**Name of Journal:** *World Journal of Gastrointestinal Surgery*

**Manuscript NO:** 85336

**Manuscript Type:** ORIGINAL ARTICLE

***Retrospective Study***

**Efficacy of ileus tube combined with meglumine diatrizoate in treating postoperative inflammatory bowel obstruction after surgery**

Yang W *et al*. Combination therapy for EPISBO

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**Author contributions:** YangW initiated the project, designed the experiment, performed postoperative follow-up and recorded data, and wrote the original manuscript; Pu J conducted collated data, assisted with the statistical analysis, and revised the paper; all authors reviewed and approved the paper; and all authors have read and approved the final manuscript.

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**Received:** May 21, 2023

**Revised:** July 3, 2023

**Accepted:** July 29, 2023

**Published online:** September 27, 2023

**Abstract**

BACKGROUND

Early postoperative inflammatory small bowel obstruction (EPISBO) is easy to be complicated after colorectal cancer surgery. Both intestinal obstruction catheter and meglumine can treat EPISBO.

AIM

To investigate the efficacy of an intestinal obstruction tube combined with meglumine diazo in treating EPISBO of colorectal cancer.

METHODS

Data from 60 patients with colorectal cancer and intestinal obstruction admitted to the Proctology Department of our hospital from April 2018 to May 2022 were collected and analyzed and divided into three cohorts according to different treatment regimens. Cohort A (*n* = 20) received a transnasal intestinal obstruction catheter with panumglumine, and cohort B (*n* = 20) received a transnasal intestinal obstruction catheter with liquid paraffin. Cohort C (*n* = 20) received oral treatment with meglumine. The clinical efficacy, first exhaust/defecation time, length of hospital stay, gastrointestinal decompression time, relief time of abdominal pain, and relief time of abdominal distension were compared among the three cohorts. The levels of C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), monocyte chemotactic protein-1 (MCP-1), serum albumin, and transferrin were compared among the three cohorts before and after treatment. The occurrence of adverse reactions in the three cohorts was compared.

RESULTS

Compared with cohort C, the successful treatment rate of cohort A was significantly higher. There were statistically significant variations in the time of first exhaust/defecation, length of hospital stays, gastrointestinal decompression time, relief time of abdominal pain, and relief time of abdominal distention among the three cohorts. Compared with cohort C, cohort A’s first exhaust/defecation time, hospitalization time, gastrointestinal decompression time, abdominal pain relief time, and abdominal distension relief time was reduced (*P* < 0.05). After treatment, serum CRP, TNF-α, IL-6, and MCP-1 expression levels increased, and serum albumin and serum transferrin levels increased in the three cohorts. The serum albumin level in cohort A was higher than in cohort C. Compared with cohort B and cohort C, the serum transferrin level in cohort A increased (*P* < 0.05). Compared with cohort C, the total incidence of adverse reactions in cohorts A and B was significantly higher (*P* < 0.05). The incidence of adverse reactions was similar between cohort A and cohort B.

CONCLUSION

Using an ileus tube combined with meglumine diatrizoate can effectively treat postoperative inflammatory ileus obstructions after surgery colorectal cancer and improve prognosis, inflammatory response, and nutritional status.

**Key Words:** Ileus tube; Meglumine diatrizoate; Colorectal cancer; Inflammatory bowel obstruction; Early postoperative inflammatory small bowel obstruction

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**Citation:** Yang W, Pu J. Efficacy of ileus tube combined with meglumine diatrizoate in treating postoperative inflammatory bowel obstruction after surgery. *World J Gastrointest Surg* 2023; 15(9): 1950-1958

**URL:** https://www.wjgnet.com/1948-9366/full/v15/i9/1950.htm

**DOI:** https://dx.doi.org/10.4240/wjgs.v15.i9.1950

**Core Tip:** Early postoperative inflammatory small bowel obstruction (EPISBO) patients with colorectal cancer that were difficult to re-operate were mostly treated with conservative therapy. Transnasal ileus catheter has better hypotensive effect and has been widely used in the treatment of EPISBO. However, the effect of combined ileus catheter and meglumine in the treatment of EPISBO has not been discussed in detail. The objective of this study was to compare the efficacy of oral meglumine for EPISBO, ileus catheter alone and ileus catheter combined with meglumine for EPISBO. The effect of intestinal obstruction catheter combined with meglumine in the treatment of EPISBO is better than that of treatment alone.

