Research Article

Effects of Vitamin C Combined with Growth Inhibitors on Gastrointestinal Bleeding in Cirrhosis

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Received 28 May 2022; Revised 3 July 2022; Accepted 5 July 2022; Published 18 July 2022

Academic Editor: Mohammad Farukh Hashmi

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The purpose of this study was to investigate the effect of vitamin C combined with growth inhibitors on serum miR-130a, nitric oxide (NO), and hemostasis in the treatment of upper gastrointestinal bleeding (UGIB) in cirrhosis. Eighty patients with cirrhosis UGIB treated in our hospital from March 2021 to March 2022 were selected and divided into two groups using the random number table method. The control group received growth inhibitor treatment, while the observation group was given vitamin C combined with growth inhibitor treatment for 3 d. The hemostatic effect, serum laboratory indexes (miR-130a, NO), liver function indexes (aspartate aminotransferase (AST), alanine aminotransferase (ALT)), adverse effects, and 24 h hemostasis rate were compared between the two groups. The hemostasis time in the observation group was shorter than that in the control group, and the blood transfusion volume was lower than that in the control group. There was no statistical difference regarding the portal blood flow, miR-130a, NO, AST, and ALT indexes between the two groups before treatment. After treatment, the portal blood flow, miR-130a, NO, AST, and ALT indexes in both groups were lower than those before treatment, and all of them were lower in the observation group than in the control group. Adverse reactions showed no significant difference between the two groups of patients with cirrhosis UGIB, while the 24 h hemostasis rate in the observation group (97.50%) was significantly higher than that in the control group (77.50%). Vitamin C combined with growth inhibitor was effective in the treatment of cirrhotic UGIB, which could effectively shorten the hemostasis time, reduce the transfusion volume and portal blood flow, and improve miR-130a, NO, and liver function levels of patients, with higher safety, and is worthy of clinical promotion.

1. Introduction

Cirrhosis is diffuse liver fibrosis caused by chronic liver diseases such as alcoholic liver disease, hepatitis B, and hepatitis C, accompanied by regenerative nodules, resulting in distorted and deformed liver lobules and microvascular structures. The disease imposes a heavy global health economic burden. Studies [1] have reported 1.16 million deaths per year from cirrhosis, with age-standardized mortality rates showing an increasing trend each year. Upper gastrointestinal bleeding (UGIB) is a common high-risk complication of cirrhosis, and its etiology can be divided into esophageal varices (OV) and nonvariceal bleeding. Domestic scholars have reported [2] that the incidence of OV in patients with UGIB has increased from 6.4% to 15.1% in recent years.

Relevant foreign studies [3] reported that OV occupied about 90.60% of patients with cirrhotic UGIB. Once cirrhosis and UGIB are comorbid, it indicates a high risk of entering the decompensated phase and adverse prognostic outcomes such as hemorrhagic shock or death [4]. Some studies have reported [5] that there is a close relationship between the severity of symptoms and the degree of liver function impairment in patients with cirrhotic UGIB and their mortality. Therefore, active treatment of patients with cirrhotic UGIB is clinically considered to be beneficial in improving the quality of their prognosis. In recent years, it has been reported [6] that growth inhibitors have been
shown to be effective in the treatment of cirrhotic UGIB because of their ability to stop bleeding and reduce portal hypertension.

It has also been reported [7] that vitamin C is effective in improving the function of endothelial cells in the liver sinusoids and can also be used in the treatment of cirrhotic UGIB. Although the therapeutic effect of vitamin C and growth inhibitors has been clinically proven, the effect of the combination of the two drugs has not been reported, and their therapeutic effect still needs to be further demonstrated. Based on this, this study will analyze the effect of vitamin C combined with growth inhibitor in the treatment of patients with cirrhotic UGIB and the pathway of influence, with the aim of clarifying the advantages of vitamin C combined with growth inhibitor treatment and providing a more ideal treatment strategy for patients. This study was approved by the Ethical Committee of Zhejiang Province Hospital of Zhejiang Province. All participants signed the relevant consent forms before the study.

