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Effect of pre-injection of Shenfu injection on the hemodynamics of elderly patients with hypertension undergoing laparoscopic radical resection of colorectal cancer

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Abstract

To investigate the effect of pre-injection Shenfu injection on the hemodynamics of radical resection of colorectal cancer in elderly patients with hypertension. The candidates were randomly divided into control group (receiving pre-injection of sodium chloride injection) and research group (receiveing pre-injection of Shenfu injection) before anesthesia induction. The perioperative hemodynamic changes and use of vasoactive drugs were compared. Mean arterial pressure (MAP), diastolic blood pressure (DBP) and systolic blood pressure (SBP) values in the research group were lower than those in the control group at the time of tracheal tube extraction ($P < 0.05$). The use rate of antihypertensive drugs in the research group was lower than those in the control group ($P < 0.05$). Pre-injection of Shenfu in elderly hypertensive patients had no influence on anesthesia effect and it can reduce the volatility of hemodynamic parameters, decrease the use of vasoactive drugs.

Keywords: Shenfu injection; hypertention; laparoscope; colorectal cancer; haemodynamics.

Practical Application: Pre-injection of Shenfu in elderly hypertensive patients can reduce the fluctuation of hemodynamic indicators and regulate the patients' blood pressure bilaterally during anesthesia induced intubation.

1 Introduction

In recent years, the incidence of colorectal cancer has gradually increased (Balthazar et al., 2021; Gaspar-Pintiliescu et al., 2020; Rafiq et al., 2020). Laparoscopic radical surgery is currently the main treatment used in clinical practice with the advantage of rapid recovery and less trauma, however, respiratory and circulatory system is greatly affected by carbon dioxide pneumoperitoneum, especially in elderly hypertensive patients (Price et al., 2017; Li et al., 2018). Hypertension is a major risk factor for perioperative cardiovascular and cerebrovascular accidents in elderly patients, and hypertension is one of the common diseases in the elderly (Kyada et al., 2016). Intraoperative surgical traction and anesthesia-induced tracheal intubation can cause tachycardia and hypertension in patients. Once cardiac excessive or hypertension reaction appeared in the process of anesthesia induction or operation, it will cause the increase of blood pressure and myocardial oxygen consumption, even many serious complications, such as cerebral infarction, heart failure, especially in elderly patients with hypertension (Hart, 2018; Lang et al., 2017).

With the increase of age, myocardial atrophy and compliance decline and other changes happened on the heart, leading to the thickening of the artery and aortic wall around the heart, which will result in increasing peripheral resistance, hardening of the arteries, reducing the running speed of calcium ions in cardiac contractile protein, and compared with young people, the cardiac output of the elderly can reduce 30-50% and the compensation ability of heart decreased (Ming, 2018; Liu et al., 2017).

Life safety and prognosis in elderly patients are directly related to perioperative hemodynamic stability. Therefore, in order to maintain the stability of vital signs of elderly patients during perioperative period and ensure the safety of elderly patients, it is necessary to minimize the incidence of adverse stress response to reduce the physiological and psychological stimulation of the body (Sun et al., 2018). The core components of Shenfu injection are ginsenosides and aconitine alkaloids, which are refined from the famous Shenfu soup. Related drug research confirmed that Shenfu injection has the function of restoring vascular function, exciting α-receptor, increasing cardiac output, increasing myocardial contractility, increasing Ca2+ concentration in cardiomyocytes, increasing Ca2+-ATPase activity in cardiomyocytes, and exciting myocardium (Ismail et al., 2020; Yuwa-Amornpitak et al., 2020; Mostafa et al., 2021). A large dose of Shenfu injection can reduce blood pressure, and a smaller dose can increase blood pressure. At lower doses, aconitine alkaloids have a one-time effect on raising blood pressure (Zhao et al., 2017; Hao et al., 2017).

Here, patients with hypertension and colorectal cancer were pre-injected with Shenfu injection before laparoscopic radical operation to investigate the effect of Shenfu injection on the hemodynamics in elderly patients.

