

Effect of Xiangbin Prescription in Gastrointestinal Function After Gynecological Abdominal Surgery: a Randomized Controlled Trial

Yuyan Wu

Guangzhou University of Traditional Chinese Medicine: Guangzhou University of Chinese Medicine
<https://orcid.org/0000-0002-7906-9099>

Jinxuan Lin

fu jian yi ke da xue fu shu di er yi yuan: Second Affiliated Hospital of Fujian Medical University

Haiping Zeng

Guangzhou University of Traditional Chinese Medicine: Guangzhou University of Chinese Medicine

Yi Chen

Guangdong Provincial Hospital of Traditional Chinese Medicine

Zhiqiang Chen

Guangdong Provincial Hospital of Traditional Chinese Medicine

Qicheng Chen

Guangdong Provincial Hospital of Traditional Chinese Medicine

Zhi Jiang

Guangdong Provincial Hospital of Traditional Chinese Medicine

Jianling Huang

Guangdong Provincial Hospital of Traditional Chinese Medicine

Lixing Cao (✉ lixingcao@126.com)

Guangdong Provincial Hospital of Traditional Chinese Medicine <https://orcid.org/0000-0002-4402-6160>

Research

Keywords: Xiangbin prescription, gynecologic laparoscopic surgery, gastrointestinal function, fast recovery

Posted Date: July 7th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-660427/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

**Effect of Xiangbin Prescription in Gastrointestinal function after
Gynecological Abdominal Surgery: A Randomized Controlled Trial**

Yuyan Wu, Jinxuan Lin, Haiping Zeng, Yi Chen, Zhiqiang Chen, Qicheng Chen, Zhi Jiang,
Jianling Huang, Lixing Cao*

***Correspondence:** lixingcao@126.com

Affiliations: Department of gynaecology, the Second Affiliated Hospital of
Guangzhou University of Traditional Chinese Medicine (Guangdong Provincial
Hospital of Traditional Chinese Medicine), Guangzhou 510120, China.

ABSTRACT

Background: Recovery of gastrointestinal function after gynecological abdominal surgery is a major clinical problem. An effective intervention to promote the rapid recovery of gastrointestinal function postoperatively is lacking. This randomized trial investigated whether Xiangbin prescription (XBP) was feasible in terms of efficacy and safety on gastrointestinal function recovery in patients after gynecological abdominal surgery.

Methods: A randomized controlled study was conducted, in which 190 patients with gynecological abdominal surgery who met the inclusion and exclusion criteria were enrolled. They were assigned randomly to XBP group, chewing gum group or blank control group, and respectively received the following treatments: took the XBP twice a day, chewed a piece of gum for about 15 minutes each 4 hours, or received conventional western basic treatment, starting on postoperative day 1 until defecation. Three groups were compared in terms of primary outcomes including the time of the first defecation and the time of the first flatus and secondary outcomes including the level of Ghrelin (GHRL) and the incidence of postoperative complications. Meanwhile, the safety of this trial was evaluated.

Results: There was no statistical difference in baseline characteristics among the three groups. For the time of the first flatus, XBP group (22.33 ± 6.68 h) showed less time compared with the chewing gum group (23.06 ± 7.37 h), while it was shorter than that in the blank control group (25.86 ± 7.93 h) with significant difference ($P < 0.05$). As for the time of the first defecation, XBP group (38.65 ± 12.96 h) showed shorter time

significantly compared with both the chewing gum group (47.29 ± 14.50 h) and the blank control group (54.01 ± 20.32 h) ($P < 0.05$). For the postoperative GHRL levels, XBP group was higher than that in the chewing gum group with no significant difference and had more significant improvement of the GHRL levels at postoperative day 3 compared with the blank control group ($P < 0.05$). For postoperative complications, XBP group had lower incidence than the other two groups but with no significant difference. For safety evaluations, no serious adverse events occurred in the three groups.

Conclusions: XBP could promote the recovery of gastrointestinal function after gynecological abdominal surgery and it is overall safe.

Trial registration: This trial was retrospectively registered by Chinese Clinical Trial Registry with the identifier number, ChiCTR1900026327, at September 30, 2019. <http://www.chictr.org.cn/>.