2. Patients and Methods

2.1. Patients. Eighty patients with cirrhotic UGIB attending our hospital from March 2021 to March 2022 were selected, and the sequence generated by the random number table was divided into two groups of 40 cases each. Inclusion criteria were as follows: (1) patients had a clear previous history of cirrhosis (refer to the Guidelines for the Diagnosis and Treatment of Cirrhosis [8]); (2) patients met the diagnostic criteria for cirrhotic UGIB in the Guidelines for the Prevention and Treatment of Esophageogastric Variceal Bleeding in Portal Hypertension in Cirrhosis [9] (signs of active bleeding from varices were confirmed by endoscopy); (3) patients had stable vital signs and signed an informed consent form. Exclusion criteria were as follows: (1) patients with a previous history of bleeding from varices in the esophagus or a history of liver transplantation; (2) patients with cirrhotic UGIB induced by malignant tumors in the lower gastrointestinal system or by peptic ulcers and other etiologies; (3) patients who were unable to cooperate with the treatment or who were allergic to the drugs used in this study.

2.2. Method. Both groups were given conventional treatment, including strategies for hemostasis, restoration of blood volume (depending on the patient’s bleeding condition with definite volume expansion and blood transfusion), and liver protection. Meanwhile, the control group was given growth inhibitor (manufacturer: Shenzhen Squire Pharmaceutical Co. Ltd. (Shenzhen, China), specification: 2 mg, State Drug Qualifier: H20064372) treatment, configured with 3 mg growth inhibitor 12 h solution (dissolved in saline), followed by a slow intravenous push of 0.25 mg (equipped with 1 ml saline dissolved), followed by a continuous infusion of 0.25 mg/h. When the bleeding has stopped, the dose is continued for 3 d of continuous treatment. In the observation group, vitamin C (manufacturer: Shenzhen Squire Pharmaceutical Co. Ltd., specification: 2 ml: 0.25 g, State Drug quantification: H42020663) was given in combination with growth inhibitor. The duration of intravenous drip was 3 d in both groups.

2.3. Outcome Measures. The hemostatic effect was compared between the two groups: the hemostatic time, blood transfusion volume, and portal vein blood flow were recorded. Portal vein blood flow was measured by Doppler ultrasound (manufacturer: Samsung Madison Co. Ltd. XW80A). Serum laboratory parameters were compared between the two groups: indicators included miR-130a and NO, and NO levels were measured by indirect colorimetry (kit source: Wuhan EliRuide Biotechnology Co. Ltd., Wuhan, China). Quantitative reverse transcription-polymerase chain reaction (qRT-PCR) (RNA extraction kit source: Invitrogen, GrandIsland, NY, USA) was used to test miR-130a expression, which was strictly performed as required by the kit. Liver function indicators were compared between the two groups: aspartate aminotransferase (AST) and alanine aminotransferase (ALT), (manufacturer: Mindray BS230). The adverse reactions and 24 h hemostasis rate were compared between the two groups: the total incidence rate of nausea, vomiting, abdominal distension, palpitation, and other adverse reactions was counted, and the 24 h hemostasis rate (24 h hemostasis patients/total sample size) was counted.

2.4. Statistical Analysis. Statistical Product and Service Solutions (SPSS) 23.0 (IBM, Armonk, NY, USA) was applied for statistical analysis. An independent sample t-test was used for comparison between groups for measurement data obeying normal distribution, and an independent sample t-test was used for comparison within groups, all expressed as (x ± s). The count data were tested by χ² and expressed as rate (%), and rank series were tested by rank-sum (Z). P < 0.05 indicates a statistical difference.

3. Results

3.1. Comparison of Baseline Data between the Two Groups. There was no statistically significant difference in the baseline data of cirrhotic UGIB patients between the two groups (P > 0.05) (Table 1).

3.2. Comparison of Hemostatic Effect between the Two Groups. There was no significant difference in portal vein blood flow between the two groups before treatment (P > 0.05) (Table 2); the hemostatic time in the observation group was higher than that in the control group, and the blood transfusion volume and portal vein blood flow after treatment were lower than those in the control group (P < 0.05) (Figure 1).