**INTRODUCTION**

Early postoperative inflammatory small bowel obstruction (EPISBO) is a common postoperative complication following treatment for colorectal cancer. EPISBO is an adhesive intestinal obstruction caused by intestinal wall edema and inflammatory exudation caused by abdominal surgery, intestinal tube injury, and leakage of contents. In patients with colorectal cancer undergoing radical surgery, the intestinal canal is exposed for a long time, and abdominal bleeding and foreign bodies can lead to inflammation. Many inflammatory cells accumulate, eventually leading to inflammation and adhesion[1,2].

If not treated in time, this enhanced inflammatory state can lead to short bowel syndrome, intestinal fistula, infection, and other serious complications. Several studies have shown that EPISBO mainly occurs within two weeks after surgery, and the main clinical manifestations include abdominal distention, cessation of anal exhaust, and defecation.

Clinical-based EPISBO therapy remains conservative, including fasting/water restriction, parenteral nutrition support, and reoperation that can damage the intestine. Traditional nasogastric tube decompression can only remove gastric juice. Additionally, it is difficult to drain the contents of the small intestine, resulting in a long conservative treatment time for early postoperative inflammatory ileus. While semi-effective, some patients have a poor curative effect.

The transnasal ileus tube could drain fluid in the small intestine, reducing edema and intestinal pressure. Meglumine diatrizoate has the characteristics of hypertonicity and has been shown to induce no apparent adverse reactions. After decompression through the intestinal obstruction catheter, angiography can significantly reduce the dilution of contrast medium by intestinal effusion and improve the effectiveness of diagnosis and treatment[3-5]. In addition to being used as a contrast agent, oral administration of meglumine diatrizoate can reduce intestinal wall edema, dilate the small intestine at the distal end of obstruction, stimulate gastrointestinal peristalsis, and relieve intestinal obstruction. This study aimed to probe the therapeutic efficacy of ileus tubes and meglumine diatrizoate for treating EPISBO after surgery for colorectal cancer.

**MATERIALS AND METHODS**

***Ethics***

This study was approved by the Ethics Committee of Lanzhou Second People’s Hospital. Due to the retrospective design, patient consent was not required.

***General information***

Data from 60 patients with colorectal cancer and intestinal obstruction admitted to the Proctology Department of our hospital from April 2018 to May 2022 were collected and analyzed. The patients were divided into three cohorts, namely A (*n* = 20), B (*n* = 20), and C (*n* = 20), according to different treatment regimens. Cohort A comprised 14 males and 6 females, with a mean age of 57.95 ± 3.10 years (50-64 years). Within this cohort, these patients presented with the following obstruction locations: Four cases of obstruction in the rectum, six in the descending colon, and 10 in the sigmoid colon. Regarding TNM staging, 10 cases were identified as stage II and 10 as stage III. Cohort B comprised 12 males and 8 females, with a mean age of 59.10 ± 3.46 years (53-65 years). Within this cohort, the patients presented with the following obstruction locations: Two cases of obstruction in the rectum, seven cases in the descending colon, and 11 cases in the sigmoid colon. Regarding TNM staging: Seven cases were identified as stage II and 13 as stage III. Lastly, cohort C comprised 16 males and four females, with a mean age of 60.20 ± 4.29 years (51-68 years). Within this cohort, the patients presented with the following obstruction locations: Six rectum cases, five descending colon cases, and nine sigmoid colon cases. Regarding TNM staging: 11 cases were identified as stage II and nine as stage III.

