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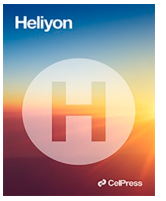

Research article

Comparison of the use of a spiral nasojejunal tube and transendoscopic enteral tubing in washed microbiota transplantation via the mid-gut route

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ABSTRACT

Background: Methods for washed microbiota transplantation (WMT) through the mid-gut include transendoscopic enteral tubing (TET) and manual spiral nasojejunal tube (SNT) placement have not been studied.

Methods: This prospective interventional study was performed at a single centre. Patients were divided into the SNT and mid-gut TET groups based on their conditions and wishes. In the SNT group, an SNT was passively inserted into the stomach, and abdominal X-rays were taken within 24 h to confirm tube placement in the small intestine. In the mid-gut TET group, mid-gut TET was placed in the small intestine for gastroscopy. Data on the clinical efficacy of WMT, intubation time, cost, overall comfort score, adverse reactions, etc., were collected from the two groups.

Results: Sixty-three patients were included in the study (SNT group (n = 40) and mid-gut TET group (n = 23)). The clinical efficacy of WMT in the SNT and mid-gut TET groups was 90 % and 95.7 %, respectively (P = 0.644). Compared with the mid-gut TET group, the SNT group showed a shorter operation time (120 s vs. 258 s, P = 0.001) and a lower average cost (641.7 yuan vs. 1702.1 yuan, P = 0.001). There was no significant difference in the overall comfort score or the incidence of common discomfort symptoms between the two groups.

Conclusion: The different implantation methods have different advantages; compared with mid-gut TET placement, manual SNT placement provides some benefits.

1. Introduction

With further research on the relationship between intestinal flora and diseases, an increasing number of studies have shown that faecal microbiota transplantation (FMT) can be used to treat diseases related to intestinal flora imbalance, such as digestive system

Abbreviations: WMT, washed microbiota transplantation; TET, transendoscopic enteral tubing; SNT, spiral nasojejunal tube; FMT, faecal microbiota transplantation; BMI, body mass index.

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diseases, which include ulcerative colitis [1], Crohn's disease [2], irritable bowel syndrome [3], functional constipation [4], radiation enteritis [5], hepatitis B [6], cirrhosis [7], and hepatic encephalopathy [8]. FMT can also be used to treat diseases other than those of the digestive system, such as metabolic diseases and obesity [9], and neuropsychiatric system diseases, such as autism [10] and essential tremor [11]. FMT is performed by initial manual isolation, capsule community transplantation and washed microbiota transplantation (WMT). WMT is based on an automatic purification system (GenFMTer FMT Medical, Nanjing, China) [12]. This system, which can significantly reduce FMT-related adverse events, has been applied in many FMT centres in China [13].

Microbiota suspensions can be applied by the transplantation of capsules into the upper, middle or lower digestive tract [12]. Methods for WMT via the upper gastrointestinal route include the use of transgastroscopy and placement of a nasogastric tube [14]; methods for WMT via the middle gastrointestinal route include the use of transendoscopy, placement of a spiral nasojejunal tube (SNT), and placement of mid-gut transendoscopic enteral tubing (TET). Capsules can also be transmitted to the lower gastrointestinal tract via colonoscopy, an enema, or TET placement via colonoscopy. Different transplantation approaches may have different therapeutic effects on recurrent *Clostridium difficile* infection, irritable bowel syndrome, inflammatory bowel disease, etc. [14–16]. Age, disease status, general condition, compliance, cost-effectiveness, and comfort during administration all affect the selection of the transplantation route by doctors and patients [17].

In 2016, Peng et al. proposed the use of TET in FMT. TET can be placed into the caecum during a colonoscopy, with one end fixed in the caecum and the other end left in the body, to perform repeated FMT [18]. To date, colonic TET has three major applications in clinical practice and research: frequent and timely delivery of microbiota and medications; drainage and decompression for colonic perforation and ileocolic obstruction; and sampling for microbial research [19]. TET can also be placed into the small intestine during gastroscopy. In 2018, Long et al. published a prospective study on the rapid placement of TET using gastroscopy in the *Journal of BMC Gastroenterology*, with a high success rate and few adverse reactions [20]. These results indicate that the endoscopic placement of mid-gut TET is a novel, convenient, reliable and safe method that can solve the problem of FMT for patients who cannot tolerate intestinal preparation or colonoscopy.

The nasojejunal tube was originally used for drug delivery [21]; it is currently also used for diagnostic procedures [22], decompression [23] and feeding [24,25]. In 2014, a study that compared the efficacy of FMT via a nasogastric tube with that of FMT via a nasojejunal tube in patients with *Clostridium difficile* infection reported a 100 % basic cure rate for FMT via a nasogastric tube compared with 80 % primary and 93.3 % secondary cure rates for FMT via a nasogastric tube. The results showed that a nasojejunal tube was better than a nasogastric tube for the treatment of FMT [26]. During FMT via an SNT [8,27,28], microbes directly enter the small intestine without passing through the stomach; this approach prevents microbial stimulation that can cause stomach discomfort and vomiting, which in turn can lead to aspiration, aspiration pneumonia and other complications. FMT can also avoid bacterial contact with liquids, such as gastric juice, thus preventing bacterial destruction by stomach acid, which affects the therapeutic effect of FMT.

