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Clinical effect of combination of octreotide and omeprazole in children with acute upper gastrointestinal bleeding and the levels of serum creatinine and serum urea nitrogen

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Abstract: Pediatric upper gastrointestinal bleeding refers to an acute massive hemorrhage of the upper digestive tract and biliary tract, which is a common clinical emergency in pediatrics. This study aimed to evaluate the clinical effect of octreotide combined with omeprazole in pediatric upper gastrointestinal bleeding. Totally 84 cases of pediatric upper gastrointestinal bleeding admitted to Ningbo Women and Children's Hospital from November 2019 to April 2021 were divided into groups according to the admission order. The control group received omeprazole treatment and the observation group received octreotide plus. The total clinical effective rate of children in the observation group was higher than that of the control group. The observation group was superior to the control group with respect to the average hemostasis time, hemostasis rate, rebleeding rate and length of stay after treatment. The observation group witnessed a significantly better quality of life than the control group. For children with acute upper gastrointestinal bleeding, the combination of omeprazole and octreotide yields a promising effect in the adjustment of blood creatinine and serum urea nitrogen levels and hemostasis, which is worthy of clinical application.

Keywords: Pediatric upper gastrointestinal bleeding, octreotide, omeprazole, curative effect, serum creatinine, serum urea nitrogen.

INTRODUCTION

Upper gastrointestinal bleeding, one of the common diseases in gastroenterology, is characterized by sudden onset, critical and urgent conditions and rapid progress (Kamboj *et al.*, 2019) and may occur at any age, which poses a great threat to the patient's physical and mental health and life safety in a short period of time. Systemic diseases, peptic ulcers, gastrointestinal mucosal inflammation and tumors are the contributory factors for upper gastrointestinal bleeding (Poddar, 2019). The clinical manifestations are mainly hematemesis, melena and bloody stools, and decreased appetite. Furthermore, children are more susceptible to the disease, and massive bleeding would occur during an acute attack. Improper and delayed treatment will give rise to shock and even death in children (Lirio, 2016), which underlines the significance of reasonable drug therapies. Herein, the effectiveness of omeprazole combined with octreotide therapy was investigated to explore better treatment methods for upper gastrointestinal bleeding.

MATERIALS AND METHODS

General information

Totally 82 children with acute upper gastrointestinal hemorrhage admitted to Ningbo Women and Children's Hospital from November 2019 to April 2021 were selected and grouped according to the order of admission time. In the control group (n=41), there were 22 males and 19 females, with an average age of average (9.11±2.13) years. The bleeding volume of patients in the control group ranged 100-755ml, with an average of (421.02±19.85) ml and in terms of causes of bleeding, there were 10 cases of duodenal ulcer, 15 cases of gastric ulcer, 11 cases of acute gastric mucosal lesions and 5 cases of ruptured esophagus and fundus varicose veins. In the observation group (n=41), there were 23 males and 18 females, with an average age of (9.22±2.18) years. The bleeding volume of patients in the observation group ranged 121-760ml, with an average of (430.02±19.99) ml, and in terms of causes of bleeding, there were 9 cases of duodenal ulcer, 16 cases of gastric ulcer, 10 cases of acute gastric mucosal lesions and 6 cases of rupture of esophageal and gastric varices. There was no statistically significant difference between the two groups in general information (P>0.05). The family members knew and signed the consent form before enrollment. This study was approved by the ethics committee of Ningbo Women and Children's Hospital, with the approved no. of CLS2018-12/214. The ethical principles of *Declaration of Helsinki* were followed (Shrestha and Dunn, 2020).

Inclusion criteria

Aged 3~14 years old; Met the relevant diagnostic criteria in *Internal Medicine*, all manifested as hematemesis,

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melena and other symptoms; bleeding volume <800ml; confirmed by gastroscopy, X-ray barium meal, etc.;

Exclusion criteria

Combined with cardiovascular and cerebrovascular diseases, vital organ dysfunction, malignant tumors; drug allergies; mental disorders; cognitive and communication disorders.