Keywords: Xiangbin prescription, gynecologic laparoscopic surgery, gastrointestinal function, fast recovery

BACKGROUND

Gynecologic laparoscopic surgery has been widely used in the treatment of gynecological diseases, such as gynecological malignant tumors, uterine fibroids, adenomyosis, endometriosis, etc^{1, 2}. Generally, gynecological surgery will not cause direct damage to the intestine, but surgical stimulation and anesthesia will also lead to the occurrence of postoperative ileus (POI)³. The reported rate of incidence varies from different authors and literature, however, is currently between 10-30% for

abdominal surgery⁴. POI is a temporary disorder of gastrointestinal function, the clinical manifestations of whom include nausea, vomiting, abdominal distension, abdominal pain and failure to flatus or defecation, leading to postoperative morbidity and increase hospital stay⁴⁻⁷. Ultimately, POI would brought massive financial burden to society and families⁸.

However, there is still a lack of effective intervention measures for preventing POI after gynecologic surgery. Nowadays, with the development of traditional Chinese medicine (TCM), an increasing number of researches have shown that TCM has good efficacy in promoting the recovery of postoperative gastrointestinal function.

Xiangbin prescription (XBP) is a self-designed prescription developed according to the classical theory of TCM combined with years of accumulated clinical experience in Guangdong Provincial Hospital of Traditional Chinese Medicine. A previous study has shown that XBP may show significant effects in promoting gastrointestinal motility in healthy individuals⁹. To evaluated the efficacy and safety of XBP for patients who underwent gynecological surgery, this randomized controlled trial was designed and completed.

METHODS

Study design

This study was designed as a randomized controlled trial which was registered by Chinese Clinical Trial Registry with the identifier number, ChiCTR1900026327.

Patients matched with the inclusion and exclusion criteria were enrolled between October 2017 and March 2018 at Guangdong Provincial Hospital of Traditional Chinese Medicine. The inclusion, exclusion, and elimination criteria for patients are shown in **Table 1**. This study was approved by the ethical committee of Guangdong Provincial Hospital of Traditional Chinese Medicine(NO.B2017-153-01). All patients signed the informed consent form.

Table 1. *Inclusion, exclusion, and elimination criteria*

Inclusion criteria	<ul style="list-style-type: none"> Undergone gynecological laparoscopic surgery Aged between 18 and 65 years old Operation duration 0.5–4.5 h Anesthesia duration 1.0–5.0 h TCM syndrome Qi deficiency, Qi stagnation, blood stasis and bowel-qi obstruction Provided informed consent
Exclusion criteria	<ul style="list-style-type: none"> Malignant tumors requiring extended radical surgery Serious cardiovascular, liver, kidney, brain, lung co-morbidity and other combined diseases Mental illness Allergic to the intervention Severe malnutrition defined as serum albumin < 21g/L; pre-albumin < 0.10g/L Need for second abdominal surgery with severe intestinal adhesion Blood loss during surgery > 400 mL Serious complications occurring within 6 hours after surgery Current participation in or past participation in other clinical trials within one month prior to this study Considered inappropriate to participate in this study by the clinical investigators
Elimination criteria	<ul style="list-style-type: none"> Do not meet the inclusion criteria, but mistakenly included The condition had worsened that could not be controlled in 3 days Had other complications because of interventions, including severe allergy or serious adverse events Refused to continue the treatment, regardless of the reason

Randomization

The random cards were prepared according to the output random distribution by the PEMS 3.1 software and put into opaque envelopes, on the surface of which we coded numbers. The order of enrolled patients corresponded to the numbers on the envelopes. Each enrolled patient was intervened according to the random number. The randomization was coded numerically with 1 for XBP group, 2 for chewing gum group, and 0 for blank control group. The random card was kept by the research team while the random number was issued by the specific person.

Professional training was provided to all researchers, including filling Case Report Forms normatively, research work manual and research program. We gained the trust and cooperation of patients to improve clinical compliance. We established record cards, one for each person, which were recorded and checked timely by the chief doctor, chief nurse and the patient, so as to ensure the integrity and accuracy of the research report and the quality of clinical research. All the authors vouch for the veracity and completeness of the data and analyses.

Blinding

Due to the different interventions in this study, one was oral traditional Chinese medicine and the other was chewing gum, so the blinding methods was not suitable for patients and evaluators.

Intervention

Eligible patients were randomly assigned to the XBP group, chewing gum group and the blank control group. In the XBP group, on the basis of conventional therapies

XBP should be taken 2 packs a day and 150ml each time at 9:00 am and 4:00 pm from the first postoperative day until defecation. In the chewing gum group, each patient was given a packet of sugar-free mint gum, chewing once every 4 hours when awake after surgery, and one tablet each time for about 15 minutes, until defecation. In the blank group, patients only accepted basic therapies without other intervention.

Observation indicators

Primary outcomes

The primary outcomes of the study were time to first defecation and flatus after the surgery. Time to first defecation and flatus was from the time when the surgery was completed until the first observed passage of stool and the first observed passing of flatus, respectively. Patients were monitored daily until the 7th postoperative day (or the day of discharge).