At present, there have been no studies comparing the advantages and disadvantages of manual SNT placement and endoscopic mid-gut TET catheterization in WMT. Therefore, the purpose of this study was to analyse the clinical effectiveness, patient comfort, complications, and economic costs of the above two approaches in WMT and to provide a reference index by which clinicians and patients can appropriately select the route for middle gastrointestinal catheterization.

2. Methods

This prospective interventional study was conducted at the First Affiliated Hospital of Guangdong Pharmaceutical University from January 2019 to November 2019. All patients who needed to undergo WMT through the mid-gut route were continuously included if they met the following inclusion criteria: age 18–85 years; any sex; tube indwelling duration of more than 2 days and refusal of extubation. Patients were excluded if they had a severe cardiopulmonary or brain disease, oesophageal stenosis, a nasolaryngological tumour or nasolaryngological strictures, a mental disorder or an inability to cooperate with the interviewees(Fig. 1). All participants

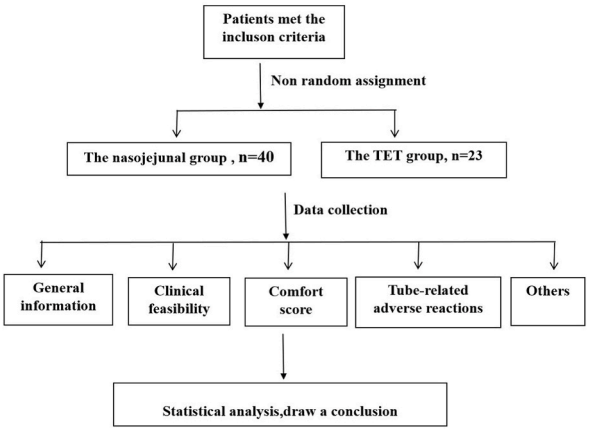

Fig. 1. Flow diagram.

signed an informed consent form to undergo WMT and participate in this study at the time of inclusion. This study was approved by the First Affiliated Hospital of Guangdong Pharmaceutical University: Medical Ethics Review [2019] No. 92. The trial was registered at http://www.chictr.org.cn (# ChiCTR1900025057).

Based on the patients' willingness to receive treatment via an SNT or mid-gut TET, the physician assigned them to the SNT group or mid-gut TET group. In the SNT group, an SNT was passed passively into the stomach, and an abdominal X-ray was obtained 24 h later to confirm whether the head end was placed in the small intestine; if the head was not in the small intestine, another radiograph was taken 48 h later, and if the head was still not in the small intestine, endoscopic placement was performed. In the mid-gut TET group, the TET was placed in the small intestine under painless gastroscopy. The SNT or mid-gut TET was removed manually after 3 consecutive days of WMT.

3. Procedures

The method of catheterization in the SNT group was as follows. The SNT (CH10; Flocare Bengmark, Nutricia, Fig. 2) was 145 cm in length, 3.23–3.28 mm in outer diameter, and 1.95–2.10 mm in inner diameter. After simple training, the clinician applied the passive waiting method according to the procedure outlined in the manufacturer's instructions. If the SNT did not move into the digestive tract after a long period of time, an appropriate dose of metoclopramide hydrochloride (10 mg, intramuscular injection) was administered. An abdominal X-ray was obtained 24 h later to confirm whether the tip of the head had reached the small intestine; if not, an X-ray was obtained again 48 h later. Two experienced imaging doctors jointly determined whether the SNT had reached the small intestine, and if the judgement was inconsistent or difficult, the SNT contrast method was used for confirmation.

The method of catheterization in the mid-gut TET group was as follows. The mid-gut TET (Fig. 3, FTT-DT-N-27/1350) was normal drug administration tubing with a diameter of 2.7 mm and a length of 1350 mm from FMT Medical, Nanjing, China. The operators were endoscopists who were skilled in gastroscopy and were required to have completed approximately 300 endoscopies. According to the method of mid-gut TET catheterization under gastroscopy described by Long et al. [20], after the patient was prepared for painless gastroscopy, the mid-gut TET was placed in and below the lower part of the duodenum under direct gastroscopy and fixed.