2 Materials and methods

2.1 Patients

Eighty patients, with both hypertension and colorectal cancer, who need to receive laparoscopic radical surgery from January 2018 to June 2019 were randomly divided into research group and control group (n=40 in each group). The general data of the two groups were comparable (Table 1, $P>0.05$). This study

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Table 1. Clinical data of two groups.

		Research group	Control group
Age (year)		73.7 ± 8.4	73.9 ± 8.2
Weight (kg)		57.5 ± 6.96	58.9 ± 6.74
KPS before sugery		74.15 ± 9.53	73.59 ± 8.86
Duration of surgery (min)		83.6 ± 35.9	87.22 ± 32.4
Gender	Male	23	25
	Female	17	15
Duke	A	12	10
	B	19	23
	C	9	7
	D	0	0

Note: Duke A: No muscularis was involved and no lymph nodes were involved. Duke B: Beyond the muscularis, extension into the periintestinal tissues did not involve lymph nodes. Duke C: In addition to the above alterations, lymph node metastasis has occurred. Duke D: Distant metastases or unresectable by surgery.

was approved by the Ethics Committee of the first affiliated hospital of shantou university medical college. All patients signed informed consent.

Inclusion criteria included that all patients were patients with primary hypertension, taking antihypertensive drugs daily in regular, blood pressure control well, and diagnosed with colorectal cancer by pathology and colonoscopy, all patients need to receive laparoscopic radical resection without surgical contraindications, all patients underwent elective surgery under general anesthesia, all patients aged ≥ 65 years, graded cardiac function I-II, no history of drug allergy, no long-term use of sedative drugs and analgesic drugs, normal liver and kidney function, no history of mental illness, expected survival > 3 months, no serious heart and brain diseases, no history of other malignant tumors, and no radiotherapy or chemotherapy 1 month before treatment

Exclusion criteria included that patients were allergic constitution, ASA grade > III, weight extremes in either direction, drug addicts, long-term use of sedative and analgesic drugs, secondary hypertension, with endocrine disease, allergic or severe adverse reactions to Shenfu, severely infected, poor compliance, conservative treatment, severe systemic metastasis, difficult tracheal intubation, recent angina and severe arrhythmia causing hemodynamic changes.

2.2 Anesthetization

All patients were required regular fasting and banned drinking for 8 hours before surgery and intravenously injected with 0.4 mg penehyclidine hydrochloride before anesthesia induction (Chengdu Lisite Pharmaceutical Co., Ltd.). Then, the venous access was routinely established and the sodium potassium magnesium calcium glucose injection solution was input with an infusion rate of 10-12 $mL \cdot kg^{-1} \cdot h^{-1}$ (Jiangsu Hengrui Pharmaceutical Co., Ltd.). The bispectral index, pulse oximetry, non-invasive blood pressure, and electrocardiogram were continuously monitored. The patients in research group were pre-injected with Shenfu injection before induction of anesthesia (China Resources Sanjiu (Ya'an) Pharmaceutical Co., Ltd, 1 $mL \cdot kg^{-1}$). The patients in control group was pre-injected with 0.9% sodium chloride injection before induction of anesthesia (Guangdong Kelun Pharmaceutical Co., Ltd., 1 $mL \cdot kg^{-1}$). Ten minutes after the injection in both groups, anesthesia induction was started using benzenesul fasuccinic acid (Dongying (Jiangsu) Pharmaceutical Co., Ltd., 0.2 $mg \cdot kg^{-1}$), citrate Fentanyl injection (Yichang Renfu Pharmaceutical Co., Ltd., 0.4 $\mu g \cdot kg^{-1}$), 1% propofol injection through intravenous target-controlled infusion (TCI) controlled infusion with a plasma concentration of 2.5 g /mL (Corden Pharma SPA), and remifentanil hydrochloride with a plasma concentration of 4 ng/mL (Yichang Renfu Pharmaceutical Co., Ltd.). After the tracheal intubation, the anesthesia machine was used to control the breathing, and the electric double frequency index was reduced to 40-60 and the tidal volume was 8 $mL \cdot kg^{-1}$. All patients were continuously input with sodium potassium magnesium calcium glucose injection or/and succinylated gelatin injection at an infusion rate of 10-12 $mL \cdot kg^{-1} \cdot h^{-1}$ (Shenyang Beilang Pharmaceutical Co., Ltd.) (Wang et al., 2018). All patients were treated with TCI after intubation, and the target concentration was set according to the bispectral index (Zhang et al., 2017). If the systolic blood pressure of patients is lower than 20% of the baseline value or less than 90 mmHg, the patient is given an intravenous injection of 10 mg of ephedrine injection (Xinjiang Kuche Ephedrine Products Co., Ltd.). If the patient's heart rate is lower than 55 per min, the patient is given 0.2mg atropine (Shanghai Hefeng Pharmaceutical Co., Ltd.) intravenous injection (Yuan et al., 2018). The anesthesia depth of all patients was monitored by the bispectral index of EEG and the target concentration of propofol and remifentanil was adjusted according to the change of bispectral index to maintain the value of bispectral index at 40-60. The concentration of anesthetic drugs began to decrease moderately from 10 minutes before the surgery (Shao & Sun, 2018).