Secondary outcomes

The secondary outcomes included GHRL and the incidence of complications related to PGID such as nausea, vomiting, abdominal pain and abdominal distention, etc. Patient compliance was also evaluated.

Safety evaluation

Safety observation items included recording of adverse events, such as rash, headache, dizziness, and testing of general safety indicators, electrocardiogram, blood routine, urine routine, liver and kidney function include. Adverse events were recorded truthfully at any time. For all adverse events, patients were withdrawn from

the study if necessary.

Statistical analysis

SPSS 18.0 was used for statistical analysis of the data. The statistical analyses were performed on an intention-to-treat (ITT) basis. All analyses were based on the ITT population. The enumeration data were described by proportion and rate, while the measurement data were described by $\bar{x} \pm s$, Median and interquartile range. *Pearson's* Chi-square or *Fisher's* exact tests was performed to compare the qualitative parameters between groups. Using ANOVA or Kruskal-wallis test to compare between groups of continuous variable. $P < 0.05$ was considered to be statistically significant. All statistical tests were two-tailed with a significance level set at $\alpha = 0.05$.

RESULTS

Patient demographic and baseline characteristics

A total of 190 patients were included in this study, all of whom were randomly assigned. Twenty-two patients were excluded: In the chewing gum group, 8 patients asked for external application with Chinese medicine due to postoperative abdominal pain at postoperative day 1 while 5 patients refused to chew gum. In the blank control group, 5 patients had postoperative fever at postoperative day 1 while 4 patients were unwilling to continue the clinical study. Eventually, 168 patients were collected in the ITT set in the aggregate, including 55 patients in the XBP group, 57 patients in the chewing gum group and 56 patients in the blank group. The study flowchart is shown in **Fig. 1**. Patient baseline characteristics are shown in **Table 2**.

There was no statistically significant difference between groups ($P > 0.05$), which showed that three groups were comparable in patient demographic and baseline characteristics.