4. WMT

Patients did not require antibiotics before WMT, and fasting was not needed. Proton pump inhibitors (such as esomeprazole 30 mg + normal saline 100 ml) were administered intravenously 1 h before the injection of bacteria (to reduce the inactivation of bacteria

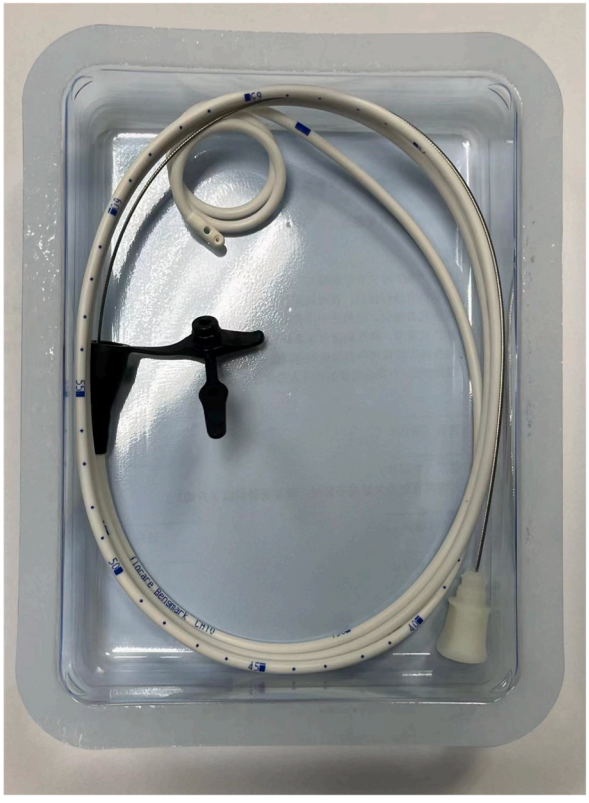

Fig. 2. Spiral nasojejunal tube.

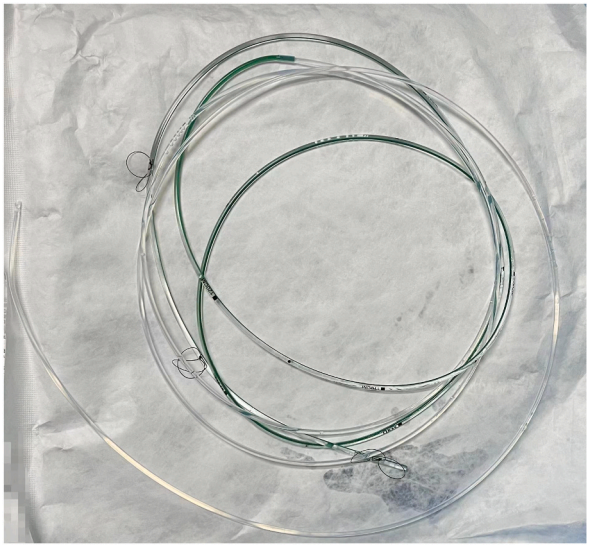

Fig. 3. Mid-gut transendoscopic enteral tubing.

when moving through the stomach). Metoclopramide hydrochloride (10 mg) was injected intramuscularly (to reduce adverse reactions such as vomiting or abdominal distension caused by irritation of the gastrointestinal tract by the bacterial fluid). The patients were in a sitting position when the bacterial solution was being injected. The injection process was slow, requiring an injection time of at least 30 min for 200 ml of bacterial solution. After the injection, the patient was asked to remain sitting or standing for at least 2 h. One course of treatment was administered once a day for 3 days.

5. Data collection

Once patients were enrolled, data including sex, age, body mass index (BMI), and diagnosis were collected from the two groups. The following main observation indices were recorded after enrolment: ① The cost of treatment in the two groups. The cost in the SNT group included the SNT, insertion operation, hydrochloric acid amine methoxychlor tome, X-ray film cost, and bed fee if there was a delay in the tube reaching the small intestine or if the tube failed to reach the small intestine, resulting in a switch to another method of catheterization. The cost in the mid-gut TET group included the mid-gut TET, insertion operation, the cost of painless gastroscopy and the cost of catheterization via another method after catheterization failure.② Clinical effectiveness, defined as successful insertion of the SNT or mid-gut TET into the small intestine within 48 h, with no unplanned tube release or blockage during tube retention and an indwelling time meeting the requirements of clinical WMT. ③ Comfort score, ranging from 0 to 10, with 0 indicating severe, unbearable pain and 10 indicating almost no discomfort, as evaluated by the patient. Secondary outcome measures included the following: tube-related adverse reactions, including nausea, vomiting, nasal discomfort, pharyngeal discomfort, pharyngeal bleeding, nasopharyngeal bleeding, pharyngeal pain, effects on patient sleeping, eating or drinking, tube extubation or rupture, and nausea or vomiting, abdominal pain, nasopharyngeal pain or discomfort during extubation. The timing of catheterization in the two groups was started when the SNT or mid-gut TET entered the nasal cavity and ended when the guide wire was removed in vitro; additionally, the operator experienc level was recorded. The comfort score of SNT insertion and the amount of metoclopramide hydrochloride used in the SNT group were also recorded.