***Inclusion and exclusion criteria***

Patients with complete case data that presented with symptoms including abdominal distension, abdominal pain, vomiting, stop of exhaustion, and defecation, had a palpable mass in the right lower abdomen, had no signs of peritonitis, and weakened or absent bowel sounds were included. Furthermore, only patients whose X-ray examination showed intestinal effusion, abdominal computed tomography examination showed intestinal wall edema, thickening, and extensive exudation were included.

Patients with intestinal obstruction caused by intestinal hernia or intussusception, intestinal obstruction or cancerous obstruction caused by mesenteric disease or intestinal paralysis, or patients with hematological diseases, severe infections, and immune diseases were excluded. Furthermore, pregnant and nursing women, patients with neurological diseases, and patients allergic to drugs used in this study were excluded.

***Treatment***

Cohort A was administered a transnasal ileus tube combined with meglumine diatrizoate, cohort B was administered a transnasal ileus tube combined with liquid paraffin, and cohort C was administered oral meglumine diatrizoate. All three cohorts were given primary treatment, which consisted of fasting and gastrointestinal decompression, early deep vein nutrition treatment to maintain water, electrolyte, and acid-base balance, the correction of hypoalbuminemia and anemia, administration of omeprazole and octreotide to inhibit the secretion of digestive juices. Lastly, a broad-spectrum antibiotic was administered as an anti-infection treatment.

**Cohort A:** The ileus tube was placed and connected to an external negative pressure suction device, and 100-150 mL of 76% meglumine was injected into the lesion through the ileus tube for intestinal angiography. The ileus tube was retained for continuous negative pressure suction for patients with extensive weakened intestinal peristalsis and apparent pleural effusion. For patients with segmental intestinal peristalsis caused by local adhesion, and if distal intestinal peristalsis was expected, the tube provided enteral nutrition through the obstruction site, and negative pressure drainage was performed through the lateral hole. Parenteral nutrition support was given during treatment.

**Cohort B:** The transnasal ileus tube was inserted into the stomach under gastroscopy and delivered to the distal descending part of the duodenum with the help of a guide wire or foreign body forceps. Approximately 15 mL of sterilized water was injected into the front balloon and relaxed the tube; the external nasal edge was not fixed. The tube was connected to a negative pressure suction device, and 50-80 mL of liquid paraffin was injected through the negative pressure suction port of the tube. The patient was told to move around more, turn over on the bed, and the tube was sent to the obstruction position through intestinal peristalsis.

**Cohort C:** Patients were administered 100 mL of meglumine orally, and abdominal signs and disease changes were strictly monitored.All three cohorts were treated twice a day, and the conditions of the three cohorts were monitored following seven days of therapy.

***Treatment outcomes to be assessed***

Baseline data, clinical efficacy, the time of first exhaust/defecation, length of hospital stays, gastrointestinal decompression time, abdominal pain relief time, abdominal distension relief time, laboratory indicators, nutritional indicators, and the occurrence of adverse reactions were collected and assessed. The clinical efficacy, the time of first exhaust/defecation, length of hospital stays, gastrointestinal decompression time, abdominal pain relief time, and abdominal distension relief time were compared among the three cohorts. The levels of C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), monocyte chemotactic protein-1 (MCP-1), serum albumin, and transferrin were compared among the three cohorts before and after treatment and the occurrence of adverse reactions in the three cohorts was compared.

***Efficacy evaluation criteria***

Cases where the clinical symptoms and signs of the patient disappeared, and the abdominal vertical position plain film showed normal were defined as “cured” following treatment. Cases where the clinical symptoms and signs disappeared, and the abdominal vertical position plain film showed that the intestinal tube was slightly inflated or had a small amount of liquid level were defined as receiving “effective” treatment. Finally, cases whose clinical symptoms, signs, and abdominal vertical position plain film did not meet the above criteria were defined as responding “ineffectively” to treatment. Totally effective treatment = cure + effective[6].