Fig. 1 Flowchart for the study

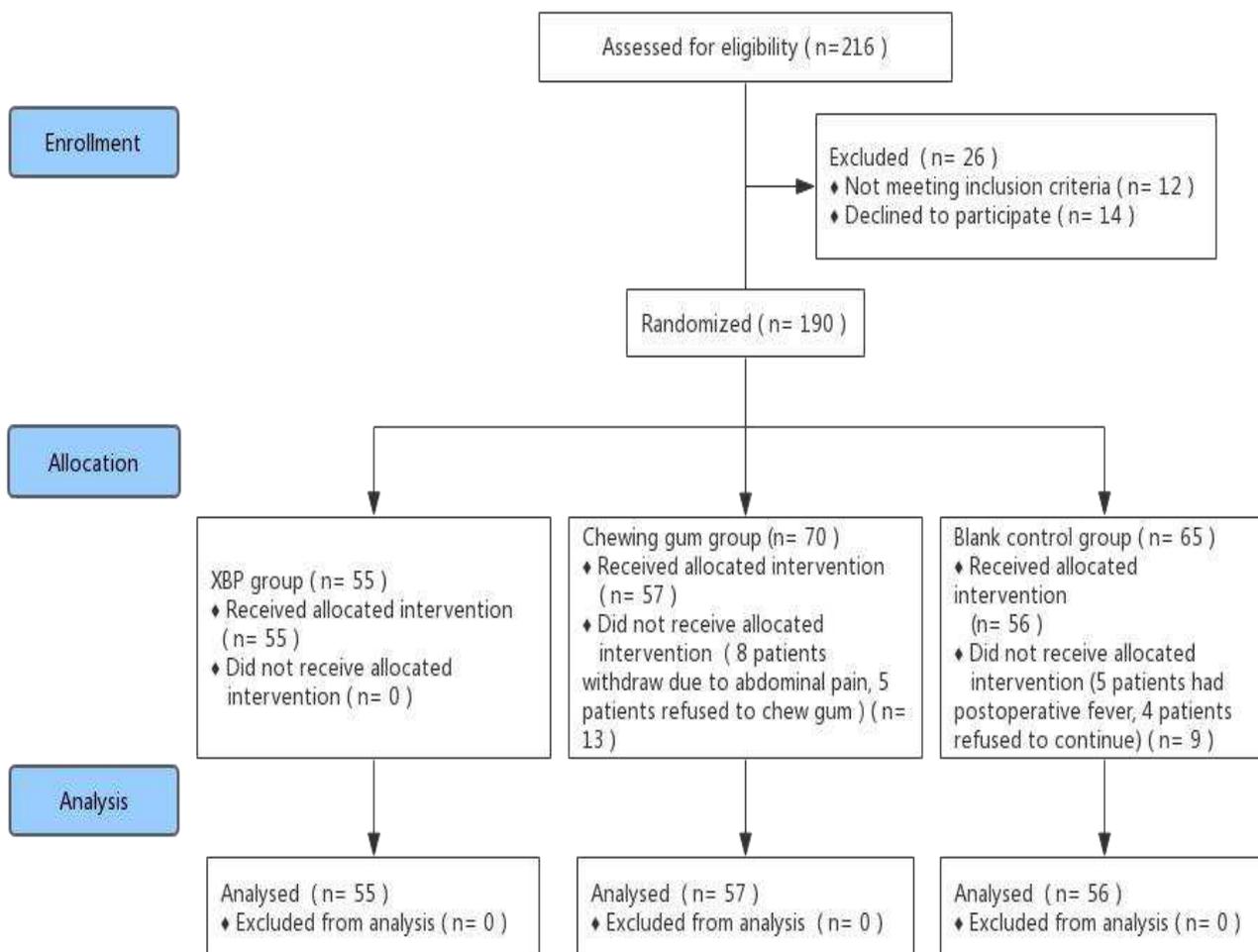


Table 2. Demographic and baseline characteristics

Variables		XBP group	Chewing gum group	Blank control group	<i>P</i>
		n = 55	n = 57	n = 56	
Age Mean (SD) year		42.29 (9.85)	40.51 (11.84)	41.43 (10.74)	0.686
Age stratification, n (%)	18~45	32 (58.2)	34 (59.6)	37 (66.1)	0.661
	46~65	23 (41.8)	23 (40.4)	19 (33.9)	
Underlying disease [◇] , n (%)	Yes	12 (21.8)	19 (33.3)	14 (25.0)	0.363
	No	43 (78.2)	38 (66.7)	42 (75.0)	
History of abdominal surgery [*] , n (%)	Yes	15 (27.3)	16 (28.1)	14 (25.0)	0.930
	No	40 (72.7)	41 (71.9)	42 (75.0)	
Surgical time (h), n (%)	≤ 2.5	34 (61.8)	35 (61.4)	35 (62.5)	0.993
	> 2.5	21 (38.2)	22 (38.6)	21 (37.5)	
Anesthesia time(h), n (%)	≤ 3.0	16 (29.1)	18 (31.6)	20 (35.7)	0.752
	> 3.0	39 (70.9)	39 (68.4)	36 (64.3)	
Ways of operation, n (%)	LTH	27 (49.1)	26 (45.6)	20 (35.7)	0.335
	Non-LTH	28 (50.9)	31 (54.4)	36 (64.3)	

SD: standard deviation; LTH: laparoscopic total hysterectomy.

[◇] including hypertension, diabetes, breast hyperplasia, breast cancer, etc.

^{*} including cesarotomy, myomectomy, appendicectomy, salpingectomy, etc.

The clinical outcomes

Primary outcomes

Overall comparison(**Table 3**). The difference of time to first flatus among the three groups was statistically significant ($P < 0.05$). The XBP group(22.33 ± 6.68 h)

had a significantly shorter time to flatus compared with patients in the blank control group (25.86 ± 7.93 h) ($P < 0.05$). The time of the first flatus in XBP group was shorter than that in chewing gum group (23.06 ± 7.37 h), but no significant difference was found.

The difference of time to first defecation among the three groups was statistically significant ($P < 0.0001$). The XBP group (38.65 ± 12.96 h) had a significantly shorter time to defecation compared with both the chewing gum group (47.29 ± 14.50 h) and the blank control group (54.01 ± 20.32 h) ($P < 0.05$).

Table 3. The primary outcome measures of overall comparison in the intention to treat population

	XBP group	Chewing gum group	Blank control group	<i>P</i>
	n=55	n=57	n=56	
Time to first flatus, h				0.03
Mean \pm SD	22.33 \pm 6.68 #	23.06 \pm 7.37 #	25.86 \pm 7.93	
Median(IQR)	23.00 (7.83)	22.42 (8.79)	24.22 (8.24)	
Time to first defecation, h				<0.0001*
Mean \pm SD	38.65 \pm 12.96 # Δ	47.29 \pm 14.50 #	54.01 \pm 20.32	
Median(IQR)	38.58 (15.75)	46.00 (15.55)	50.86 (26.00)	

* Kruskal-Wallis H test. SD: standard deviation. IQR: interquartile range.