6. Statistical analysis

SPSS 22.0 statistical software was used. Normally distributed data are reported as the mean ± standard deviation, while non-normally distributed measurement data are represented by the median and interquartile range. The independent-samples T test or nonparametric Wilcoxon rank-sum test was used for measurement data, Pearson chi-square test or Fisher's exact test was used for count data, and Kendall's Tau_B test was used for correlation analysis. All hypothesis tests were performed by bilateral analyses, and $P < 0.05$ was considered to indicate statistical significance.

7. Results

1 General information

A total of 63 patients (33 females) were included, including 40 patients in the SNT group and 23 patients in the mid-gut TET group. There were no significant differences in age, BMI or sex between the two groups (Table 1). The causes of WMT included functional

constipation in 18 patients (28.57 %), irritable bowel syndrome with diarrhoea in 12 patients (19.05 %), and functional diarrhoea in 11 patients (17.46 %) (Fig. 4).

2 Comparison of clinical effectiveness of WMT between the two groups

In all 23 patients in the mid-gut TET group, TET was successfully placed in the small intestine under painless gastroscopy, with a placement rate of 100 %. Of the 40 patients in the SNT group, the catheter reached the small intestine within 24 h in 35 patients, within 24–48 h in one patient, and after 48 h in four patients. The rate of catheterization of the small intestine within 48 h in the SNT group was 90 %. Fisher's exact test yielded $X^2 = 2.456$ and $P = 0.287$, indicating no significant difference in the rate of small intestine catheterization between the two groups.

Tube blockage occurred in both groups during tube retention, affecting 1 patient (2.5 %) in the SNT group and 2 patients (8.7 %) in the mid-gut TET group, with no significant difference between the two groups ($X^2 = 1.236$, $P = 0.548$; Table 4). One patient in the SNT group and one patient in the mid-gut TET group developed blockages; in these patients, the tube was cleared after the injection of gas and water, and WMT was continued. However, in another patient in the mid-gut TET group, the tube was not successfully cleared after the injection of gas and water. This patient was advised to have the position of the tube adjusted or to have the mid-gut TET repositioned under gastroscopy; however, the patient refused due to pharyngeal pain and foreign body sensation and opted to have the mid-gut TET replaced under colonoscopic guidance to continue WMT. The mean indwelling time in the SNT group was longer than that in the mid-gut TET group (3.4 vs. 2.3 days, $P = 0.001$; Table 2). In addition, no cases of unplanned detachment occurred in either group.

In conclusion, the clinical effectiveness in the SNT group was 90 % (4 patients did not achieve tube placement in the small intestine within 48 h), and that in the mid-gut TET group was 95.7 % (in 1 patient, the blockage could not be cleared), with no significant difference between the two groups ($X^2 = 0.639$, $P = 0.644$).

3 Comparison of catheterization comfort

The overall comfort scores in the two groups during tube retention were 7 (5–8) vs. 8 (6–9), with no significant difference ($P = 0.063$; Table 2). Endoscopic catheterization in the mid-gut TET group was performed under painless anaesthesia, so the degree of catheterization comfort was not evaluated. The comfort score in the SNT group was 7.5 (6–8); 22.5 % (9/40) of patients with a comfort score less than or equal to 5 reported that the procedure was relatively painful, and two of them said that the pain was unbearable and refused to choose this method of treatment again. Overall, 77.5 % (31/40) of patients had scores greater than or equal to 6, indicating that most patients had no marked pain and could tolerate the procedure.

4 Relationship between the use of metoclopramide hydrochloride and SNT arrival in the small intestine

Sixteen patients in the SNT group received metoclopramide hydrochloride after catheterization (experimental group), including 5 who received 20 mg of metoclopramide hydrochloride and 11 who received 10 mg of metoclopramide hydrochloride; these patients were compared with patients who did not receive metoclopramide hydrochloride (control group, 24 patients) (Table 3). The proportions of patients who underwent catheterization with the tube reaching the small intestine within 24 h were 75 % and 95.7 % (experimental group vs. control group), respectively. There was no significant difference in the rate of small intestine catheterization with an SNT according to the use of metoclopramide hydrochloride ($X^2 = 0.138$, $P = 3.810$, Fisher's exact test).

5 Comparison of adverse reactions to catheterization

There were no serious adverse reactions during catheterization or catheter retention in either group, and there were no complications, such as abdominal pain, nosebleeds, extubation difficulty or tube fracture, in either group. Moreover, no anaesthesia-related adverse events occurred during mid-gut TET catheterization under gastroscopy, and no gastroscope-related adverse events, such as oesophageal perforation or gastric perforation, occurred. Adverse reactions in the two groups included the following: nausea or vomiting; nasal or pharyngeal discomfort; pharyngeal bleeding; pharyngeal pain; effects on sleeping, eating or drinking; abdominal pain; and nasal pharyngeal pain or discomfort during extubation. These adverse reactions were mild, self-limiting and did not require

Table 1
Basic information of the two groups of patients.