***Statistical methods***

SPSS 20.0 was employed for analyzing/processing datasets, with measurement data reflecting mean ± SD. The independent sample *t*-test was used for comparisons across cohorts, and the paired *t*-test was used for comparison pre-/post-therapy within cohorts. Counting datasets reflected frequency/composition ratio. The comparison of disordered classification data used the chi2 test or Fisher’s exact probability method, and the rank sum test compared rank data. A *P* value < 0.05 was deemed to confer statistical significance.

**RESULTS**

***Comparative analyses for clinical efficacy among all cohorts***

The effectiveness rate of cohort A was significantly elevated compared to cohort C. The effective rates across cohorts “A and B” and “B and C” were similar (Table 1).

***Comparative analyses for prognosis among all cohorts***

There were statistically significant differences in the time of first exhaust/defecation, length of hospital stays, gastrointestinal decompression time, relief time of abdominal pain, and relief time of abdominal distention among all cohorts (Table 2). Compared to cohort C, the time of first exhaust/defecation, length of hospital stays, gastrointestinal decompression time, relief time of abdominal pain, and relief time of abdominal distention in cohort A were significantly reduced (Table 2).

***Comparative analyses for inflammatory factor expression pre-/ post-therapy in all cohorts***

Pre-therapy, all cohorts had a similar secretion of serum biomarkers, including CRP, TNF-α, IL-6, and MCP-1 expression. Post-therapy, serum CRP, TNF-α, IL-6, and MCP-1 expression in all cohorts were increased, and the indexes in cohort A were significantly elevated compared to cohort B and C, while cohort B expression profiles were significantly upregulated compared to cohort A (Table 3).

***Comparative analyses for nutritional status of all cohorts pre-/ post-therapy***

Pre-therapy, serum albumin, and serum transferrin levels were similar among all cohorts. However, post-therapy, serum albumin and serum transferrin levels in all cohorts were increased. Specifically, the serum albumin level in cohort A was significantly elevated compared to cohort C, and the serum transferrin level in cohort A was significantly elevated compared to cohort B and C (Table 4).

***Comparative analyses for the incidence of adverse reactions among all cohorts***

The widespread occurrence of adverse events within cohorts A and B was significantly elevated compared to cohort C. Additionally, the occurrence of adverse events between cohorts A and B was similar (Table 5).

**DISCUSSION**

EPISBO pathogenesis after colorectal cancer surgery is mainly related to neuroinhibitory effects, hormones, hypoalbuminemia, inflammatory response, and anesthesia. Intestinal wall tissue damage during surgery can lead to infiltration of a high quantity of macrophages/neutrophils, combined with the release of increased levels of IL-6 and CRP, forming aseptic inflammation. Such inflammatory substances inhibit the inhibition of gastrointestinal vagal nerve and gastrointestinal peristalsis disorder[7-9]. Additionally, inflammatory factors can excite gastrointestinal sympathetic nerves, leading to intestinal wall congestion and mechanical obstruction[10-12]. The rise of intestinal canal pressure can result in intestinal blood circulation disorder, eventually leading to intestinal perforation, necrosis, and abdominal infection. Reoperation can further damage the intestinal canal, leading to postoperative infection and bleeding. Therefore, conservative therapy is often used in clinical therapy of the disease.

