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Simo decoction versus domperidone suspension for post-pyloric spiral nasoenteric tube placement: A multicenter, randomized, noninferiority trial

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Background

- Enteral access should be attained and enteral nutrition (EN) initiated within 24-48 h of admission in the critically ill patient who is unable to maintain volitional intake.
- Oral intake or nasogastric feeding is most appropriate when starting EN, switching to post-pyloric feeding for patients at high risk for aspiration, with high gastric residual volumes or with intolerance of gastric feeding.

Background

- Using a self-propelled spiral nasoenteric tube for post-pyloric feeding has emerged as a promising approach.
- RCTs had demonstrated that several prokinetic agents, including erythromycin, metoclopramide and domperidone, improve the success rate of post-pyloric placement of spiral nasoenteric tubes.
- Several RCTs have concluded that the combination of simo decoction and acupuncture is effective for promoting the recovery of gastrointestinal function after surgery.

Background

- However, there is limited evidence that simo decoction facilitates trans-pyloric migration of spiral nasoenteric tubes.
- Therefore, a non-inferiority RCT was designed to evaluate whether simo decoction is an acceptable alternative to domperidone suspension in facilitating post-pyloric placement of spiral nasoenteric tubes in critically ill adults.

Methods --- Study design

- A prospective, open-label, parallel, and noninferiority RCT conducted at ICUs of six university hospitals in Guangdong Province, China.
- The study protocol, designed in accordance with the CONSORT statement , was approved by the ethic committees of all of the participating centers .
- Informed consent was obtained from each patient or his/her legal authorized representative before the intervention.

Methods --- Patients

纳入标准：

- Adult patients consecutively admitted to ICUs
- With indication for EN and elevated gastric residual (single measurement > 150 ml or 12 h cumulative volume > 500 ml)

Methods --- Patients

排除标准：

- Indications for percutaneous gastrostomy or jejunostomy
- Oesophageal varices or history of major gastroesophageal surgery
- Active upper gastrointestinal bleeding
- Severe nasopharyngeal injuries or stenosis
- Severe coagulopathy

Methods --- Patients

排除标准：

- Gastric malignancy, peptic ulcer or intestinal mechanical obstruction
- Pregnancy
- Contraindications of simo decoction or domperidone suspension
- History of allergy to meglumine diatrizoate

Methods --- Randomization

- Enrolled patients were randomized in a 1:1 ratio by computergenerated random numbers to simo decoction or domperidone suspension arms in blocks of 8 to minimize the allocation bias.
- None of the investigators was aware of the randomization list prior to group allocation, as well as blocks numbers or blocks sizes at any moment in order to maintain allocation concealment.

Methods --- Study intervention

- Patients were randomly assigned to receive either simo decoction 20 ml q8h, or domperidone suspension 20 mg/20 ml q6h for 24 h, administered via the tube immediately when it was inserted into stomach.

Methods ---Data collection

- Demographic characteristics, diagnosis, concomitant drug, APACHE II, SOFA, AGI, Nutritional Risk Score 2002, length of hospital stay before ICU admission, length of ICU stay before randomization and length of receiving EN before randomization were collected.
- The tube tip position confirmed by abdominal X-ray 24 h after tube insertion.

Methods ---Data collection

- The exact location of the tube tips was documented.
- Adverse events including the side effects of study drugs and tube insertion complications were also evaluated and documented.