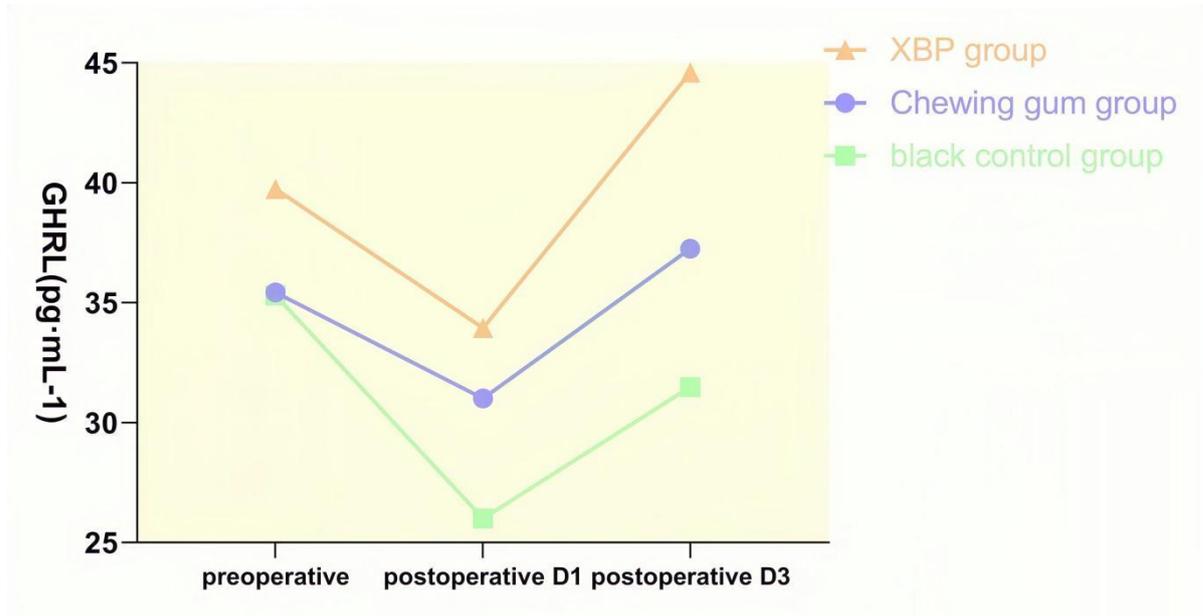
$P < 0.05$ versus blank control group; Δ $P < 0.05$ versus chewing gum group.

Secondary outcomes

Compared the GHRL levels with three groups of different detection point (preoperative, postoperative day 1 and postoperative day 3), the GHRL levels of three groups of postoperative patients were lower than before operation, and elevated at postoperative day 3. The difference of GHRL levels among three groups was statistically significant ($P < 0.05$). Comparison among three groups manifested that the GHRL levels in the XBP group was significantly higher than that in the blank control group at postoperative day 3, and the difference was statistically significant (P

< 0.05). The improvement in the XBP group was more efficiency than chewing gum group, but no significant difference was found ($P > 0.05$). (Fig. 2)

Fig. 2 GHRL levels



For the incidence of postoperative complications, the morbidity in the XBP group was similar to the chewing gum group and decreased compared with the blank control group, but it was not statistically significant. In conclusion, XBP can reduce the incidence of postoperative complications to a certain extent (Table 4).

Table 4. The incidence of postoperative complications

		XBP group(%) n=55	chewing gum group(%) n=57	blank control group(%) n=56	χ^2	P^*
abdominal distention and pain	Yes	3(5.5)	2(3.5)	9(16.1)	5.895	0.043
	No	52(94.5)	55(96.5)	47(83.9)		
nausea and vomiting	Yes	1(1.8)	1(1.8)	4(7.1)	2.530	0.327
	No	54(98.2)	56(98.2)	52(92.9)		
postoperative fever	Yes	22(40.0)	26(45.6)	30(53.6)	2.078	0.368
	No	33(60.0)	31(54.4)	26(46.4)		

* Pearson's Chi-square test.

Safety evaluation

There was no local or systemic adverse reactions such as headache, dizziness or rash occurred in the three groups during the treatment. Compared with pretreatment, it is nothing abnormal for the liver and kidney function, electrocardiogram, blood routine and urine routine of the three groups after surgery. XBP is safe to use.