Conservative EPISBO therapy includes fasting, gastrointestinal decompression, spasmolysis and analgesia, and correction of water, electrolyte, and acid-base balance disorders. A traditional nasogastric tube decompression can only aspirate gastric juice but cannot drain the contents of the small intestine, the therapeutic cycle is long, and the therapeutic effect is poor. A transnasal ileus tube can be delivered into the duodenum under the guidance of a gastroscope. Peristalsis and water sac can promote the tube to move to the distal part of the small intestine and reach the proximal part of the obstruction site for decompression. The transnasal ileus tube can quickly play the role of intestinal hypotension, relieve intestinal edema, and promote gastrointestinal function recovery. Water injection by the posterior airbag and water pumping by the anterior airbag can ensure the unidirectional movement of the contrast agent, promote further determination of obstruction location and nature, and promote intestinal decompression. Meglumine diatrizoate was initially used as a contrast agent and, recently, was employed within therapy for intestinal obstruction in several studies with sound therapeutic effects[13-15]. The hypertonic 76% meglumine diatrizoate solution assists in transferring interstitial fluid to the intestinal lumen, relieving intestinal wall edema. In addition, meglumine diatrizoate helps determine the size and shape of intestinal filling. According to relevant studies, meglumine diatrizoate can improve local microcirculation, protect intestinal mucosal barrier function, and relieve inflammation. Furthermore, the body can quickly metabolize an appropriate amount of meglumine diatrizoate in a short period with reasonable safety, leading to high clinical tolerance.

This investigation’s dataset outcomes demonstrated that cohort A’s effective rate was significantly elevated compared to cohort C. Furthermore, the effective rate across cohorts “A and B” and “B and C” were similar. Compared to cohort C, the time of first exhaust/defecation, length of hospital stays, gastrointestinal decompression time, relief time of abdominal pain, and relief time of abdominal distension in cohort A were significantly reduced. Together, these results indicate that combined therapy has a better effect on EPISBO after colorectal cancer surgery and can more effectively promote the recovery of gastrointestinal function and shorten the therapy time.

The therapy plan of the ileus tube combined with meglumine diatrizoate injection combines the therapeutic advantages of the ileus tube and meglumine diatrizoate. Using an ileus tube, meglumine diatrizoate can quickly reach the site of intestinal obstruction, dilute intestinal obstruction contents, relieve intestinal stenosis, recover gastrointestinal function, and avoid further aggravation of intestinal obstruction. Thus, this method can effectively shorten the hospital stay and reduce clinical manifestations in patients. Cohort B was administered an ileus tube combined with liquid paraffin, which also took advantage of the dual advantages of an ileus tube and liquid paraffin. Therefore, cohorts A and B’s clinical efficacy and prognosis were better than cohort C, who were administered oral meglumine diatrizoate alone.

CRP is synthesized by stem cells, and its expression level can be abnormally elevated when the body is subjected to inflammatory stimulation or stress response[16,17]. Lymphocytes and fibroblasts produce TNF-α, and endothelial cells, which can enhance the chemotaxis of neutrophils, release inflammatory factors, aggravate the body’s inflammatory response, and exacerbate tumor cellular proliferative rate, leading to patient condition deterioration. IL-6 is an inflammatory cytokine produced by endothelial cells, lymphoid cells, and mononuclear macrophages, which can regulate inflammatory response and induce stem cells to synthesize CRP. MCP-1 can reduce the speed of gastrointestinal motility through inhibitory adrenergic nerve pathway activity and is abnormally expressed in various inflammatory responses, affecting gastrointestinal neuromuscular movement. Additionally, several studies have shown that MCP-1 expression level is intimately linked with the severity of intestinal obstruction[18-20]. This investigation revealed that serum CRP, TNF-α, IL-6, and MCP-1 levels in all cohorts were significantly increased post-therapy. In contrast, the levels of each index in cohort A were elevated compared to cohort B and C, and the levels of each index in cohort B were significantly elevated compared to cohort A. These data indicate that an ileus tube combined with meglumine diatrizoate for treating EPISBO after colorectal cancer surgery could effectively relieve the inflammatory response of patients and that the effect is better than instances where an ileus tube combined with liquid paraffin therapy and meglumine diatrizoate is used alone. This observation may be because, compared with liquid paraffin, meglumine diatrizoate can play a particular therapeutic effect in addition to the contrast effect in the therapy of EPISBO; thus, the combination of ileus tube and meglumine diatrizoate has a better therapeutic effect. We hypothesize that the mechanism underlying this effect may be because the ileus tube combined with meglumine diatrizoate relieves the body’s inflammatory response, improving clinical symptoms.