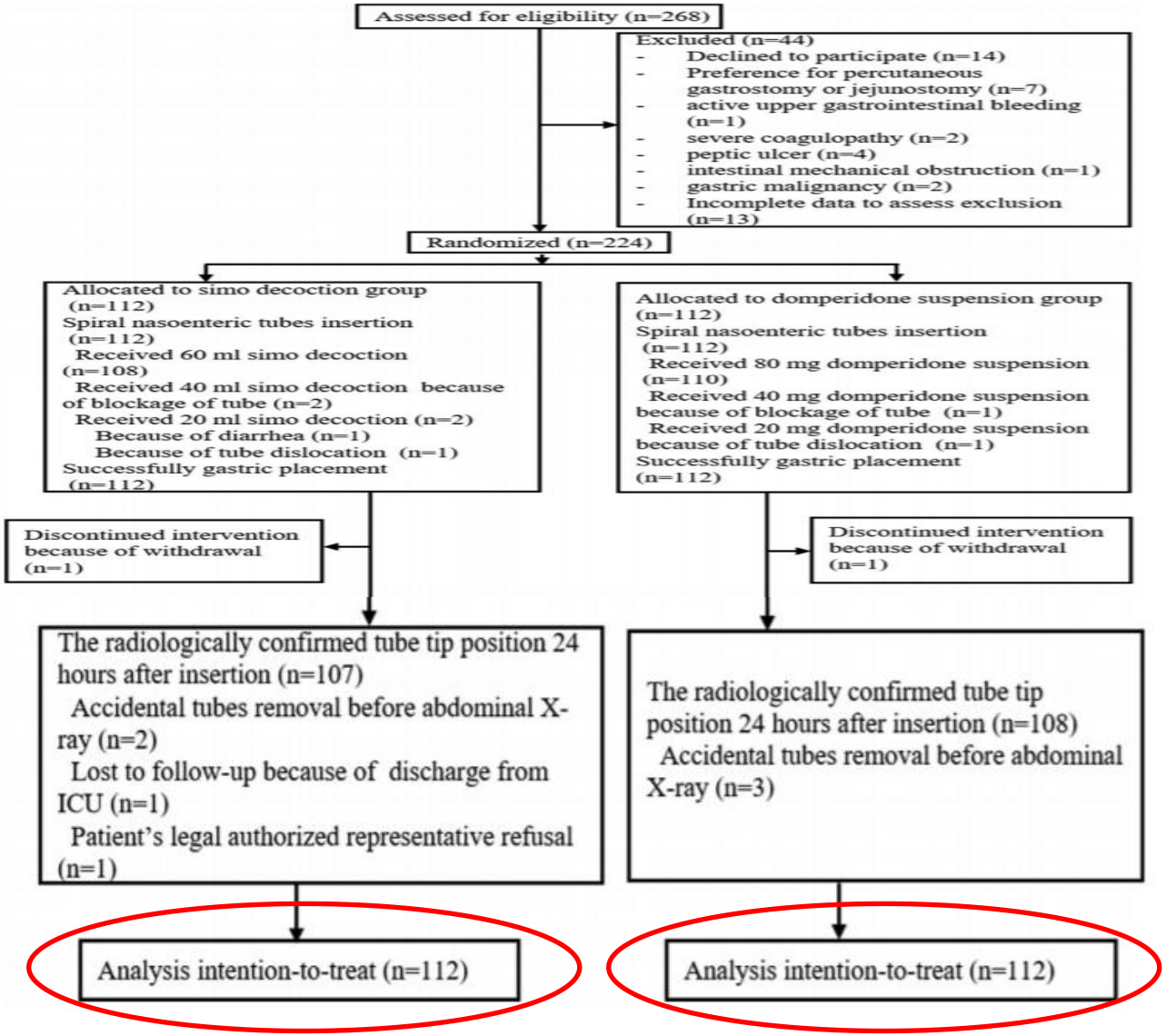
Methods ---Study outcomes

- The primary outcome was procedure success defined as postpyloric placement .
- The secondary outcomes were the success rates of postD1, postD2, postD3
- Length of ICU stay
- Mortality in ICU

Statistical analysis

- A sample size of 102 patients per group was calculated by PASS software.
- For continuous variables, the normality of data was assessed by the ShapiroeWilk test.
- The Student's t test for continuous variables with normal distribution.
- Statistical analysis was performed using SPSS 22.0 and SAS 9.4.

Results --- Enrollment



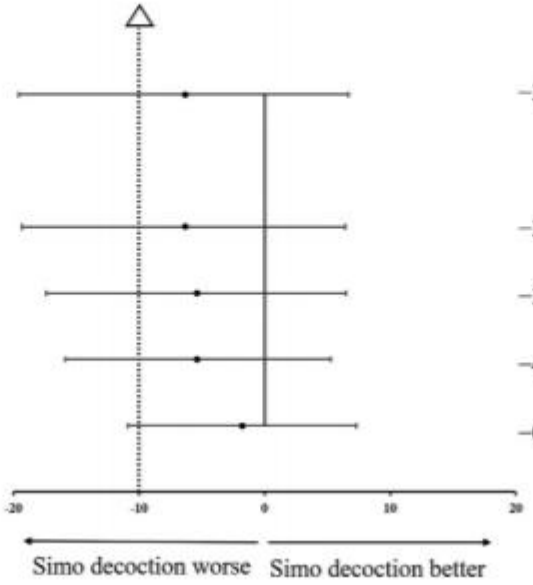
Results ---Baseline characteristics

Table 1
Demographics and clinical characteristics of study population.