3.3. Serum Laboratory Parameters and Liver Function Parameters Were Compared between the Two Groups. Before treatment, there was no significant difference in miR-130a, NO, AST, and ALT indicators between the two groups of cirrhotic UGIB patients (P > 0.05); after treatment, miR-
The pathogenesis of cirrhosis UGIB is mainly related to cirrhosis portal hypertension, impaired liver function, coagulation-anticoagulation mechanism disorders, and portal vein internal diameter, when cirrhosis continues to progress into the decompensated stage, it will destroy the normal liver blood sinusoidal structure and function, affecting the portal blood return, prompting the tissue pressure to increase, the internal diameter due to blood stasis widening, forming the esophagogastric fundus. The more severe the injury, the more serious the destruction of the normal structure of the blood sinusoids will be, leading to the accumulation of blood in the upper gastric collateral circulation and the formation of esophageal varices and the occurrence of UGIB [10]. For patients with cirrhotic UGIB, clinical treatment principles are based on hemostasis and reduction of portal vein pressure, prevention and control of complications, and prolongation of survival, with pharmacological treatment strategies preferred.

Growth inhibitor belongs to the synthetic hormone class (cyclic peptide substances) and is a commonly used clinical hemostatic drug. Its mechanism of action is to regulate the gastrointestinal internal environment, acting directly on the visceral vascular smooth muscle to induce local arterial contraction and reduce its portal blood flow and pressure; by inhibiting the secretion of vasodilating substances (including vasoactive intestinal peptide and substance P), it produces local vasoconstrictive effects, and then plays an effective role by inhibiting the secretion of vasodilating substances (including vasoactive intestinal peptides and substance P), it produces a local vasoconstrictive effect, which then effectively reduces intestinal vascular resistance and blood flow; at the same time, it can also inhibit the secretion of gastric acid, gastrin, and other irritating substances, which is conducive to repairing the gastrointestinal mucosa [11–13].

Vitamin C is an effective scavenger of reactive oxygen species and has the effect of promoting the formation of antibodies and collagen in the body. Its mechanism of action is to improve the body’s immune resistance by participating in amino acid metabolism, neurotransmitters, protein synthesis, and immune function mechanisms; it helps maintain the integrity of blood vessels while reducing the capillary permeability, accelerates blood coagulation, and strengthens hematopoietic function [14]. The results of this study showed that the hemostasis time in the observation group was shorter than that in the control group, and the blood transfusion volume and portal blood flow after treatment were lower than those in the control group (P < 0.05). Vitamin C is an

Table 1: Comparison of the baseline data of the two groups (n, ± s).

| Group            | Number of subjects | Male/ female | Age (years) | Etiology of cirrhosis (hepatitis B/ alcoholic cirrhosis/hepatitis C) | Child–Pugh classification (A/B/C) | Duration of cirrhosis (years) |
|------------------|--------------------|--------------|-------------|---------------------------------------------------------------------|----------------------------------|--------------------------------|
| Observation group| 40                 | 25/15        | 51.47 ± 6.82 | 14/15/11                                                            | 10/14/16                         | 4.39 ± 0.77                   |
| Control group    | 40                 | 27/13        | 51.74 ± 6.51 | 16/15/9                                                             | 9/13/18                          | 4.57 ± 0.71                   |

X²/ t/ Z

| Group | Number | t | P value |
|-------|--------|---|---------|
| Observation group | 40 | 2.800 | 0.006 |
| Control group | 40 | 0.902 | 0.333 |

Figure 1: The hemostatic effect was compared between the two groups.

130a, NO, AST, and ALT indicators in the two groups were lower than those before treatment, and the observation group was significantly lower than the control group (P < 0.05) (Table 3 and Figure 2).

3.4. Comparison of Adverse Reactions and 24 h Hemostatic Rate between the Two Groups. There was no significant difference in the adverse reaction rate between the two groups (P > 0.05), while the 24 h hemostasis rate in the observation group (97.95%) was significantly higher than that in the control group (77.50%) (P < 0.05) (Table 4).