DISCUSSION

With the increasing development of surgical technology, gynecological surgery has become one of the important treatments of gynecological diseases. For example, Hysterectomy is one of the most common gynecological operations, with more than 600,000 cases per year in the United States according to statistics, and nearly one third of women will have hysterectomy before the age of 60¹⁰. Although the advancement in laparoscopic surgery and the application of fast track surgery has greatly reduced the incidence of postoperative complications, POI can not be avoid due to the surgical trauma, anesthesia, and peritoneal stimulation¹¹. The recovery time of gastrointestinal function after gynecological surgery is one of the key factors affecting the length of hospital stay.

The pathogenesis of POI is known as complex and multifactorial¹². From the perspective of TCM, POI belongs to the syndrome of intermingled deficiency and excess because operation will consume qi and injury fluid while abdominal distension and obstruction occurred. When it comes to modern medicine, surgical stress injury

leads to complex pathophysiological changes in hemodynamics, metabolism, neuroendocrine and other aspects. Compensatory anti-inflammatory response syndrome will be triggered when the body releases a large number of inflammatory mediators, leading to transient trauma or postoperative immune dysfunction¹³. In terms of the mechanism of postoperative gastrointestinal function recovery, GHRL is well established to exert gastroprokinetic effects¹⁴. Previous study has proved that XBP can stimulate duodenal and jejunal motility and increase the concentrations of plasma motilin and GHRL¹⁵. This study has detected the gastrointestinal function related hormone GHRL in the three groups, showing that the GHRL levels in XBP group was significantly higher than that in the blank control group on the postoperative day 3. It is suggested that the mechanism of XBP promoting gastrointestinal function recovery after gynecological abdominal surgery may be through regulating GHRL levels which was consistent with the conclusion of our previous experiment.

To prevent POI, many efforts have been taken. In modern medicine, antibiotics, restricted fluids, early activity and nutrition are used to promote rapid postoperative recovery after abdominal gynecologic surgery¹⁶⁻¹⁸. Generally the common gastrointestinal motility drugs, such as morbutoline, cisapride, metoclopramide and alvimopan, are restricted in clinical use by the cardiac system adverse reactions and extrapyramidal reactions, which are mainly used for internal medicine treatment^{19, 20}. However, none of these measures has been completely successful⁵. As an alternative to sham feeding, chewing gum had been proved to be an effective measure to

ameliorate gastrointestinal function and decrease complications such as nausea, vomiting and ileus after gynecological surgery²¹. Another clinical study also indicated that chewing gum in the postoperative could shorten the duration of the intestinal movement, the time of first flatus and defecation time of patients who had undergone cesarean operation²². In our study, the data revealed that the first flatus time of the XBP group was similar to that of chewing gum group. However, XBP decreased the time to defecation by more than 7 h compared with gum chewing, which was demonstrated that XBP was benefit to accelerate the postoperative recovery of gastrointestinal function of patients who have undergone gynecological surgery and was superior to gum chewing for to some extent.

Components of XBP include *Lindera aggregata* Kosterm (Wuyao), *Panax ginseng* (Renshen), *Areca catechu* L. (Binlang), *Prunus persica* Batsch (Taoren), and *Fructus amomi* (Sharen). Published in *A Supplement to Materia Medica(bencao shiyi)*, Wuyao has the effect of moving qi to relieve pain and warming kidney for dispelling cold²³. Alkaloids are believed to be the main active components. An animal trial showed that *Lindera radix* ethanol extract treatment can significantly reduce NF-kB and LPS levels, suppress the inflammatory response and ameliorate intestinal ultrastructure injury²⁴. As a kind of Chinese medicine with high medicinal value, ginseng has been shown to improve the symptoms of intestinal mucosa atrophy, reduce the effect of intestinal mucosa secretions, and protect the intestinal mucosa²⁵. As a M receptor agonist, Arecoline can promote the secretion of gastrointestinal glands, especially enhance gastric emptying²⁶. Taoren has been confirmed to promote blood circulation, removes

blood stasis, and moistens and loosens the bowels. Sharen can promote the release of motilin and substance P in the body so as to improve gastrointestinal function after gastric surgery²⁷. Our previous research also showed that alkaloids may be the main substances in promoting gastrointestinal motility of XBP²⁸.

There were some limitations in our study that should be mentioned. First of all, the sample size is not large enough so that some data did not have significant statistical differences as expected or skewed in some extent. In addition, due to the obvious difference in the intervention methods, blind design was not adopted in this study, which may lead to differential misclassification bias. Besides, too few research indicators. Summing up the above, in the later study, we will expand the sample size and carry out the trial by using the method of randomized double-blind control with placebo to improve the authenticity and credibility of the research results. Furthermore, later studies can add indicators like electroencephalogram observations of patients and in terms of mechanism research, animal experiments, cell experiments or muscle strip experiments can be designed to further explore the mechanism in multiple ways.