Methods

After admission, blood transfusion was given to replenish blood volume, fluids were administered to maintain water and electrolyte balance, and routine examinations were performed. After admission, transfusion was given to replenish blood volume, infusion of fluids was administered to maintain water and electrolyte balance, and routine examinations were performed. Symptomatic administration of gastric mucosal protective agents and anti-infective therapy was administered and eating and drinking were prohibited during bleeding. The control group received 40mg omeprazole (manufacturer: Beijing Taiyang Pharmaceutical Co., Ltd., approval no. H19990114, specification 20mg) in 100ml of normal saline by intravenous drip twice a day. The observation group received 40mg omeprazole and 0.1mg octreotide (manufacturer: Beijing Bai'ao Pharmaceutical Co., Ltd., approval no. H20061309, specification: 1ml: 0.1mg) in 100ml of normal saline. A micro-pump injection was adopted at a rate of 0.25mg/h for 12 hours. Both groups continued medication for one week.

During treatment, the patients' diet was under strict control. After successful hemostasis, a light diet was maintained and stimulating foods were averted to prevent irritation of the digestive tract. For those with shock, low-flow oxygen inhalation was given, the mouth was regularly cleared to maintain oral hygiene. The respiration, heart rate, blood pressure, blood in the stool, liver and kidney function, and blood gases of patients were continuously monitored and recorded for 24 hours. In case of no cessation of bleeding or unabated bleeding after three days of medication, gastroscopic hemostasis was performed immediately.

Observation indicators

1) Clinical efficacy: If hematemesis, melena and bleeding symptoms completely disappeared after medication, no active bleeding occurred for 24 hours, the fecal occult blood test was negative, and the diet returned to normal, the treatment efficacy was considered cured. If hematemesis and melena symptoms after medication disappeared, the gastrointestinal bleeding slowly stopped after 72 hours, and the stool occult blood test was weakly positive a week later, the treatment efficacy was considered effective. If hematemesis, melena and other symptoms did not improve, gastroscopy showed that the gastrointestinal tract was still bleeding, and the stool occult blood test was positive, the treatment efficacy was considered ineffective. Total effective rate = (cured + effective)/n*100%.

2) Adverse reactions: The adverse reactions of the children after medication, such as blood pressure drop, vomiting, anorexia and irregular heartbeat were observed and recorded.

3) Hemostasis: The average bleeding time, 24h hemostasis rate, 48h rebleeding rate and hospitalization time of the two groups were recorded and compared.

4) Clinical indicators: The changes in serum creatinine, serum urea nitrogen and hemoglobin levels of the two groups of children were detected and compared.

5) Quality of life: The Generic Quality of Life Inventory-74 (GQOLI-74) (Ai, 2021) was used to evaluate the children's life status after treatment, including physiological functions, emotional functions, social functions, and material life status. The full score is 100 points, with higher score indicating a better quality of life.

STATISTICAL ANALYSIS

The statistical software SPSS23.0 was used for data analysis. The count data were expressed as (%) and analyzed by χ^2 test. The measurement data were represented by ($\bar{x}\pm s$) and analyzed by the t-test. $P<0.05$ indicated that the difference was statistically significant.

RESULTS

Comparison of clinical efficacy and adverse reaction rate

The total effective rate of the observation group after medication was remarkably higher than that of the control group ($P<0.05$). No significant difference was found in theincidence of adverse reactions between the two groups after medication ($P>0.05$), see table 1.

Comparison of hemostasis

The average hemostasis time and hospital stay of children in the observation group were shorter than those of the control group and their hemostasis rate was higher than that of the control group; the 48-hour rebleeding rate was lower than that of the control group (all $P<0.05$, table 2).

Comparison of clinical indicators

Before treatment, there was no significant difference in serum creatinine, serum urea nitrogen, and hemoglobin levels between the two groups of children. After treatment, the improvement of serum creatinine, serum urea nitrogen and hemoglobin levels in the observation group was significantly better than that of the control group ($P<0.05$), as listed in table 3.

Comparison of quality-of-life scores

Table 4 shows that markedly higher GQOLI-74 scores of children were observed in the observation group after treatment in contrast to the control group.

