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Effects of Luo Han Guo on throat complications associated with tracheal intubation: a randomized controlled trial

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Abstract

Objectives: Conventional treatment for throat complications after surgery involves the use of hormone therapy, which has variable effects. This study was performed to investigate the effects of oral administration of Luo Han Guo decoction for throat complications after tracheal intubation during general anesthesia for laparoscopic radical hysterectomy.

Methods: Beginning at 6 h after surgery, patients in the experimental group were administered 30 mL of a Luo Han Guo decoction; the control group received black tea. Patients in both groups were evaluated using a Visual Analogue Scale for the degree of throat soreness at 2, 12, 24, and 48 h after surgery; coughing and expectoration were evaluated at 48 h after surgery.

Results: This study included 203 patients: 102 in the experimental group and 101 in the control group. Compared with controls, the experimental group had significantly lower evaluation scores at 12, 24, and 48 hours postoperatively. Moreover, at 48 hours postoperatively, coughing and expectoration were significantly reduced in the experimental group, compared with in the control group.

Conclusions: Administration of a Luo Han Guo decoction can effectively reduce throat pain, hoarseness, throat swelling, cough, and sputum after tracheal intubation during general anesthesia.

Keywords

Tracheal intubation, throat complications, Luo Han Guo, nursing care, hoarseness, cough, sputum, pain measurement, laparoscopy, general anesthesia

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Introduction

Tracheal intubation is one of the most widely used methods to deliver anesthesia. However, tracheal intubation is an invasive procedure.[1] Intubation of the tracheal tube can damage the vocal cords, tracheal mucosa, and inflatable cuff of the trachea, leading to respiratory tract mucosal congestion and edema; some patients emerge with a sore throat and/or hoarseness.[2] Previous studies of tracheal intubation have shown that a sore throat can occur in 40% to 60% of patients,[3] while hoarseness occurs in 50.1% to 100% of patients.[4] Such complications affect patient satisfaction with surgery and postoperative rehabilitation; they may intermittently carry a risk of mortality.[5] Many treatments have been applied,[6–8] but there remains a lack of a simple and safe approach for effective prevention of these complications, as well as alleviation of clinical symptoms.

Luo Han Guo is a medicinal herb, also known as "Oriental God Fruit," that is commonly used in Traditional Chinese Medicine to moisten the lungs, clear away heat, and relieve coughing. It is also used to treat diabetes, bronchitis, tonsillitis, pharyngitis, acute gastritis and asthma.[9] It may also be used as a beverage and seasoning.[10,11]

The present study aimed to observe the effect of orally administered Luo Han Guo decoction in patients with throat pain after general anesthesia for tracheal intubation. We hypothesized that Luo Han Guo decoction may provide a safe and effective method to reduce throat complications, and that this study could provide a theoretical basis for clinical treatment and nursing of such patients to improve their postoperative comfort.

Methods

Data collection and ethical approval

This randomized controlled study was approved by the Medical Ethics Committee of the Guigang City People's Hospital and registered in the Chinese Clinical Trial Register (registration no. ChiCTR-INR-17012203; URL: http: //www.chictr.org.cn/enindex.aspx). The study complied with the CONSORT guidelines. Patients provided written informed consent prior to enrollment in the study. From January 2017 to May 2018, our hospital's gynecology unit identified patients with cervical cancer who were scheduled to receive tracheal intubations during general anesthesia for laparoscopic radical hysterectomy. The criteria for inclusion in the present study were as follows: 1) oral tracheal intubation for anesthesia delivery within 10 minutes, for completion of a one-time operation; 2) intraoperative tracheal intubation of a throat structure with a Cormack–Lehane grade of I–II;[12] 3) general anesthesia intubation duration for 4 hours; 4) postoperative anesthesia recovery period; 5) "Steward score" after surgery of $\geq$4 points;[13] 6) recovery of the swallowing reflex; 7) tracheal tube removal; 8) preoperative use of expectorant drugs (both oral and inhalation); 9) postoperative anti-inflammatory treatment using a cefuroxime sodium injection; 10) use of sufentanil injection (1 μg/kg/day) for postoperative analgesia. The exclusion criteria were as follows: 1) presence of a throat disorder; 2) presence of cardiovascular and cerebrovascular complications; respiratory insufficiency; liver, kidney, or immune system complications; severe infection; severe anemia; or other serious complications; 3) drug use for allergy or intolerance; 4) intubation complicated by a respiratory tract infection; 5) incomplete intubation; 6) intubation difficulty due to soft throat tissue abnormalities; 7) multiple intubations; 8) a history of steroid use; 9) presence of a postoperative indwelling gastric tube; 10) diagnosis of diabetes; 11) history of frequent vomiting; 12) presence of pregnancy or possible pregnancy. The suspension criteria were as follows: 1) noncompliance with the research protocol;

2) development of exclusionary conditions during the course of the study; and 3) patient request for termination.