4. Discussion

The pathogenesis of cirrhosis UGIB is mainly related to cirrhosis portal hypertension, impaired liver function, coagulation-anticoagulation mechanism disorders, and portal vein internal diameter, when cirrhosis continues to progress into the decompensated stage, it will destroy the normal liver blood sinusoidal structure and function, affecting the portal blood return, prompting the tissue pressure to increase, the internal diameter due to blood stasis widening, forming the esophagogastric fundus. The

Table 2: Comparison of the hemostatic effect between the two groups (±s).

| Group            | Number of subjects | Hemostasis time (hr) | Blood transfusion volume (ml) | Portal vein flow (mL/min) |
|------------------|--------------------|----------------------|-------------------------------|--------------------------|
| Observation group| 40                 | 17.35 ± 8.74         | 1091.27 ± 24.31               | 814.32 ± 93.49           |
| Control group    | 40                 | 22.69 ± 8.31         | 173.78 ± 29.85                | 816.17 ± 92.15           |

Post treatment Before treatment

| Group            | Number of subjects | NO (umol/ L) | AST (U/L) | miR-130a | ALT (U/L) |
|------------------|--------------------|-------------|-----------|----------|-----------|
| Observation group| 40                 | 92.15 ± 814.32 | 29.85 ± 8.74 | 6.82 ± 8.74 | 1091.27 ± 24.31 |
| Control group    | 40                 | 24.31 ± 816.17 | 6.51 ± 8.74 | 6.82 ± 8.74 | 1091.27 ± 24.31 |

P indicates comparison with that before treatment, P < 0.05.
**Table 3: Comparison of serum laboratory parameters and liver function parameters between the two groups (n = 40, x ± s).**

| Group          | miR-130a Before treatment | miR-130a Post treatment | NO (μmol/L) Before treatment | NO (μmol/L) Post treatment | AST (U/L) Before treatment | AST (U/L) Post treatment | ALT (U/L) Before treatment | ALT (U/L) Post treatment |
|----------------|---------------------------|-------------------------|-------------------------------|---------------------------|----------------------------|---------------------------|----------------------------|---------------------------|
| Observation group | 8.57 ± 1.44               | 1.79 ± 0.35*            | 124.37 ± 18.95               | 91.37 ± 10.29*            | 89.48 ± 15.67              | 20.35 ± 6.74*             | 90.27 ± 16.34               | 18.64 ± 6.51*             |
| Control group   | 8.51 ± 1.47               | 2.81 ± 0.37*            | 125.68 ± 18.11               | 115.67 ± 10.32*           | 88.39 ± 16.14              | 33.48 ± 6.95*             | 90.11 ± 16.73               | 32.74 ± 6.87*             |
| t               | 0.184                     | 12.666                  | 0.316                        | 10.546                    | 0.307                      | 8.577                     | 0.043                      | 9.422                     |
| P value         | 0.854                     | 0.001                   | 0.753                        | 0.001                     | 0.760                      | 0.001                     | 0.966                      | 0.001                     |

* indicates comparison with that before treatment, *P* < 0.05.

**Figure 2: Comparison of adverse reactions and 24 h hemostasis rate between the two groups.**

**Table 4: Comparison of serum laboratory parameters and liver function parameters between the two groups (n, %).**

| Group          | Number of subjects | Nausea and vomiting | Abdominal distention | Palpitations | Total occurrence | 24 h hemostasis rate |
|----------------|-------------------|---------------------|----------------------|--------------|------------------|---------------------|
| Observation group | 40                | 1 (2.50)            | 1 (2.50)             | 1 (2.50)     | 3 (7.50)         | 39 (97.50)          |
| Control group   | 40                | 1 (2.50)            | 0 (0.00)             | 1 (2.50)     | 2 (5.00)         | 31 (77.50)          |
| X²              | —                 | —                   | —                    | —            | —                | 0.644               |
| P value         | —                 | —                   | —                    | —            | —                | 1.7                 |

5. Conclusions

Vitamin C combined with growth inhibitor is effective in the treatment of cirrhosis UGIB, which can effectively shorten the hemostasis time, reduce the transfusion volume and portal blood flow, improve miR-130a, NO, and liver function level of patients, with high safety, and is worthy of clinical promotion.