Table 1: Comparison of clinical efficacy and adverse reaction rate (n, %)

Groups	N	Cured	Effective	Ineffective	Total effectiveness	Total
Observation group	41	31 (75.61)	9(21.95)	1(2.44)	40 (97.56)	2(4.88)
Control group	41	28(68.29)	6(14.63)	7(17.07)	34(82.92)	4(9.76)
χ^2	-	-	-	-	4.986	0.719
P	-	-	-	-	0.026	0.396

Table 2: Comparison of hemostasis ($\bar{x}$ ±s, %)

Groups	N	Mean hemostasis time (h)	Hospital stay (d)	Hemostasis rate	Rebleeding rate
Observation group	41	20.88±2.51	5.72±1.44	35(85.36)	3(7.32)
Control group	41	39.55±3.88	8.03±2.17	26(63.41)	11(26.83)
t	-	25.869	5.679	5.185	5.513
P	-	0.000	0.000	0.023	0.019

Table 3: Comparison of clinical indicators ($\bar{x}$ ±s)

Groups	N	Blood creatinine (μmol/L)		Urea Nitrogen (mmol/L)		Hemoglobin (g/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	41	80.25±6.57	102.71±9.32	13.54±3.77	6.09±2.11	89.44±4.88	105.77±6.55
Control group	41	80.24±6.62	91.43±7.85	13.38±3.84	8.96±2.98	89.73±4.59	99.11±5.42
t	-	0.007	5.927	0.190	5.033	0.277	5.016
P	-	0.994	0.000	0.849	0.000	0.782	0.000

Table 4: GQOLI-74 score comparison ($\bar{x}$ ±s, points)

Groups	N	Physiological function	Emotional function	Social function	Material life
Observation group	41	91.15±7.51	91.72±7.44	91.58±7.98	90.49±7.37
Control group	41	82.05±6.44	82.02±6.67	81.91±6.85	81.82±6.76
t	-	5.889	6.216	5.887	5.551
P	-	0.000	0.000	0.000	0.000

DISCUSSION

Acute upper gastrointestinal bleeding generally refers to the acute bleeding caused by the pathological changes in the digestive tract on the ligament of flexion, such as the esophagus, stomach, and duodenum (Gralnek *et al.*, 2015; Farrar, 2018). It is a critically ill acute disease, with the main symptom of hematemesis and black stools. During the onset, continuous bleeding in the digestive tract is frequently seen, which eventually leads to shock due to excessive blood loss (Maia *et al.*, 2021). Children are vulnerable to the disease in the clinical setting, which poses a high risk of death in light of its serious bleeding and urgent situation. Therefore, the exploration of effective treatment measures remains a critical issue to be addressed in clinical practice to control the bleeding volume and bleeding speed and lower the clinical fatality rate (Nasher *et al.*, 2017).

The pathogenesis of acute upper gastrointestinal bleeding is relatively complicated. The previous clinical treatment mainly relied on the combination of three-cavity two-bladder tube compression with pituitrin treatment to stop bleeding (Hernández-Gea *et al.*, 2018). Although this method can temporarily control the bleeding, it will give rise to erosion of the gastric fundus and esophageal mucosa consequent to long-term compression, leading to recurrence of bleeding in the later stage, which even threatens the life of the patient. With the advancement and development of medical technology, endoscopic hemostasis is a preferred method with favorable treatment efficiency. However, the effect of endoscopic treatment has been reported to be unsatisfactory in children, which, as a result, necessitates drug treatment (Aoki *et al.*, 2019).