Items	SNT group (n = 40)	Mid-gut TET group (n = 23)	P value
Age (mean ± standard deviation)	58.8 ± 15.62	52.57 ± 15.21	1.54[a]
Sex (n, %)			
Male	21 (52.5 %)	9 (37.5 %)	0.306[b]
Female	19 (47.5 %)	14 (62.5 %)	
BMI (median; IQR, kg/m^2)	21.21 (19–24.57)	21.2 (18.86–26.37)	0.578[b]

Note.
[a] T test analysis of independent samples.
[b] Nonparametric Wilcoxon signed-rank test.

Table 2
Statistical analysis of the intubation time, overall comfort score, indwelling time, and operator level in the two groups.

Items	SNT group (n = 40)	Mid-gut TET group (n = 23)	P
Intubation time (median; IQR, s)	120 (62.25–237.5)	258 (180–326)	0.001[a]
Overall comfort score (median; IQR, score)	7 (5–8)	8 (6–9)	0.063[a]
Indwelling time (median, days)	3.4	2.3	0.001[a]
Cost (yuan)	641.7	1702.1	0.001
Operator level			0.001[b]
Resident physician (n)	17	0	
Attending physician (n)	23	12	
Associate chief physician (n)	0	11	

Note.
[a] Nonparametric Wilcoxon signed-rank test.
[b] Fisher's exact test for sample sizes (T) less than 5.

Table 3
Relationship between the use of metoclopramide hydrochloride and the success rate of SNT placement in the small intestine.

Use of metoclopramide hydrochloride	Arrival within 24 h	No arrival within 24 h	P	X^2
Yes (N = 16)	12	4	0.138	3.810
No (N = 24)	23	1		

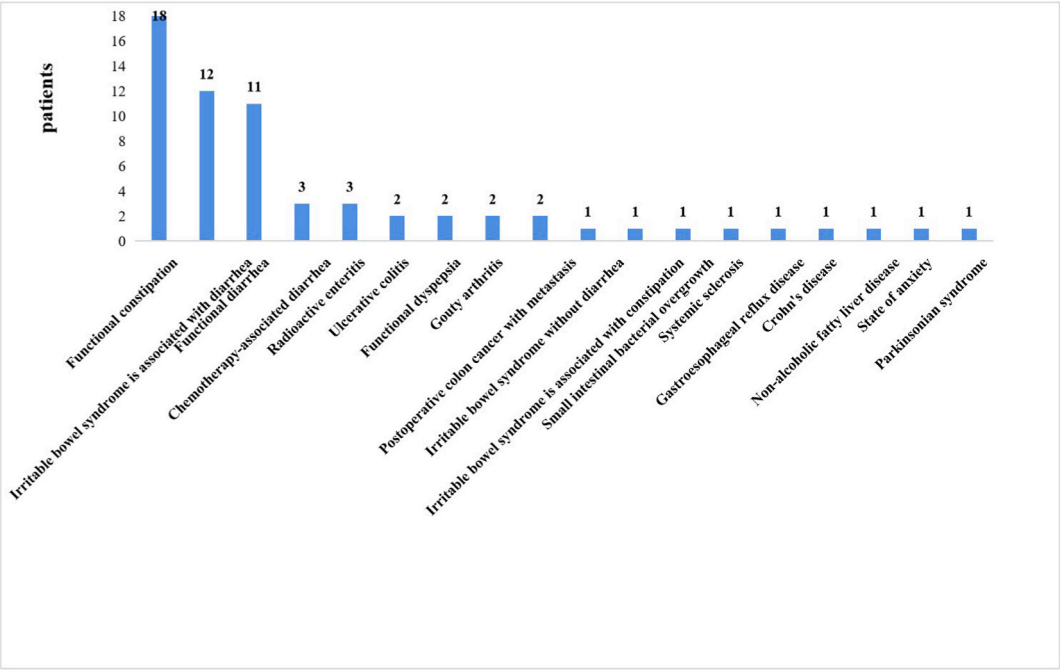

Fig. 4. Patient distribution by aetiology.

special treatment after extubation. There was no significant difference in adverse reactions between the two groups (all $P > 0.05$, chi-square test; Table 4).

6 Comparison of tube insertion cost and time

The average cost in the SNT group was obviously lower than that in the mid-gut TET group (641.7 yuan vs. 1702.1 yuan, Z = −6.904, P = 0.001). In the SNT group, catheterization was performed by a resident or attending physician after simple training. Seventeen patients (42.5 %) were catheterized by a resident, and 23 patients (57.5 %) were catheterized by an attending physician. Mid-gut TET placement under gastroscopy was performed by an endoscopist who was trained and skilled in gastroscopy; TET placement was performed by an attending physician in 12 patients (52.2 %) and an associate chief physician in 11 patients (47.8 %). We assumed a catheter placement score of 1 for resident physicians, 2 for attending physicians, and 3 for associate chief physicians.

