PR) 45/minute). His PR increased to 66/minute by 12 hours after octreotide was discontinued.

Conclusion: Octreotide can cause significant cardiovascular side effects. Bradycardia and cardiac conduction blocks may affect the hemodynamics of a child with acute GI bleeding.

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Introduction

In children and adolescents causes of upper gastrointestinal bleeding (UGIB) include erosive esophagitis, esophageal varices, gastritis, peptic ulcer disease, coagulation disorders, dieulafoy lesions (angiodysplasia), and caustic ingestions [1]. Throughout the world, the mortality rate for UGIB in children can range from 5% to 15% [1]. Initial treatment of UGIB is the stabilization of the general condition which should precede any instrumental investigation (usually endoscopy). The pharmacological treatment of UGIB includes 3 classes of drugs: acid suppression drugs (proton pump inhibitors), vasoactive drugs (terlipressin, somatostatin, and octreotide), and non-selective β-blockers (propranolol, nadolol, and carvedilol) [1]. Octreotide is an analog of somatostatin. It acts on the somatostatin receptors, which couple to phospholipase C via inhibitory G proteins, and causes vascular smooth muscle contraction [2]. It selectively causes splanchnic vasoconstriction and decreases portal blood flow, thereby indirectly decreasing variceal blood flow [1]. In children, intravenously octreotide is effective in decreasing acute gastrointestinal (GI) bleeding in children at dosages of 2-5 mcg/kg per hour administered by continuous infusion [1]. GI side effects are common which include diarrhea, nausea, abdominal discomfort, and gallbladder abnormalities. Other side effects are hypoglycemia, hyperglycemia, itching, headache, and dizziness [2]. Octreotide is used to control UGIB and has been used in many GI disorders [3]. Al-Hussaini observed significant adverse effects in 4 out of 21 children who were treated with Octreotide. They are hyperglycemia, growth hormone deficiency, hypertension, Q-T interval prolongation, and ventricular fibrillation [3]. Infrequently, mild bradycardia has been reported after octreotide administration [4]. Herewith we are reporting an adolescent boy who presented with shock due to a bleeding ulcer in the duodenum posterior wall. He was treated with octreotide infusion and endoscopy revealed an ulcer oozing with the visible vessel, the oozing ulcer was managed with adrenaline 5 ml injection, and the vessel ulcer base was coagulated by using coagulation grasper, which achieved hemostasis (Forrest 1 b duodenal ulcer). He developed severe bradycardia during octreotide infusion (pulse Rate 45/minute) and the pulse rate increased to 66/minute after stopping the octreotide.

Case Report

A 16-year-old boy presented with hematemesis and melena for one day referred to the district hospital. There was no history of drug ingestion/ fever/jaundice. His past medical history and birth history were unremarkable. There was no significant family history. His weight and height were 32.5 kgs and 155 cms (both are less than 3 rd centile according to the CDC growth chart), respectively. He was managed there with IV DNS 80 ml/hour, InjOndansetron 4 mg, Inj pantoprazole 30 mg, and Inj Vitamin K 5 mg. After 2 hours, he had one episode of a large amount of melena and developed shock. He was given 3 boluses of 10 ml/kg of NS given, 350 ml of PCV transfusion and referred to our hospital.

When he was admitted to our hospital about 6 hours after the onset of symptoms, the child was in shock. His vital signs were: temperature 99^{0}F, RR 20/minute, pulse rate(PR) 152/minute, low volume with cold peripheries, CFT more than 4 seconds and blood pressure (BP) only systolic 60 mm recordable. The child's shock was managed with two pints of PCV (packed cell volume), 1 FFP (fresh frozen plasma) and a noradrenaline infusion (0.5 microgram/kg/minute). Intravenous octreotide infusion at a dose of 1 microgram/kg/hour was started, along with pantoprazole infusion (1mg/kg/minute). Intravenous administration of the antibiotics InjPipericillin+Tazobactum and Injamikacin was started. The investigations are depicted in table 1. Abdominal ultrasonography, chest x ray and echocardiography were reported normal.