EPISBO patients, after colorectal cancer surgery, are prone to malnutrition. Parenteral nutrition can provide adequate nutritional support to patients and reduce the incidence of complications. However, long-term enteral nutrition can damage the intestinal microbial barrier function, cause entheogenic infection, and affect the postoperative recovery of patients. Therefore, enteral nutrition is generally given to patients with intestinal obstruction to improve their nutritional status and promote the recovery of gastrointestinal function. In this study, serum albumin and serum transferrin levels in all cohorts increased post-therapy. Specifically, the serum albumin level in cohort A was significantly elevated compared to cohort C and the serum transferrin level in cohort A was significantly elevated compared to cohort B and C. These results suggest that an ileus tube combined with meglumine diatrizoate in the therapy of EPISBO after colorectal cancer surgery can effectively improve the nutritional status of patients. Because the transnasal ileus tube can effectively shorten the recovery time of the gastrointestinal function and provide enteral nutrition as soon as possible, the nutritional status of patients in cohort A was better than in cohort B and C. The incidence of total adverse reactions in cohorts A and B was significantly elevated compared to cohort C. The incidence of adverse reactions was similar across cohort A and cohort B. The higher incidence of adverse reactions observed in cohorts A and B could be attributed to using the ileus tube in these groups.

This study has several limitations. First, this is a retrospective study with a small sample size; unintentional biases may have been introduced. Further large-scale, multi-center prospective studies are expected to explore the effect of ileus tubes combined with meglumine diatrizoate in the therapy of EPISBO after colorectal cancer surgery and provide references for clinical treatment.

**CONCLUSION**

In conclusion, the use of an ileus tube combined with meglumine diatrizoate in the therapy of EPISBO after colorectal cancer surgery can effectively shorten the length of hospital stay, promote the recovery of gastrointestinal function, and relieve the inflammatory response of the body, with good therapeutic effect and clinical application value.

**ARTICLE HIGHLIGHTS**

***Research background***

Early postoperative inflammatory small bowel obstruction (EPISBO) is easy to be complicated after colorectal cancer surgery. Both intestinal obstruction catheter and meglumine can treat EPISBO. Extensive application of parenteral nutrition support, traditional nasogastric tube, intestinal obstruction catheter and meglumine in EPISBO treatment. Research significance is to explore a new method for the treatment of EPISBO after colorectal cancer surgery.

***Research motivation***

The main topics is treatment of EPISBO after colorectal cancer surgery. There is a clinical need to explore more effective therapies to treat EPISBO after colorectal cancer surgery. The significance of this study is to confirm the effectiveness of the new method of ileus catheter combined with meglumine for the treatment of EPISBO after colorectal cancer surgery, encourage clinical teams to continue to explore more effective treatment methods for EPISBO after colorectal cancer surgery, and promote the continuous progress of medical technology.

***Research objectives***

To compare the effects of different treatment methods for EPISBO, and to observe the advantages of intestinal obstruction catheter combined with meglumine in the treatment of EPISBO. The combination of intestinal obstruction catheter and meglumine in the treatment of EPISBO after colorectal cancer surgery can significantly improve the short-term prognosis, inflammatory status and nutritional status of patients, which confirms that this treatment method has a good therapeutic effect, and provide a new reference for future clinical treatment of EPISBO after colorectal cancer surgery.

***Research methods***

Clinical data of patients were retrospectively analyzed and divided into three groups according to different treatment methods. One-way analysis of variance, paired sample *t*-test and Chi-square test were used to statistically analyze the general data, clinical efficacy, short-term prognostic indicators, inflammatory factors, nutritional status indicators and incidence of adverse reactions of patients in the three groups. The feature of retrospective study is to explore the cause through the results, and it is easier to obtain the case data.