Table 4
Comparison of adverse reactions between the two groups.

Adverse reactions	SNT group		Mid-gut TET group		X^2	P
	+	−	+	−		
Blockage	1	39	2	21	1.236	0.548
Nausea or vomiting during indwelling	7	33	3	20	0.217	0.734
Pharyngeal discomfort	30	10	21	2	2.518	0.183
Nasal discomfort	17	23	14	9	1.972	0.160
Pharyngeal bleeding	1	39	2	21	1.236	0.548
Pharyngeal pain	13	27	8	15	0.034	0.853
Effects on sleep	9	31	7	16	0.485	0.486
Effects on eating or drinking	17	23	9	14	0.068	0.794
Nausea or vomiting during extubation	1	39	3	20	2.73	0.134

Note. Fisher's exact test for $T < 5$; Pearson chi-square test for $T \geq 5$. All *P* values were greater than 0.05.

Analysis of the scores in the two groups by Fisher's exact test indicated a significant difference in the level of the catheterization physician between the two groups ($X^2 = 31.684$, $P = 0.001$; Table 2). The time needed for tube insertion in the SNT group and the mid-gut TET group was 120 s (62.25–237.5) vs. 258 s (180–326), indicating that significantly less time was needed for manual SNT insertion than mid-gut TET catheterization under gastroscopy ($Z = -3.758$, $P = 0.001$). Resident physicians (157 s, 106.5–302) required significantly more time than attending physicians (103 s, 60–180) in the SNT group (($Z = -2.195$, $P = 0.028$), but there was no significant difference in the degree of pain felt by the patients during the process of catheterization ($P = 0.195$). In the mid-gut TET group, there was no significant difference in the time required for endoscopic mid-gut TET placement between the attending and associate chief physicians (281 s vs. 249 s, $Z = -0.893$, $P = 0.372$; Table 5).

7 Advantages and disadvantages of SNT and mid-gut TET use in WMT

Comparison of the two methods showed that both an SNT and mid-gut TET can be used for satisfactory WMT, with the same overall comfort score and incidence of adverse reactions. However, both approaches have advantages and disadvantages. SNT insertion into the stomach is performed in direct view of the patient while the patient is awake, and there is some discomfort. Abdominal X-rays are obtained within 24 h to confirm tube placement in the small intestine. If the tube has not arrived, the patient needs to wait for another 24 h. If the tube still has not arrived, the patient needs to undergo gastroscopy to place the SNT in the small intestine, which prolongs the length of hospital stay and increases medical costs. However, the results of this study showed that 95 % of the patients in the SNT group tolerated bedside catheterization, and the arrival rate within 24 h was 87.5 %. Compared with mid-gut TET placement, SNT placement is simpler and faster to perform, less expensive, and does not carry the risks of gastroscopy or anaesthesia. Although patients will not feel uncomfortable during mid-gut TET placement under painless gastroscopy, whether the patient can tolerate gastroscopy and anaesthesia needs to be assessed, and fasting before the examination is needed. Doctors must also have experience with gastroscopy in more than 300 patients, and this method is more expensive; however, upper gastrointestinal diseases can be observed (Table 6).

8. Discussion

This prospective and controlled clinical trial showed that there were no significant differences in clinical efficacy, adverse reactions, or overall comfort scores between manual SNT placement at the bedside and mid-gut TET placement under gastroscopy, but there were significant differences in the financial cost, catheter insertion time, and level of the operating physician (Table 6).

Compared with mid-gut TET placement under gastroscopy, SNT placement is simple, with lower requirements for operating physicians. In this study, catheter insertion was mainly performed by residents and attending physicians, and the time for catheter insertion by attending physicians was markedly shorter than that for residents ($P = 0.001$), which may be related to operator proficiency. In the mid-gut TET group, catheterization was performed mainly by attending physicians or associate chief physicians who were skilled in gastroscopy (having performed endoscopy in at least 300 patients), and there was a significant difference in the physician level ($P = 0.001$) between the two groups. Similar results were described in a paper published by Long et al. on endoscopic mid-gut TET placement [20]. Similar to in our study, the operator was required to be a physician skilled in performing gastroscopy;

Table 5
Analysis of the intubation time and discomfort scores by operator level in the two groups.

Groups	Items		Median; IQR	Z	P
SNT group (n = 40)	Intubation time (seconds)	Resident physician	157 (106.5–302)	−2.195	0.028
		Attending physician	103 (60–180)		
	Discomfort score (score)	Resident physician	8 (6–8)	−1.295	0.195
		Attending physician	7 (5–8)		
Mid-gut TET group (n = 23)	Intubation time (seconds)	Attending physician	281 (185–334.25)	−0.893	0.372
		Associate chief physician	249 (168–307.79)		

Table 6
Similarities and differences between SNT and mid-gut TET use in WMT.