2.3 Observation index

During the operation, the pulse oximetry, heart rate, and non-invasive blood pressure were recorded per 5 minutes. The bispectral index was monitored throughout the surgery. The bispectral index, pulse oximetry, heart rate, and non-invasive blood pressure, including mean arterial pressure (MAP), diastolic blood pressure (DBP), and systolic blood pressure (SBP), were recorded at the four stages of admission, immediately before intubation, 5min after intubation and immediately after tracheal tube extraction. The usage rates of nitroglycerin, ephedrine and atropine was compared between the two groups.

2.4 Statistical analysis

The data was analyzed by SPSS18.0. The count data were conducted by X^2 (%) test and the measurement data were performed by t test ($x \pm s$) test. And $P<0.05$ indicated a significant difference.

3 Results

3.1 No significant differences in bispectral index and heart rate between the two groups

There were no differences in the bispectral index and heart rate between the two groups at the four stages of admission, immediately

Table 2. Comparison of bispectral index and heart rate between the two group(n=20, $\overline{x} \pm s$).

		Admission	Immediately before intubation	5 min after intubation	Immediately after tracheal tube extraction
Bispectral index	Control group	96.11 ± 1.3	45.71 ± 6.0	47.81 ± 5.6	78.94 ± 4.4
	Research group	95.51 ± 2.7	44.94 ± 5.4	47.44 ± 4.4	79.94 ± 4.0
Heart rate	Control group	80.94 ± 15.8	76.64 ± 13.5	81.57 ± 15.7	89.97 ± 15.9[a]
	Research group	80.24 ± 11.2	76.61 ± 9.2	75.51 ± 10.1	84.84 ± 9.9

Note: [a]represent the comparison with the admission intra-group (P<0.05).

Table 3. Comparison of blood pressure between the two group(mmHg, $\overline{x} \pm s$).

		Admission	Immediately before intubation	5 min after intubation	Immediately after tracheal tube extraction
MBP	Control group	98.86 ± 12.5	73.05 ± 11.2[a]	78.02 ± 17.7[a]	112.32 ± 16.3[a]
	Research group	95.06 ± 13.7	74.85 ± 12.2[a]	80.26 ± 11.1[a]	101.02 ± 9.3[b]
DBP	Control group	78.29 ± 12.0	61.59 ± 10.4[a]	63.25 ± 14.2[a]	88.72 ± 13.5[a]
	Research group	74.69 ± 12.2[d]	62.05 ± 10.6[ad]	66.19 ± 10.1[ad]	79.82 ± 9.6[bc]
SBP	Control group	140.72 ± 17.8	96.29 ± 15.6[a]	107.52 ± 28.0[a]	160.72 ± 26.5[a]
	Research group	136.22 ± 20.8	106.02 ± 17.0[ab]	109.02 ± 16.1[ad]	144.19 ± 14.0[b]

Note: [a]represent the comparison with the admission intra-group (P<0.05). [b]represent the comparison with control group (P<0.05).

before intubation, 5min after intubation and immediately after tracheal tube extraction, respectively (P>0.05). The heart rate at the immediately after tracheal tube extraction was higher than that at the stage of admission in the control group (P<0.05) (Table 2).