The reasonable use of drugs for children with acute upper gastrointestinal bleeding has become the key issue in clinical research. The pH value of the stomach juice has been reported as one of the gastrointestinal bleeding factors. To be specific, a low pH value will compromise the hemostatic effect and a pH value greater than 6 will lead to a normal blood coagulation function in the body, which will induce platelet aggregation to achieve good hemostasis (Thomson *et al.*, 2015). Therefore, acid inhibitors are considered the first-line drugs for clinical medication to ameliorate the acidic environment, abate gastric acid secretion, and further adjust the pH value of the stomach juice (Scherdin *et al.*, 2021). Omeprazole is a

commonly used acid-suppressing drug that can effectively inhibit the secretion of gastric acid, protect the mucosa of the digestive tract, reduce the fibrin solubility of the mucosa, and promote blood coagulation (Iida *et al.*, 2015). The acid suppression effect of omeprazole is to interfere with gastric parietal cell acid secretion by reducing the H+-K+-ATPase activity, with a long-lasting and strong acid suppression effect. It increases the pH of the stomach juice and reduces the stomach and esophagus mucosal damage. Blood in the digestive tract at a gastric fluid pH above 6.0 will rapidly form a blood clot, which consequently achieves hemostasis (Abed *et al.*, 2020). However, monotherapy with omeprazole yields mediocre treatment results and is not suitable for patients with excessive bleeding, high body oxygen consumption, and symptoms such as syncope and shock, which entails combined drug treatment (Hunt and Scarpignato, 2018).

Herein, octreotide was applied in combination with o omeprazole. Octreotide is synthetic octapeptide somatostatin that inhibits the secretion of glucagon, enhances the sensitivity of blood vessels and improves the contractility of vascular smooth muscle, thereby reducing portal pressure and achieving local hemostasis (Lamberts and Hofland, 2019). Octreotide also accelerates blood clot contraction and coagulation, promotes platelet aggregation, prevents gastroesophageal reflux, improves gastric mucosal blood supply, accelerates mucosal repair, and prevents rebleeding triggered by the rupture of the blood clot. Moreover, it features a good tolerance and a safety profile, with a long-lasting efficacy and few adverse reactions such as occasional hypoglycemia and headaches (Malla *et al.*, 2020). The gastric acid is the major cause of upper gastrointestinal bleeding, which highlights the importance of inhibition of gastric acid secretion, adjustment of the pH value in the stomach juice, and the protection of the gastric mucosa. In this study, the combined treatment of octreotide and omeprazole was used in observation group and the results showed that the total effective rate of treatment and quality of life scores of the observation group were significantly higher than those of the control group, and the hemostatic effect, blood creatinine, urea nitrogen, and hemoglobin indicators after medication were significantly better than that of the control group, while the adverse reaction results of the two groups were not significantly different. These results confirm that the combined treatment yields a promising curative effect, with high drug safety, and plays a positive role in improving the efficiency of hemostasis and shortening the bleeding time.

This study confirmed that the improvement effect of serum creatinine, serum urea nitrogen and hemoglobin levels in the observation group was significantly better than that of the control group. Urea nitrogen is synthesized in the liver, and its concentration in the blood is related to gastrointestinal bleeding. Serum creatinine is a metabolite; when bleeding occurs, the protein breakdown in the child's body will increase, which will lead to an increase in the level of urea nitrogen. Accordingly, its changes show great potential as an evaluation criterion for the prognostic effect of hemostasis (Kumar *et al.*, 2017). Scientific choice of drug combination therapy can rapidly shorten the visceral clotting time to achieve hemostasis, with few adverse reactions and a low rebleeding rate. Additionally, it also shortens the hospital stay, reduces medical costs, and accelerates recovery.

CONCLUSION

From our study, the combination of octreotide and omeprazole for the treatment of children with acute upper gastrointestinal bleeding helps repair the damaged gastrointestinal mucosa, reduces the amount of bleeding, boosts the post-treatment quality of life of the children, and accelerates the recovery of digestive tract function.

REFERENCES

Abed MN, Alassaf FA, Jasim MHM, Alfahad M and Qazzaz ME (2020). Comparison of antioxidant effects of the proton pump-inhibiting drugs omeprazole, esomeprazole, lansoprazole, pantoprazole and rabeprazole. *Pharmacology,* **105**(11-12): 645-651.

Ai H (2021). A randomised controlled trial: Effect of the meticulous nursing model on the treatment compliance and quality of life of patients with upper gastrointestinal bleeding. *Ann. Palliat Med.,* **10**(8): 8737-8745.