Differences	SNT	Mid-gut TET[a]
X-ray examination	+[b]	-[c]
Risk of gastroscopy and anaesthesia	–	+
Discomfort during tube placement	+	–
Requirements for patients	Can tolerate bedside catheterization	Can tolerate anaesthesia and gastroscopy; fasting
Requirements for physicians	Resident or attending physician	Attending physician or associate chief physician skilled in gastroscopy
Observation of upper gastrointestinal lesions	–	+
Financial cost	Less expensive	More expensive
Time cost	Shorter	Longer
Risk of catheterization failure and prolonged hospital stay	+	–
Similarities	Clinical effectiveness of WMT, overall comfort score, incidence of adverse reactions.	

Note.
[a] Mid-gut TET, TET placement into the small intestine under painless gastroscopy.
[b] +, yes.
[c] -, no.

however, in the Long study, the catheterization time was shorter for senior endoscopists than for general endoscopists (3.3 min vs. 5.5 min), and the success rate was 98.8 %. In contrast, in our study, there was no significant difference in the time of catheter insertion (249 s vs. 281 s), and the success rate was 100 %. In terms of medical expenses, the average cost incurred in the mid-gut TET group (1702.1 yuan) was nearly three times that in the SNT group (641.7 yuan). Because of the simple operation involved in SNT placement, the catheterization time was significantly shorter in the SNT group than in the mid-gut TET group, and the placement time in the mid-gut TET group did not include the duration of anaesthesia, gastroscopy, or postoperative recovery from anaesthesia. However, patients in the mid-gut TET group underwent gastroscopy, which enabled the identification of upper gastrointestinal lesions. At present, there have been no relevant studies comparing the economic benefits of the two catheterization methods. Our study revealed that bedside SNT placement is better than gastroscopic mid-gut TET placement in terms of cost, labour and time and is recommended for mid-gut WMT.

In this study, TET placement in the small intestine under gastroscopy was successful, but the SNT could only enter the stomach. Because of its special spiral structure, the auxiliary SNT meets the treatment needs when it is placed into the small intestine [29]. According to previous research on the passive placement of an SNT, the success rate of reaching the small intestine within 24 h varies from 52.2 % to 82.7 % [29–32], but the rate of placement in the small intestine significantly increases by more than 85 % with the use of gastrointestinal motility drugs, gastric steam injection or water injection and changes in body position [31,33–35]. In our study, the success rate of SNT placement in the small intestine within 24 h was 87.5 % (35/40), which is relatively consistent with the success rates reported in the literature. There were three cases of tube blockage in the two groups, two of which were resolved by gas and water injection. However, one case was not resolved after the injection of gas and water; the patient refused adjustment of the catheter under gastroscopy, and the exact cause of the blockage was unknown. Notably, there is a risk of blockage in any tube [35,36]. According to research reports, the incidence of obstruction during the application of an SNT ranges from 9 % to 35 % [36,37]. In this study, the incidence of blockage was only 2.5 % (1/40). Negligence of the nursing staff in the catheter maintenance is the most important potential cause of blockages [38]. The following technical factors can also easily lead to tube obstruction: insufficient water irrigation (especially after medication or feeding) and the infusion of drugs (especially crushed tablets in a narrow cavity). However, there have been no related reports on the blockage of TET used for FMT [39]. In this study, two cases of blockage (8.7 %) occurred in the mid-gut TET group. These cases could have occurred because the remaining bacterial liquid in the tube led to blockage, the distal end of the pipe was blocked by food, or the tube became bent in the stomach.

Because SNTs are placed at the bedside and mid-gut TET is placed under gastroscopy, which is an invasive operation through the nose and throat, patients can develop a violent illness, when the latter method is applied [40]. In the process of placement, the indwelling catheter and tube drawing process are likely to cause adverse reactions, including tube placement in the nasal mucosa or nasopharyngeal submucosal channel; pharyngeal lesions; tube malpositioning; injury or perforation of the mucosa in the oesophagus, stomach or small intestine; nausea, vomiting, or abdominal pain; and effects on sleeping or eating, nasal congestion, or nasal discharge during tube retention [41]. Because mid-gut TET is placed under painless gastroscopy, this study investigated only subjective discomfort during SNT insertion. The results showed that the median comfort score was 7.5 points, and 77.5 % of the patients had a score greater than or equal to 6, indicating that most of the patients tolerated the procedure well. Second, there was no significant difference in the degree of discomfort felt by patients according to the operator level. In a study of 2267 patients treated with modified blind SNT-based FMT, the patients scored 2.6 and 2.7 (mild pain) on the digital evaluation scale for pain perception during catheter placement and retention, respectively [42]. Most patients can undergo manual SNT placement at the bedside, and improvements in operator proficiency and care can reduce patient discomfort during catheter insertion. In terms of adverse reactions, the above article showed that patients experienced nasopharyngeal pain (8.4 %), foreign body sensations in the throat (13.2 %), rhinorrhoea (2 %), and mild nasal bleeding (1 %). In Professor Zhang's observational study on mid-gut TET placement, the operation-related adverse events were mild pharyngeal bleeding (1.2 %) and limited epistemic bleeding (4.6 %), while the catheter-related adverse events included