CONCLUSION

XBP was verified to be benefit to promote the recovery of gastrointestinal function after gynecological surgery, whose mechanism may be through the regulation of GHRL level. Further more, XBP can reduce the incidence of

postoperative complications to a certain extent, which is worthy of promotion and application in clinical practice.

LIST OF ABBREVIATIONS

XBP: Xiangbin prescription; POI: Postoperative ileus; TCM: Traditional Chinese medicine; ITT: Intention-to-treat; SD: Standard deviation; IQR: Interquartile range; GHRL: Ghrelin.

DECLARATIONS

Ethics approval and consent to participate

This study was approved by the ethical committee of Guangdong Provincial Hospital of Traditional Chinese Medicine (NO.B2017-153-01) and retrospectively registered by Chinese Clinical Trial Registry with the identifier number, ChiCTR1900026327. Every participant endorsed informed consent voluntarily.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analysed during the current study are available in the ResMan repository, <http://www.medresman.org.cn/>.

Competing interests

All authors declare that there have no competing interests.

Funding

The Special Fund for the Construction of National and Regional Traditional Chinese Medicine Diagnosis and Treatment Centers (letter of state administration of Traditional Chinese Medicine, 2018, 205, Gastrointestinal Surgery Department in Guangdong Provincial Hospital of Traditional Chinese Medicine); the Special Fund for Clinical Research of Guangdong Provincial Hospital of Traditional Chinese Medicine, YN10101902; the Special Fund for Clinical Research of Guangdong Provincial Hospital of Traditional Chinese Medicine, YN10101911; Guangzhou University of Traditional Chinese Medicine, 2018, 6–18.

Authors' contributions:

Zhiqiang Chen, Lixing Cao, Yi Chen, Jianling Huang: Conception and design of the study; contribution;

Yuyan Wu, Jinxuan Lin: Contributed equally as first authors; assembly, analysis and interpretation of data;

Yuyan Wu, Haiping Zeng: Figures design; drafting or revision of the manuscript;

Zhi Jiang, Qicheng Chen: Case quality control;

All authors had access to the study data and had reviewed and approved the final manuscript.

Acknowledgements

Not applicable.

REFERENCES

1. Almeida JP, Suppiah S, Karekezi C, Marigil-Sanchez M, Wong JS, Vescan A, Gentili F, Zadeh G. Rates and Routes of Hysterectomy for Benign Indications in Austria 2002–2014. *Geburtshilfe Und*

Frauenheilkunde 2017;77:482-486.

2. Andreas Chrysostomou, Dusan Djokovic, William Edridge, van Herendael. BJ. Evidence-based guidelines for vaginal hysterectomy of the International Society for Gynecologic Endoscopy (ISGE). *European Journal of Obstetrics & Gynecology and Reproductive Biology* 2018;231:262-267.

3. Correia MITD, Liboredo JC, Consoli MLD. The role of probiotics in gastrointestinal surgery. *Nutrition* 2012;28:230-234.

4. Venara A, Neunlist M, Slim K, Ba Rbieux J, Colas PA, Hamy A, Meurette G. Postoperative ileus: Pathophysiology, incidence, and prevention. *Journal of Visceral Surgery* 2016;153:439-446.

5. Bragg D, El-Sharkawy AM, Psaltis E, Maxwell-Armstrong CA, Lobo DN. Postoperative ileus: Recent developments in pathophysiology and management. *Clinical Nutrition* 2015;34:367-376.

6. Quiroga-Centeno AC, Jerez-Torra KA, Martin-Mojica PA, Castaneda-Alfonso SA, Castillo-Sanchez ME, Calvo-Corredor OF, Gomez-Ochoa SA. Risk Factors for Prolonged Postoperative Ileus in Colorectal Surgery: A Systematic Review and Meta-analysis. *World J Surg* 2020;44:1612-1626.

7. Lee MJ, Vaughan-Shaw P, Vimalachandran D, ACPGBI GRG. A systematic review and meta-analysis of baseline risk factors for the development of postoperative ileus in patients undergoing gastrointestinal surgery. *Annals of the Royal College of Surgeons of England* 2020;102:194.

8. Shogan BD, Chen J, Duchalais E, Collins D, Chang M, Krull K, Krezalek MA, Larson DW, Walther-Antonio MR, Chia N, Nelson H. Alterations of the Rectal Microbiome Are Associated with the Development of Postoperative Ileus in Patients Undergoing Colorectal Surgery. *Journal of Gastrointestinal Surgery* 2020;24:1663-1672.