Study design and grouping

The study was performed in a double-blind manner. The decoction of Luo Han Guo in the experimental group and the black tea in the control group were prepared uniformly by nurses who did not participate in the clinical trial; the appearance and color of the oral agents in the two groups were thus confirmed to be consistent and the dosages were unified. Medical staff who participated in the clinical study did not know the composition of the oral agents received by the patients throughout the study; they only were able to access the number of the drug in the enrollment record. After all observations in this study were completed, a third party received the unblinded data in June 2018, and the relevant data were subjected to statistical analysis.

Methods of monitoring and medication

Patients returned to the ward after surgery and were placed in a supine position at an angle of 30 degrees for 4 hours. Patients received continuous oxygen at 2 to 3 L/min. Heart rate, blood pressure, and pulse oximetry were continuously monitored using the PM9000 multi-parameter monitoring system (Mindray, Shenzhen, China). Postoperative care included anti-inflammatory treatment (intravenous injection of 0.9% normal saline and 100 mL of 0.5 g cefuroxime sodium, twice per day) and fasting for 6 hours postoperatively.[14] For 6 hours postoperatively, patients in the experimental group were administered an oral 30% Luo Han Guo decoction (300 g dried Luo Han Guo boiled in 1000 ml water for 10 minutes)[0.5–1.0 g/kg/day; 30-mL bolus, three times per day (0800, 1200, 1600) for 48 hours].[15,16] Patients were permitted 30 minutes to consume the Luo Han Guo decoction and were not permitted to ingest food during the treatment. If no coughing was observed and the patient developed a dry mouth, the dosage was increased to 50 mL and the same schedule was followed. Patients in the control group were provided black tea to drink, in accordance with their conditions and dry mouth symptoms. At 24 hours postoperatively and after the first defecation, both groups of patients received a semi-liquid diet, and were gradually permitted to eat normal food.

For analysis parameters, please see Table 1.

Data analysis

All statistical analyses were performed using SPSS software version 19.0 (IBM Corp., Armonk, NY, USA). Using the intention-to-treat approach, data were expressed as the mean ± standard deviation, and a t-test was used to compare experimental and control groups. The count data were expressed as the rate (%). A chi-squared (χ^2) test was used to compare categorical group data, with $\alpha = 0.05$ and $P < 0.05$ considered indicative of a statistically significant difference. The estimated sample size formula was $n = \frac{8 \times p \times q}{(p1-p2)^2}$. Here, $p1$ and $p2$ represent the estimated cure rates in the pilot study and intervention study, respectively; $p = (p1+p2)/2$, $q = 1-p$, and $p1 = 0.86$, according to preliminary experiments. If the cure rate is 95% after intervention (i.e., $p2 = 0.95$), the sample size is $n = 102$ per group.

Results

Sample size and response rate

Two hundred three (203) patients were enrolled in this study. Using the random number table method, 102 patients were assigned to the experimental group and 101 to the control group. Two patients in

Table 1. Analysis parameters.

Parameter	Analysis method	Assessment tools
1. Adverse reactions	Liver and kidney function were evaluated and an electrocardiogram was performed; evidence of palpitations, dizziness, itching, chest tightness, shortness of breath, nausea and vomiting, and skin rash were recorded.	
2. Cough and expectoration	Incidence of cough and expectoration at 48 h postoperatively.	
3. Degree of throat soreness	Evaluated as described previously:[11] 0 = natural swallowing; 1–4 = mild pain when swallowing; 5–6 = moderate pain when swallowing; 7–10 = severe pain when swallowing.	Visual Analogue Scale (VAS) (score of 0–10 points).
4. Degree of voice hoarseness	0 = asymptomatic; I = able to speak quietly; 2 = unable to speak or only able to speak at a whisper level.[24]	
5. Degree of swelling of the throat	At 2, 12, 24, and 48 h after surgery, laryngoscopy was performed by the same otolaryngologist to observe and evaluate the degree of swelling of the throat in the two groups. 0 = no swelling; I = mucosal congestion; II = mucosal redness and mild pain; III = significant redness and pain; IV = high degree of flaky mucosa swelling and pain.[25]	
6. Compliance with medication	The nurse recorded whether the container was emptied each time the drug was issued. Compliance = (actual medication usage / theoretical medication usage) × 100%; ≥95% = good compliance.	

Table 2. Patient characteristics.