***Research results***

Intestinal obstruction catheter combined with meglumine has a significant effect in the treatment of EPISBO after colorectal cancer surgery, showing good improvement in clinical efficacy, short-term prognosis, inflammatory status and nutritional status, providing a new treatment method for EPISBO after colorectal cancer surgery, and further prospective studies are needed to verify the effectiveness of this treatment method.

***Research conclusions***

Malnutrition in EPISBO patients can lead to a variety of complications and affect the prognosis of patients. Therefore, attention should be paid to the influence of treatment methods on the nutritional status of patients after treatment. Intestinal obstruction catheter combined with meglumine is effective in the treatment of EPISBO after colorectal cancer surgery, and the clinical treatment plan with better effect should be preferred.

***Research perspectives***

Clinical treatment plan should not only consider the therapeutic effect, but also consider the impact on the patient’s prognosis. Future research is aimed at further exploring the impact of medicine on quality of life.

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**Footnotes**

**Institutional review board statement:** This study was approved by the Ethics Committee of Lanzhou Second People’s Hospital.

**Informed consent statement:** Due to the retrospective design, patient consent was not required.

**Conflict-of-interest statement:** All the authors report no relevant conflicts of interest for this article.

**Data sharing statement:** All data generated or analyzed during this study are included in this published article.

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**Provenance and peer review:** Unsolicited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** May 21, 2023

**First decision:** June 1, 2023

**Article in press:** July 29, 2023

**Specialty type:** Gastroenterology and hepatology

**Country/Territory of origin:** China

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Elkan H, Turkey; Kaya BC, Turkey **S-Editor:** Wang JJ **L-Editor:** A **P-Editor:** Wang JJ

**Table 1 Comparative analyses for clinical efficacy among all cohorts [cases (%)]**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cohort** | **Cure** | **Effective** | **Ineffective** | **Total effective rate** |
| Cohort A (*n=*20) | 11 (55.00) | 8 (40.00) | 1 (5.00) | 19 (95.00)a |
| Cohort B (*n=*20) | 9 (45.00) | 7 (35.00) | 4 (20.00) | 16 (80.00) |
| Cohort C (*n=*20) | 7 (35.00) | 5 (25.00) | 8 (40.00) | 12 (60.00) |
| *χ2* values |  |  |  | 7.267 |
| *P* value |  |  |  | 0.026 |

aIndicated *P* < 0.05 compared to cohort C.

There is no significant difference between group A and group B.

**Table 2 Comparative analyses for prognosis among all cohorts (*x* ± *s*)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cohort** | **Time of first exhaust/defecation (d)** | **Length of hospital stay (d)** | **Gastrointestinal decompression time (d)** | **Relief time of abdominal pain (d)** | **Relief time of abdominal distention (d)** |
| Cohort A (*n* = 20) | 7.85 ± 1.53a,b | 15.30 ± 1.95c | 11.30 ± 1.84a,b | 2.05 ± 0.51a,b | 5.55 ± 1.79a,b |
| Cohort B (*n* = 20) | 10.75 ± 2.86c | 17.10 ± 2.57c | 14.40 ± 2.74c | 3.00 ± 1.12 | 3.85 ± 1.09 |
| Cohort C (*n* = 20) | 13.05 ± 1.90 | 20.25 ± 2.53 | 16.35 ± 1.60 | 3.60 ± 1.35 | 3.55 ± 1.10 |
| *F* value | 28.749 | 22.381 | 28.933 | 10.923 | 12.458 |
| *P* value | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 |

aIndicated *P* < 0.05 when compared to cohort B.

bIndicated *P* < 0.05 when compared to cohort C.