Aoki T, Hirata Y, Yamada A and Koike K (2019). Initial management for acute lower gastrointestinal bleeding. *World J. Gastroenterol.,* **25**(1): 69-84.

Farrar FC (2018). Management of Acute Gastrointestinal Bleed. *Crit Care Nurs Clin. North Am.,* **30**(1): 55-66.

Gralnek IM, Dumonceau JM, Kuipers EJ, Lanas A, Sanders DS, Kurien M, Rotondano G, Hucl T, Dinis-Ribeiro M, Marmo R, Racz I, Arezzo A, Hoffmann RT, Lesur G, de Franchis R, Aabakken L, Veitch A, Radaelli F, Salgueiro P, Cardoso R, Maia L, Zullo A, Cipolletta L and Hassan C (2015). Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy,* **47**(10): a1-46.

Hernandez-Gea V, Berbel C, Baiges A and Garcia-Pagan JC (2018). Acute variceal bleeding: Risk stratification and management (including TIPS). *Hepatol Int,* **12**(Suppl 1): 81-90.

Hunt RH and Scarpignato C (2018). Potent acid suppression with PPIs and P-CABs: What's New? *Curr. Treat Options Gastroenterol.,* **16**(4): 570-590.

Iida H, Inamori M, Okuno K, Sekino Y, Sakai E, Okubo H, Higurashi T, Endo H, Hosono K, Yoneda M, Koide

T, Takahashi H, Goto A, Kubota K, Saito S, Maeda S, Nakajima A and Gotoh E (2015). Early effects of oral administration of esomeprazole and omeprazole on the intragastric pH. *Hepatogastroenterology,* **62**(138): 493-496.

Kamboj AK, Hoversten P and Leggett CL (2019). Upper gastrointestinal bleeding: Etiologies and management. *Mayo. Clin. Proc.,* **94**(4): 697-703.

Kumar NL, Claggett BL, Cohen AJ, Nayor J and Saltzman JR (2017). Association between an increase in blood urea nitrogen at 24 hours and worse outcomes in acute nonvariceal upper GI bleeding. *Gastrointest Endosc.,* **86**(6): 1022-1027.e1021.

Lamberts SWJ and Hofland LJ (2019). Anniversary review: Octreotide, 40 years later. *Eur. J. Endocrinol.,* **181**(5): R173-r183.

Lirio RA (2016). Management of Upper Gastrointestinal Bleeding in Children: Variceal and nonvariceal. *Gastrointest Endosc Clin. N. Am.,* **26**(1): 63-73.

Maia S, Falcão D, Silva J and Pedroto I (2021). The clinical impact of Rockall and Glasgow-Blatchford scores in nonvariceal upper gastrointestinal bleeding. *GE Port. J. Gastroenterol.,* **28**(4): 243-252.

Malla I, López S, Busquet L, Lipsich J, Sierre S, Cervio G and Cuarterolo M (2020). Long-acting release octreotide for pediatric upper gastrointestinal bleeding. *Rev. Chil. Pediatr.,* **91**(2): 251-254.

Nasher O, Devadason D and Stewart RJ (2017). Upper gastrointestinal bleeding in children: A tertiary United Kingdom children's hospital experience. *Children* (Basel), **4**(11): 95.

Poddar U (2019). Diagnostic and therapeutic approach to upper gastrointestinal bleeding. *Paediatr Int. Child Health,* **39**(1): 18-22.

Scherdin Y, Halldestam I and Redeen S (2021). Incidence and mortality related to gastrointestinal bleeding, and the effect of tranexamic acid on gastrointestinal bleeding. *Gastroenterology Res.,* **14**(3): 165-172.

Shrestha B and Dunn L (2020). The declaration of helsinki on medical research involving human subjects: A review of seventh revision. *J. Nepal Health Res. Counc.,* **17**(4): 548-552.

Thomson MA, Leton N and Belsha D (2015). Acute upper gastrointestinal bleeding in childhood: Development of the Sheffield scoring system to predict need for endoscopic therapy. *J. Pediatr. Gastroenterol. Nutr.,* **60**(5): 632-636.