Variables	Simo decoction group (n = 112)	Domperidone suspension group (n = 112)
Age (years)	67 (51–75)	61 (50–70)
Male	66 (58.9)	68 (60.7)
Weight (kg)	61.0 ± 9.6	59.0 ± 8.8
BMI (kg/m^2)	22.6 ± 2.6	22.0 ± 2.5
Primary diagnosis		
Neurologic	63 (56.3)	68 (60.7)
Respiratory	21 (18.8)	20 (17.9)
Cardiovascular	12 (10.7)	10 (8.9)
Gastrointestinal	5 (4.5)	1 (0.9)
Multitrauma	5 (4.5)	5 (4.5)
Sepsis	4 (3.6)	3 (2.7)
Others	2 (1.8)	5 (4.5)
Use of sedatives	49 (43.8)	43 (38.4)
Use of vasopressors	18 (16.1)	23 (20.5)
Mechanical Ventilation	81 (72.3)	80 (71.4)
NRS 2002	4 (3–5)	4 (3–5)
APACHE II score	21.1 ± 6.1	21.2 ± 5.8
SOFA score	7 (5–10)	7 (5–9)
AGI grade		
0	6 (5.4)	4 (3.6)
I	39 (34.8)	32 (28.6)
II	62 (55.4)	63 (56.3)
III	5 (4.5)	13 (11.6)
Gastric residual volume		
Single measurement > 150 ml	100 (89.3)	104 (92.9)
12 h cumulative volume > 500 ml	12 (10.7)	8 (7.1)
Length of hospital stay before ICU admission (days)	4 (0–9)	2 (0–8)
Length of ICU stay before randomization (days)	2 (1–6)	3 (1–6)
Length of receiving EN before randomization (days)	1 (0–4)	1 (0–6)

Results ---Primary outcomes

	Simo decoction group (n=112)	Domperidone suspension group (n=112)	Risk difference from Domperidone suspension group (95% CI)[a]	Adjusted risk difference 95% CI [b]	*p* value for non-inferiority [c]	*p* value for difference [d]
Primary outcome						
Post-pyloric placement	46 (41.1)	53(47.3)		−3.7 (−16.3 to 9.0)	0.285	0.346
Secondary outcomes						
Post-D1 placement	40 (35.7)	47 (42.0)		−3.8 (−16.2 to 8.5)	0.281	0.337
Post-D2 placement	29 (25.9)	35 (31.3)		−3.5 (−15.1 to 8.1)	0.220	0.375
Post-D3 placement	18 (16.1)	24 (21.4)		−4.1 (−14.2 to 5.9)	0.187	0.304
Proximal jejunum placement	13 (11.6)	15 (13.4)		−0.1 (−8.8 to 8.5)	0.032	0.686



Results ---Safety

Table 2
Adverse events and clinical outcomes.

Event	Simo decoction group ($n = 112$)	Domperidone suspension group ($n = 112$)	p value
Adverse events, total	14 (12.5)	18 (16.1)	0.445
Drugs side effects	4 (3.6)	10 (8.9)	0.166
Diarrhea	3 (2.7)	6 (5.4)	0.499
Abdominal pain	1 (0.9)	1 (0.9)	1.000
Rash	0	1 (0.9)	1.000
Somnolence	0	1 (0.9)	1.000
Dysphoria	0	1 (0.9)	1.000
Tube insertion complications	10 (8.9)	8 (7.1)	0.623
Nasal mucosa bleeding	7 (6.3)	5 (4.5)	0.553
Bucking	1 (0.9)	2 (1.8)	1.000
Nausea	2 (1.8)	1 (0.9)	1.000
Clinical outcomes			
Mortality in ICU	15 (13.4)	13 (11.6)	0.686
Length of ICU stay (days)	12 (7–17)	12 (7–21)	0.534

Data presented as median (interquartile range) or n (%) unless indicated otherwise.
ICU: Intensive care unit.

Discussion

- Our trial is the first head-to-head comparison of simo decoction versus domperidone suspension as adjuvant treatment.
- There were no differences between the groups in the success rates of post-D1, post-D2, post-D3 and proximal jejunum placement, the incidences of adverse events, length of ICU stay or mortality in ICU.

Discussion

- There is a lack of evidence from randomized trials to either support or refute the routine use of simo decoction in promoting trans-pyloric migration of spiral nasoenteric tubes in critically ill patients.
- Thus, a total-dose of 60 ml (maximum dose as recommended in the drug instruction manual) of simo decoction was ultimately designed.

Discussion

- The current multicenter RCT found that the success rate of post-pyloric tube placement in the simo decoction group (41.1%) was not non-inferior to that in the domperidone suspension group (47.3%), using 10% as the non-inferiority margin.
- With regard to safety, a relatively low occurrence of suspected drug-related side effects was reported in simo decoction group (3.6%), without significant difference from the control group (8.9%).

Discussion

- No cardiac adverse effect was observed in all patients who received domperidone suspension, and other serious complications requiring special treatment were also absent in both groups.

limitations

- First, the study was not doubleblinded because of the different dosage regimens and the appearance of the two medicines.
- Second, over 50% of the patients in our trial were primarily diagnosed with neurologic diseases.
- Third, side-effects are one of the main concerns regarding herbal medication.

Conclusions

- In this trial, non-inferiority of simo decoction to domperidone suspension was not confirmed, indicating that simo decoction is not appropriate as an alternative to domperidone suspension in facilitating post-pyloric placement of spiral nasoenteric tubes in critically ill adults.

THANK YOU!

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