3.2 Comparison of blood pressure changes between the two groups

The MAP, DBP and SBP values at the immediate time of tracheal tube extraction were not different from those at the time of admission in the research group (P>0.05). The values of MAP, DBP and SBP were lower in the research group than those in the control group at the immediate time of tracheal tube extraction (P<0.05). The SBP value at the immediate time before the intubation in the research group was higher than that of the control group (P<0.05) (Table 3).

3.3 Use rate of nitroglycerin, ephedrine and atropine were lower in research group

The use rate of nitroglycerin, ephedrine and atropine in the research group was lower than that in the control group (P<0.05) (Table 4).

Table 4. Comparison of the use rate of nitroglycerin, ephedrine and atropine in the two groups (n(%)).

Group	Nitroglycerin	Ephedrine	Atropine
Control group	7(17.5)	7(17.5)	9(22.5)
Research group	0(0.0)	1(2.5)	2(5.0)
X^2	6.792	6.543	6.928
P	<0.05	<0.05	<0.05

4 Discussion

In recent years, laparoscopic radical mastectomy has been widely used in the treatment of rectal cancer, colon cancer, gastric cancer and other digestive tract tumors due to the advantage of better therapeutic effect, rapid recovery, shorter hospital stay, and smaller trauma (Oprescu et al., 2017). However, the application of the laparoscopic radical mastectomy in elderly patients, especially those with hypertension, is difficult. The main reason is that the incidence of coexisting diseases in the elderly is high, the decline of the physiological function for the body leads to the reduction of anesthesia and surgery tolerance, therefore, the elderly could not maintain the hemodynamics well during the stable operation period, which can easily lead to the increased risk of cardiovascular and cerebrovascular accidents. And the current important issue for anesthesiologists is how to maintain stable the hemodynamics in elderly hypertensive patients during anesthesia surgery (Shen & Yu, 2019).

Shenfu injection has the effect of improving microcirculation, lowering blood viscosity, increasing blood pressure, increasing cardiac output and enhancing myocardial contractility (Hart, 2018). Shenfu injection has been widely used in the assistant treatment of various shock, hypotension and heart disease because of the effects of benefiting Qi and solidifying and reversing the yang (He et al., 2018).

This study showed that though pre-injection of Shenfu injection had no significant effect on MAP, DBP and SBP values at the time of admission, the SBP before tracheal intubation in patients pre-injection with Shenfu injection was higher than that in patients pre-injection of 0.9% sodium chloride, which may be related to the effect of raising blood pressure at one time for aconitine alkaloids in Shenfu injection. The MAP, DBP and SBP values in the research group at immediately after tracheal tube extraction were no different from those at the time of admission, but all were lower than those in the control group, which may

result from the antihypotensive effect of ginsenoside in Shenfu injection. Due to the anesthetic action such as muscle inhibition effect and expanding blood vessels can lead to slow heart rate and drop of blood pressure, in addition, blood loss, surgical trauma, tracheal extubation operation, endotracheal intubation and many other factors will trigger a sympathetic adrenal medulla system excited, cardiovascular reactions, such as elevated myocardial oxygen consumption, increased blood pressure, heart rate increase, etc. In this study, compared with the control group, the blood pressure and heart rate of patients in the research group was relatively stable during operation, indicating that the bidirectional regulation of blood pressure by Shenfu injection could reduce the probability of intraoperative and postoperative cardiovascular and cerebrovascular accidents in elderly patients (Jiang et al., 2017).