9. Zhi J, Lixing C, Qicheng C, Wenfan S, Zhiqiang C. Effects of Xiangbin Recipe on gastrointestinal motility in healthy individuals. *Chinese Journal of Biomedical Engineering* 2016;22:234-238.

10. Lee MS, Venkatesh KK, Growdon WB, Ecker JL, York-Best CM. Predictors of 30-day readmission following hysterectomy for benign and malignant indications at a tertiary care academic medical center. *American Journal of Obstetrics and Gynecology* 2016;214:607.e1-607.e12.

11. Nelson G, Kalogera E, Dowdy SC. Enhanced recovery pathways in gynecologic oncology. *Gynecologic Oncology* 2014;135:586-594.

12. Harnsberger C, Maykel J, Alavi K. Postoperative Ileus. *Clinics in Colon and Rectal Surgery* 2019;32:166-170.

13. Nelson G, Kalogera E, Dowdy SC. Enhanced recovery pathways in gynecologic oncology. *Gynecologic Oncology* 2014;135:586-594.

14. Stengel A, Taché Y. Ghrelin: new insight to mechanisms and treatment of postoperative gastric ileus. *Current pharmaceutical design* 2011;17:1587-1593.

15. Jiang Z, Cao LX, Liu B, Chen QC, Shang WF, Zhou L, Li DY, Guo DA, Chen ZQ. Effects of Chinese herbal medicine Xiangbin prescription on gastrointestinal motility. *World Journal of Gastroenterology* 2017;23:2987-2994.

16. Charoenkwan, Kittipat, Matovinovic E. Early versus delayed oral fluids and food for reducing complications after major abdominal gynaecologic surgery. *The Cochrane database of systematic reviews* 2014:CD004508.

17. Güngördük K, Özdemir İA, Güngördük Ö, Gülseren V, Gokçü M, Sancı M. Effects of coffee consumption on gut recovery after surgery of gynecological cancer patients: a randomized controlled trial. *American Journal of Obstetrics and Gynecology* 2017;216:145.e1-e7.

18. Lashen H, Jones GL, Duru C, Pitsillides C, Radley S, Jacques RM, McAlindon M. Bowel dysfunction after total abdominal hysterectomy for benign conditions: a prospective longitudinal study. *European*

Journal of Gastroenterology & Hepatology 2013;25:1217-1222.

19. Bor S, Demir M, Ozdemir O, Yuksel K. A meta-analysis on the cardiac safety profile of domperidone compared to metoclopramide. *United European Gastroenterology Journal* 2018;6:1331-1346.
20. Nemeth ZH, Bogdanovski DA, Paglinco SR, Barratt-Stopper P, Rolandelli RH. Cost and efficacy examination of alvimopan for the prevention of postoperative ileus. *J Investig Med* 2017;65:949-952.
21. Xu C, Peng J, Liu S, Qi D. Effect of chewing gum on gastrointestinal function after gynecological surgery: A systematic literature review and meta-analysis. *Journal of Obstetrics and Gynaecology Research* 2018;44:936-943.
22. Akalpler O, Okumuş H. Gum chewing and bowel function after Caesarean section under spinal anesthesia. *Pakistan Journal of Medical Sciences Online* 2018;34:1242-1247.
23. Commission CP. *Pharmacopoeia of the People's Republic of China*. China Medical Science Press, 2015.
24. Lou Z, Wang J, Chen Y, Xu C, Chen X, Shao T, Zhang K, Pan H. *Linderae radix* ethanol extract attenuates alcoholic liver injury via attenuating inflammation and regulating gut microbiota in rats. *Braz J Med Biol Res* 2019;52:e7628.
25. FQDA Y. Effects of ginseng on intestinal mucosa and the levels of serum CRP, TNF- α and IL-6 in mice after infection. *China Medical Herald* 2019;04:18-21.
26. Yang YR, Chang KC, Chen CL, Chiu TH. Arecoline excites rat locus coeruleus neurons by activating the M2-muscarinic receptor. *Chin J Physiol* 2000;43:23-8.
27. Yun CYGH. Clinical study on *Amomum villosum*'s promotion of gastrointestinal function recovery after gastric operation. *Modern Journal of Integrated Traditional Chinese and Western Medicine* 2019;28:19-22+62.
28. JIANG Si-wei, ZHENG Zuo-liang, XU Fang-fang, CHEN Wei-ying, TANG Li-peng, CHEN Zhi-qiang, LIU Bo, Ben L. Simultaneous determination of four alkaloid components in Xiangbin decoction by UPLC-QqQ-MS/MS. *Chinese Journal of Experimental Traditional Medical Formulae* 2019;25:152-159.