Group	n	Age (years)	BMI (kg/m^2)	Operation time (minutes)	Intubation time (minutes)	Intraoperative blood loss (mL)
Experimental	94	47.10 ± 5.201	21.34 ± 4.076	155.73 ± 12.380	171.79 ±24.514	136.54 ±22.144
Control	95	47.25 ± 4.892	21.53 ± 3.935	156.19 ±15.340	172.44 ± 23.600	136.95 ±20.812
t		0.214	0.319	0.224	0.187	0.130
P		0.831	0.750	0.823	0.852	0.897

In Experimental and Control rows, values are mean ± standard deviation.

the experimental group and one patient in the control group were excluded during the study because those patients and their families discontinued treatment. Data from 11 patients were excluded from the analysis at 24 hours postoperatively for the following reasons: among patients in the experimental group, two for violation of the protocol, four because of abdominal distension from an indwelling gastric tube; among patients in the control group, two because of discontinuation of treatment, and three because abdominal distension from an indwelling gastric tube. A total of 189 patients were included in the final analysis: 94 in the experimental group and 95 in the control group. No significant differences were observed in terms of age, operation time, intubation time, or total blood loss (Table 2).

With the exception of the 11 aforementioned patients, none withdrew from the present study or showed abnormalities in blood pressure, heart rate, or pulse oximetry. Moreover, no adverse reactions were observed in the patients, including palpitations, dizziness, itching, chest tightness, shortness of breath, nausea and vomiting, and skin rash. At 48 hours postoperatively, three patients in the experimental group and 15 patients in the control group had cough and expectoration ($\chi^2 = 8.703$, $P = 0.003$).

Sore throat and hoarse voice scores

Sore throat and hoarse voice scores did not significantly differ between the experimental and control groups at 2 hours postoperatively. However, the scores of the experimental group were significantly lower than those of the control group at 12, 24, and 48 hours postoperatively (all $P < 0.05$; Tables 3–4).

Throat swelling

No significant differences in throat swelling were found between the two groups at 2 hours postoperatively. However, the experimental group showed more rapid recovery than the control group at 12, 24, and 48 hours postoperatively. Moreover, after 48 hours, the experimental group showed clear remission of throat swelling, and the two groups thus differed significantly (all $P < 0.05$; Table 5).

Compliance

The recovery of empty decoction containers and inventory records showed that patients were highly compliant. Rates of compliance were 100% in both the experimental and control groups.

Discussion

Throat pain and hoarseness comprise common complications after tracheal

Table 3. Degree of throat soreness at 2, 12, 24, and 48 hours postoperatively.

		Soreness at 2 hours [n (%)]				Soreness at 12 hours [n (%)]				Soreness at 24 hours [n (%)]				Soreness at 48 hours [n (%)]			
Group	n	N	Mi	Mo	S	N	Mi	Mo	S	N	Mi	Mo	S	N	Mi	Mo	S
Experimental	94	2 (2)	15 (16)	53 (56)	24 (26)	12 (13)	31 (33)	41 (43)	10 (11)	21 (22)	47 (50)	20 (21)	6 (7)	63 (67)	26 (28)	3 (3)	2 (2)
Control	95	3 (3)	17 (18)	54 (57)	21 (22)	2 (2)	19 (20)	51 (54)	23 (24)	7 (7)	30 (32)	39 (41)	19 (20)	10 (11)	40 (42)	31 (32)	14 (15)
X^2		0.529				6.352	4.091	1.917	6.040	8.392	6.641	8.606	7.633	63.614	4.334	27.758	8.135
p		0.971				0.012	0.043	0.166	0.014	0.004	0.010	0.003	0.006	0.000	0.037	0.000	0.004

Abbreviations: N, none; Mi, mild; Mo, moderate; S, severe

Table 4. Degree of hoarseness at 2, 12, 24, and 48 hours postoperatively.

		Hoarseness at 2 hours [n (%)]			Hoarseness at 12 hours [n (%)]			Hoarseness at 24 hours [n (%)]			Hoarseness at 48 hours [n (%)]		
Group	n	0*	1	2	0	1	2	0	1	2	0	1	2
Experimental	94	4 (4)	67 (71)	23 (25)	29 (31)	55 (59)	10 (10)	35 (37)	53 (57)	6 (6)	63 (67)	28 (30)	3 (3)
Control	95	3 (3)	70 (74)	22 (23)	8 (9)	65 (68)	22 (23)	10 (10)	69 (73)	16 (17)	29 (31)	55 (58)	11 (11)
X^2		0.225			15.098	2.002	5.267	6.373	5.451	5.025	25.190	15.156	4.846
p		0.893			0.000	0.157	0.022	0.012	0.019	0.025	0.000	0.000	0.028

*Scale: 0 = asymptomatic; 1 = able to speak quietly; 2 = unable to speak or only able to speak at a whisper level

Table 5. Throat swelling at 2, 12, 24, and 48 hours postoperatively.