After 1 hour in our hospital, his vital signs were: temperature 99.4^{0}F, RR 22/minute, PR 150/minute, low volume with cold peripheries, CFT more than 4 seconds and BP 80/30 mm of Hg. His ECHO was normal. The noradrenaline infusion was increased to 0.6 microgram/kg/minute and a dobutamine infusion was added at 10 micro/kg/minute. Endoscopy was performed 9 hours after admission

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with Inj Propofol 50 mg and the patient tolerated the procedure. Endoscopy revealed a bleeding ulcer in the posterior wall of the duodenum. Inj adrenaline was injected and hemostasis was achieved.

There was no new bleeding 8 hours after endoscopy. His vital signs were: temperature 99.4^0F, RR 18/minute, PR 120/minute, good volume with warm periphery, CFT less than 3 seconds and BP of 96/58 mm Hg. Octreotide and noradrenaline infusions were slowly discontinued. His vital signs were stable. After a 24-hour endoscopy, he had melena again. His vital signs were: temperature 99.6^0F, RR 20/minute, PR 140/minute normal volume, CFT less than 3 seconds, and BP 90/60 mm Hg. He was restarted onoctreotide1 microgram/kg/hour and a repeat endoscopy was done under Inj Propofol 50 mg. Endoscopy revealed an oozing ulcer with a visible vessel, which was controlled with adrenaline 5 ml injection and the vessel base of the ulcer was coagulated with coagulation forceps, achieving hemostasis (duodenal ulcer Forrest 1 b).

After 12 hours after the second endoscopy, he had a small amount of melena. His vital signs were: temperature 99^0F, RR 20/minute, pulse rate 120/minute with normal volume, BP of 96/60 mm of Hg. Given the rebleeding, the octreotide infusion rate was increased to 2 micrograms/kg/hour. After a 12-hour infusion of 2 micrograms/kg/hr octreotide, his PR was 62/minute and BP was 102/64 mm Hg. Gradually, the heart rate decreased. After another 12 hours, his PR was 45/minute, regular, with good volume and BP of 110/70 mm Hg (Figure 1A). At this point, we discontinued octreotide, and his heart rate increased to 66/minute within 12 hours. After 3 days, his heart rate was 88/minute (Figure 1B). After 3 days, he was discharged with one tablet of pantoprazole 20 mg OD.

Table 1. Laboratory data of studied patient

Investigations	At admission	Day 2	Day3	Day 6
Hb(g/dl)	6.0	10	6.0	12.8
PCV	17.4	29.3	17.6	37.8
Total Counts (cells/mm3)	38950 (N80%,L16%,M4%)	31200 (N87%L,9%,M%)	15480 (N85%,L10%,M%)	13060, (N66%,L17%,M4%)
Platelets (cells/mm3)	2.13 lakhs	1.55	1.54	2.22
CRP (U/L)	1.9	-	-	-
Blood Urea (mg/dl)	53	-	35	-
Serum Creatinine (mg/dl)	0.82	-	0.73	-
Serum Sodium(mEq/l)	137	-	134	-
Serum Potassium (mEq/l)	5.8	-	3.9	-
Serum Bilirubin (mg/dl)	0.95	-	-	-
AST (U/L)	32	-	-	-
ALT(U/L)	24	-	-	-
Alkaline phosphatase (U/L)	200	-	-	-
PT (seconds)/control, INR	17/13.3, 1.35	-	-	-
APTT (seconds)/control	55/32	-	-	-
Serum Total protein (gm/dl)	3	-	-	-
Serum Albumin(gm/dl)	2.2	-	-	-
d-dimer (FEU/ml)	0.2	-	-	-