**Table 3 Comparative analyses for inflammatory factors levels pre-/post-therapy in all cohorts (*x* ± *s*)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cohort** | **CRP (mg/L)** | **TNF-α (ng/L)** | **IL-6 (ng/L)** | **MCP-1 (ng/L)** |
| **Pre-therapy** | **Post-therapy** | **Pre-therapy** | **Post-therapy** | **Pre-therapy** | **Post-therapy** | **Pre- therapy** | **Post-therapy** |
| Cohort A (*n* = 20) | 32.84 ± 3.90 | 17.14 ± 2.27a,b,c | 10.11 ± 1.74 | 2.62 ± 0.83a,b,c | 34.92 ± 2.31 | 15.27 ± 1.15a,b,c | 213.33 ± 14.91 | 122.91 ± 19.00a,b,c |
| Cohort B (*n* = 20) | 34.40 ± 4.67 | 19.99 ± 3.51a,c | 11.03 ± 1.99 | 3.79 ± 1.06a,c | 35.59 ± 1.59 | 18.88 ± 1.58a,c | 215.24 ± 19.15 | 150.74 ± 19.76a,c |
| Cohort C (*n* = 20) | 32.27 ± 2.78 | 25.16 ± 2.41a | 10.80 ± 2.06 | 5.35 ± 0.95a | 34.92 ± 3.09 | 23.43 ± 2.26a | 211.07 ± 16.46 | 167.83 ± 15.10a |
| *F* value | 1.636 | 42.566 | 1.227 | 41.469 | 0.526 | 112.506 | 0.303 | 31.482 |
| *P* value | 0.204 | < 0.001 | 0.301 | < 0.001 | 0.594 | < 0.001 | 0.740 | < 0.001 |

aIndicated *P* < 0.05 when compared with the same cohort pre-therapy.

bIndicated *P* < 0.05 when compared with cohort B.

cIndicated *P* < 0.05 when compared with cohort C.

CRP: C-reactive protein; TNF-α: Tumor necrosis factor-alpha; IL-6: Interleukin-6; MCP-1: Monocyte chemoattractant protein-1.

**Table 4 Comparative analyses for nutritional status of all cohorts pre- and post-therapy (*x* ± *s*)**

|  |  |  |
| --- | --- | --- |
| **Cohort** | **Serum albumin (g/L)** | **Serum transferrin (g/L)** |
| **Pre-therapy** | **Post-therapy** | **Pre-therapy** | **Post-therapy** |
| Cohort A (*n* = 20) | 43.46 ± 3.33 | 49.88 ± 3.60a,c | 2.24 ± 0.53 | 3.55 ± 0.42a,b,c |
| Cohort B (*n* = 20) | 42.79 ± 4.36 | 47.90 ± 3.90a | 2.02 ± 0.55 | 3.16 ± 0.23a |
| Cohort C (*n* = 20) | 43.58 ± 2.14 | 46.68 ± 2.41a | 2.27 ± 0.49 | 2.13 ± 0.51a |
| *F* value | 0.306 | 4.596 | 1.377 | 7.000 |
| *P* value | 0.737 | 0.014 | 0.261 | 0.002 |

aIndicated *P* < 0.05 when compared with the same cohort pre-therapy.

bIndicated *P* < 0.05 when compared with cohort B.

cIndicated *P* < 0.05 when compared with cohort C.

**Table 5 Comparative analyses for adverse event occurrence among all cohorts [cases (%)]**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cohort** | **Anorexia** | **Vomiting** | **Tube obstruction** | **Rash** | **The total incidence of adverse reactions** |
| Cohort A (*n* = 20) | 1 (5.00) | 4 (20.00) | 0 (0.00) | 0 (0.00) | 5 (25.00) |
| Cohort B (*n* = 20) | 1 (5.00) | 3 (15.00) | 1 (5.00) | 1 (5.00) | 6 (30.00) |
| Cohort C (*n* = 20) | 0 (0.00) | 0 (0.00) | 0 (0.00) | 0 (0.00) | 0 (0.00) |
| Fisher’s exact probability value |  |  |  |  | 0.029 |



Published by **Baishideng Publishing Group Inc**

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