		Swelling at 2 hours [n (%)]					Swelling at 12 hours [n (%)]					Swelling at 24 hours [n (%)]					Swelling at 48 hours [n (%)]				
Group	n	0	I	II	III	IV	0	I	II	III	IV	0	I	II	III	IV	0	I	II	III	IV
Experimental	100†	0 (0)	34 (34)	31 (31)	25 (25)	10 (10)	6 (6)*	50 (50)*	28 (28)*	12 (12)*	4 (4)*	25 (25)*	65 (65)*	6 (6)*	3 (3)*	1 (1)*	83 (88)*	6 (7)*	3 (3)*	2 (2)*	0 (0)*
Control	100	0 (0)	37 (37)	29 (29)	23 (23)	11 (11)	0 (0)	33 (33)	39 (39)	20 (20)	8 (8)	6 (6)	45 (45)	30 (30)	13 (13)	6 (6)	20 (21)	47 (49)	11 (12)	12 (13)	5 (5)

†Experimental group, n = 94 at 48 hours; Control group, n = 95 at 48 hours. *Compared with the control group, $p < 0.05$

intubation anesthesia.[17] Several factors can lead to such complications. For example, a clinician who is unskilled at performing intubation could induce damage to the throat mucosa. In addition, long-term tracheal intubation can suppress throat mucosa, leading to congestion, edema, or bacterial growth in the trachea. The growth of bacteria or the presence of other microbial particles in the trachea can lead to secondary acute pharyngitis, which manifests as a sore throat, voice hoarseness, and swallowing pain; the overall result is patient discomfort.[18] Throat complications due to tracheal intubation anesthesia should be actively treated. Current interventions for a sore throat and voice hoarseness after tracheal intubation anesthesia include postoperative inhalation of a mixture of α-chymotrypsin, gentamicin, dexamethasone, and normal saline,[6,7] as well as systemic administration of steroid hormones. Several studies have reported[8] that preoperative intravenous dexamethasone can relieve the symptoms of a sore throat. However, systemic hormone drug treatment can cause adverse reactions, such as increased blood sugar and blood pressure instability, which may contribute to other complications (e.g., osteoporosis, osteonecrosis, and/or insufficient wound healing). Thus, patients with malignant tumors, liver and kidney dysfunction, and stomach ulcers should be cautiously treated with systemic hormone drugs.

In the present study, an orally administered Luo Han Guo decoction reduced throat mucosal congestion and edema associated with tracheal intubation anesthesia, thereby relieving throat soreness, voice hoarseness, cough, and other symptoms. Luo Han Guo belongs to the *Cucurbitaceae* family and is thought to exert its effects on the large intestine and lungs. Luo Han Guo can act as a laxative and is commonly used to treat constipation; however, it can also be used to treat acute bronchitis, acute tonsillitis, and pharyngitis.[19] A previous study[20] found that healthy adults administered a one-time oral dose of 30% Luo Han Guo glycoside (200 mg/kg) exhibited no changes in blood glucose levels or liver enzyme activity; thus, the investigators concluded that the conversion of Luo Han Guo glycosides to glucose is not acutely toxic. Recent pharmacological studies[21] have reported that Luo Han Guo shows antioxidative, anti-tumor, antibacterial, antifatigue, and anti-diabetic effects. Luo Han Guo can also improve hypoglycemia, hypolipidemia, liver function, immunity, and hypoxia, as well as other functions.[9]

We found that, after tracheal intubation, sore throat, voice hoarseness, throat swelling, and cough sputum were significantly improved in the experimental group treated with Luo Han Guo, compared with the control group, at 12, 24, and 48 hours postoperatively. Luo Han Guo has been shown to have anti-inflammatory and cough expectorant properties, improving sore throat, cough, sputum, hoarseness, and postoperative dryness of the throat, while also promoting gastrointestinal function recovery.[14,16,22] Thus, many patients treated with Luo Han Guo have reported reduction of pain. Luo Han Guo can be classified into several high-quality grades and a low-quality grade. Low-quality Luo Han Guo demonstrates a shaking sound. Previous studies have shown that the high-quality grades have expectorant and anti-inflammatory properties.[23] To increase the likelihood of a beneficial response to Luo Han Guo treatment, high-quality Luo Han Guo should be used.

Conclusion

This study demonstrated that Luo Han Guo can effectively reduce the symptoms of inflammatory damage caused by tracheal intubation during general anesthesia. Thus, given the side effects associated with

conventional steroid therapy, Luo Han Guo treatment may be an economical and safe alternative with minimal adverse effects, and appears worthy of further clinical application.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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