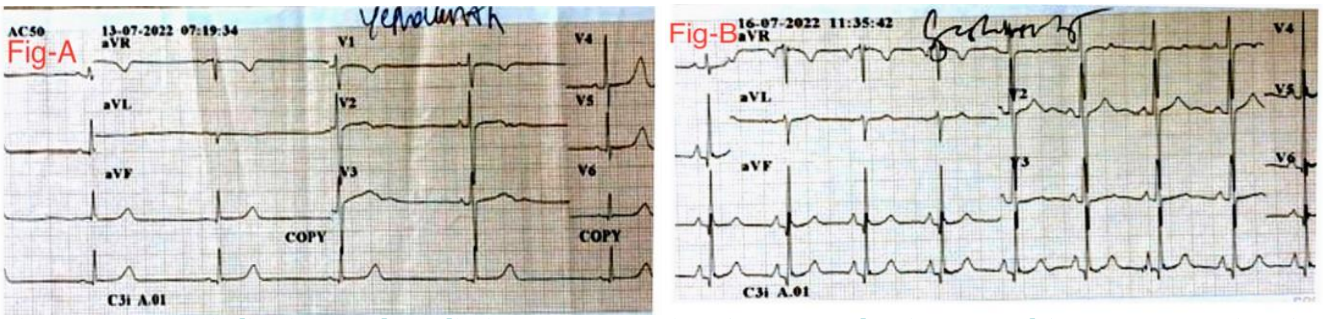

Figure 1. A: ECG indicating Bradycardia (Heart rate 45/minute), B: ECG showing Normal (Heart rate 88/minute)

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Discussion

In the current case, severe bradycardia of 45/minute was observed after octreotide infusion for UGIB. Octreotide administration can lead to mild bradycardia infrequently [4]. However, Icen et al. reported a complete heart block during octreotide infusion in a 62–year-old which was reversed by a temporary pacemaker [5]. Tuncer et al. found a complete heart block at the 60th hour of octreotide infusion, which recovered six days after cessation of octreotide [4]. The present case initially had tachycardia, but he developed bradycardia after an octreotide infusion of 2 microgram/kg/hour (65 microgram/hour). The cardiovascular effect appears to occur less frequently at 50 microgram/hour and more frequently at 250 microgram/hour doses [5]. We notice d bradycardia with a low-dose infusion rate of only 60 micrograms/hour. Yuhicoet al. also reported multiple asystolic events during an octreotide infusion at a relatively low dose [6]. Out of 21 children on octreotide treatment only one child had cardiovascular adverse effects [3]. An 8-year-old developed bradycardia which progressed into ventricular fibrillation on a high dose of octreotide (4 μg/kg/h). Electrocardiography revealed a prolonged corrected Q–T interval (0.46–0.48 second) (normal, <0.45 second). The patient was successfully resuscitated. During the follow-up after months of discontinuation of octreotide therapy, an electrocardiogram (ECG) showed persistent borderline Q–Tc intervals of 0.44-0.45 seconds, which raised the possibility of pre-existing congenital Q–T prolongation [3]. However, the Q-T interval was normal (0.44 seconds) in the current case. Among 34 children who received octreotide for the treatment of chemotherapy or acute graft versus host disease-induced diarrheal, common adverse effects observed were hyperglycemia, hyperbilirubinemia, nausea/vomiting, and abdominal cramping. The authors have not mentioned any cardiac side effects [7]. In a study by Testoni et al. regarding the safety of octreotide in hospitalized infants, the most common clinical adverse effect was hypotension [8]. Normal ranges of heart rate in children is depicted in the table 2 [9]. The mechanisms of bradycardia in octreotide infusion are not known. Octreotide increases systemic vascular resistance, and bradycardia may be a reflex response of a baroreceptor to increased systemic vascular resistance caused by octreotide. It may be a direct action of octreotide also [4, 5].

Table 2. Normal ranges of heart rate in children

Age Range [Years]	Heart Rate (Beats/minute)
Neonate	85-205
0-1	100-190
1-2	100-190
2-10	60-140
10-18	60-100

Conclusion

Octreotide can cause significant cardiovascular side effects. Bradycardia may affect the hemodynamics of a child with acute GI bleeding. Cardiac side effects are usually dose-dependent. Octreotide infusion must be started at a lower dose under electrocardiographic monitoring, preferably in an intensive care unit. The treating physician must keep an eye on cardiac side effects to avoid hemodynamic instability.

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Ethical approval

Parents gave us written informed consent for publication. There were no ethical issues to be addressed in this case report. There was no funding source for our study.

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Conflict of interest

There was no conflict of interest.

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