Data Availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.
Conflicts of Interest

The authors declare that they have no conflict of interest.

References

[1] R. Barnett, “Liver cirrhosis,” The Lancet, vol. 392, no. 10144, p. 275, 2018.
[2] M. Feinman and E. R. Haut, “Upper gastrointestinal bleeding,” Surgical Clinics of North America, vol. 94, no. 1, pp. 43–53, 2014.
[3] A. Duah, K. N. Nkrumah, and K. Tachi, “Oesophageal varices in patients with liver cirrhosis attending a major tertiary hospital in Ghana,” The Pan African medical journal, vol. 31, p. 230, 2018.
[4] M. J. Williams and P. Hayes, “Improving the management of gastrointestinal bleeding in patients with cirrhosis,” Expert Review of Gastroenterology & Hepatology, vol. 10, no. 4, pp. 505–515, 2016.
[5] K. Bishay, P. Tandon, S. Fisher et al., “Clinical factors associated with mortality in cirrhotic patients presenting with upper gastrointestinal bleeding,” Journal of the Canadian Association of Gastroenterology, vol. 3, no. 3, pp. 127–134, 2020.
[6] S. Vadera, C. Yong, L. L. Gluud, and M. Y. Morgan, “Band ligation versus no intervention for primary prevention of upper gastrointestinal bleeding in adults with cirrhosis and oesophageal varices,” Cochrane Database of Systematic Reviews, vol. 6, Article ID CD012673, 2019.
[7] M. A. Alhasoon, “The use of high dose octreotide in management of neonatal chylothorax: Review,” Journal of Neonatal-Perinatal Medicine, vol. 14, no. 4, pp. 457–461, 2021.
[8] G. P. Aithal, N. Panalijappan, L. China et al., “Guidelines on the management of ascites in cirrhosis,” Gut, vol. 70, no. 1, pp. 9–29, 2021.
[9] J. Y. Sheng, S. Liu, Y. S. Yang, and X. W. Zhang, “The progress in management of esophageal variceal bleeding in cirrhotic portal hypertension,” Zhonghua Wai Ke Za Zhi, vol. 58, no. 10, pp. 808–812, 2020.
[10] L. I. Cifuentes, D. Gattini, R. Torres-Robles, and J. C. Gana, “Band ligation versus sham or no intervention for primary prophylaxis of oesophageal varical bleeding in children and adolescents with chronic liver disease or portal vein thrombosis,” Cochrane Database of Systematic Reviews, vol. 1, Article ID D11561, 2021.
[11] T. B. Krüger, B. B. Herlofson, A. M. Lian, U. Syversen, and J. E. Reseland, “Alendronate and omeprazole in combination reduce angiogenic and growth signals from osteoblasts,” Bone Reports, vol. 14, Article ID 100750, 2021.
[12] S. Vedachalam, G. Balasubramanian, G. J. Haas, and S. G. Krishna, “Treatment of gastrointestinal bleeding in left ventricular assist devices: a comprehensive review,” World Journal of Gastroenterology, vol. 26, no. 20, pp. 2550–2558, 2020.
[13] X. Liu, X. Guo, and H. Zhou, “Octreotide acetate combined with somatostatin upregulates miR-1291 and downregulates miR-331-3p in patients with cirrhosis and upper gastrointestinal bleeding,” American Journal of Translational Research, vol. 13, no. 8, pp. 9883–9891, 2021.
[14] M. Akyildiz, S. Ersin, E. Oymaci, M. Dayıaçağ, M. Kapkac, and M. Alkanat, “Effects of somatostatin analogues and vitamin C on bacterial translocation in an experimental intestinal obstruction model of rats,” Journal of Investigative