moderate to severe pharyngeal discomfort (4.6 %), rhinorrhoea (1.2 %), and nausea (1.2 %) [20]. The hardness, thickness, diameter and material composition of the two kinds of catheters in the present study were different, but the results showed no significant difference in either the overall comfort score or adverse reactions between the groups. The most common adverse reactions in the two groups were pharyngeal discomfort (80.9 %), nasal or pharyngeal discomfort (49.2 %), and discomfort during eating (41.3 %). Additionally, 33.3 % of the patients experienced pharyngeal pain, and 25.4 % experienced sleep problems; these adverse reactions were mild and gradually resolved within one week after extubation without the need for special treatment. There was also no significant difference in the incidence of adverse reactions during tube retention between the two groups.

It has been reported that the factors affecting the entry of an SNT into the small intestine may be related to gastrointestinal motility disorders [40]. In a prospective study involving general patients ($n = 70$), the use of metoclopramide did not significantly differ from the use of a placebo (60 % vs. 49 %) in promoting SNT entry into the duodenum but did significantly differ in patients with diabetes (64 % vs. 20 %), suggesting that the use of metoclopramide helps promote SNT entry into the small intestine in patients with impaired gastrointestinal motility [43]. In addition, a meta-analysis published in 2015 evaluated how to promote SNT movement through the pylorus in 753 cases from clinical trials in 14 categories. The results showed that compared with standard methods, the use of motility drugs yielded a greater success rate, but the use of steam was more common in adults. Therefore, the authors of this study did not recommend the use of motility drugs in patients with normal gastrointestinal motility [44]. There was no significant difference in the success rate of SNT entry into the small intestine based on whether metoclopramide was used (75 % vs. 95.8 %, $p = 0.138$), indicating that the use of metoclopramide does not promote SNT entry into the small intestine and may even be counterproductive. The conclusion of that study was that the use of motility drugs in patients with normal gastrointestinal function does not consistently improve the success rate of tube placement. Unfortunately, the gastrointestinal motility of patients was not assessed in the present study.

There are several limitations to this study. The sample sizes of the two groups were small, and the position of the SNT was not determined by SNT angiography in every patient, so there may have been some misjudgements regarding the position of the tube. When comparing the time of catheterization between the two groups, the time of catheter insertion into the gastric space was calculated in the SNT group, while the time of catheter insertion into the small intestine was calculated in the mid-gut TET catheter group, indicating different goals in the two groups. In the future, a randomized controlled study with a larger sample size and a more complete survey questionnaire that includes patient preference will be designed to provide reference indicators for clinicians and patients.

9. Conclusion

This study compared manual SNT placement at the bedside with mid-gut TET placement under gastroscopy. SNT placement required less time, was less expensive, required less skill, was simpler, and carried none of the risks associated with endoscopic diagnosis and treatment or painless anaesthesia. There was no significant difference between the two methods in terms of the clinical effectiveness of WMT, overall comfort score or incidence of adverse reactions. However, compared with those in the mid-gut TET group, a small number of patients in the SNT group experienced more pain at the time of catheterization, and the success rate of entry into the small intestine was slightly lower in the SNT group, necessitating an X-ray examination to confirm tube placement. In general, the different placement methods have different advantages. Compared with mid-gut TET placement, manual SNT placement has several benefits, such as simple manual placement, low cost, good clinical effectiveness and satisfactory patient comfort, rendering SNT placement a relatively good choice for use in mid-gut WMT. However, larger studies including survey questionnaires evaluating patient preference or any other additional aspects are needed.

Statement of interests

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Ethics statement

All participants signed an informed consent form to undergo WMT and participate in this study at the time of inclusion. This study was approved by the First Affiliated Hospital of Guangdong Pharmaceutical University: Medical Ethics Review [2019] No. 92.

Data availability statement

The data will be made available upon request.

CRediT authorship contribution statement

Ya-Mei Zheng: Writing – original draft, Methodology, Investigation. **Hui-Yi Wu:** Data curation. **Meng-Meng Ye:** Investigation. **Jie-Yi Cai:** Formal analysis. **Yu Yuan:** Supervision. **Wen-Rui Xie:** Validation. **Jia-Ting Xu:** Software. **Tao Liu:** Methodology, Formal analysis. **Xing-Xiang He:** Conceptualization. **Li-Hao Wu:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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