The fluctuation amplitude of heart rate in the research group was smaller than that in the control group, and the utilization rate of nitroglycerin, ephedrine and atropine in the research group was lower than that in the control group during the operation, which may be related to the effect of ginsenoside to slow down the heart rate, so it is speculated that Shenfu injection can stabilize the heart rate.

5 Conclusion

In summary, pre-injection of Shenfu injection during laparoscopic radical resection of colorectal cancer in elderly patients with hypertension will not influence the anesthetic effect of the patients and can reduce the fluctuation of hemodynamic indicators and regulate the patients"s blood pressure bilaterally during anesthesia induced intubation.

Ethical approval

This study was approved by the Ethics Committee of the first affiliated hospital of shantou university medical college. All patients gave informed written consent to participate in the study.

Conflict of interest

The authors declare that they have no conflict of interest.

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References

Balthazar, C. F., de Moura, N. A., Romualdo, G. R., Rocha, R. S., Pimentel, T. C., Esmerino, E. A., Freitas, M. Q., Santillo, A., Silva, M. C., Barbisan, L. F., Cruz, A. G., & Albenzio, M. (2021). Synbiotic sheep milk ice cream reduces chemically induced mouse colon carcinogenesis. *Journal of Dairy Science*, 104(7), 7406-7414. http://dx.doi.org/10.3168/jds.2020-19979. PMid:33934866.

Gaspar-Pintiliescu, A., Oancea, A., Cotarlet, M., Vasile, A. M., Bahrim, G. E., Shaposhnikov, S., Craciunescu, O., & Oprita, E. I. (2020). Angiotensin-converting enzyme inhibition, antioxidant activity and cytotoxicity of bioactive peptides from fermented bovine colostrum. *International Journal of Dairy Technology*, 73(1), 108-116. http://dx.doi.org/10.1111/1471-0307.12659.

Hao, H., Kong, L., & Han, N. (2017). Effects of Shenfu injection on hemodynamics and polysaccharide coating of septic shock. *Chinese Patent Medicine*, 20, 219-222.

Hart, P. W. (2018). Shenfu injection after in-hospital cardiac arrest: a question regarding funding. *Critical Care Medicine*, 46(3), e276-e279. http://dx.doi.org/10.1097/CCM.0000000000002845. PMid:29474341.

He, W., Zhang, W., Yang, Y., & Zhang, H. (2018). Meta-analysis and syndrome analysis of clinical efficacy of traditional Chinese medicine in the treatment of colorectal cancer. *Journal of Traditional Chinese Medicine*, 59, 44-51.

Ismail, G. A., Gheda, S. F., Abo-Shady, A. M., & Abdel-Karim, O. H. (2020). In vitro potential activity of some seaweeds as antioxidants and inhibitors of diabetic enzymes. *Food Science and Technology (Campinas)*, 40(3), 681-691. http://dx.doi.org/10.1590/fst.15619.

Jiang, L., Yu, L., & Yao, R. (2017). Study on the dose-effect relationship of Shenfu injection against hemodynamics indexes of early and middle stage cardiogenic shock. *Shizhen Guo Guo Guo Yao*, 14, 229-232.

Kyada, P., Jadhav, K., Biswas, T. K., & Mehta, V. (2016). Clinical study of hypertension in elderly with special reference to risk factors and end organ damage. *International Journal of Medicine and Allied Health Sciences*, 4, 372-375.

Lang, H., Zhao, F., Hu, J., & Danese, S. (2017). Nutritional risk screening of patients with colorectal cancer and its impact on postoperative infection. *Zhongguo Yiyuan Ganranxue Zazhi*, 27, 839-841.

Li, Q., Dai, W., Jia, H., Li, Y., Xu, Y., Li, X., Cai, G., & Cai, S. (2018). Prognostic impact of hypochloremia in patients with stage I to III colorectal cancer after radical resection. *Diseases of the Colon and Rectum*, 61(11), 1273-1280. http://dx.doi.org/10.1097/DCR.0000000000001196. PMid:30239393.

Liu, H., Wu, Y., & Wang, X. (2017). Percutaneous coronary intervention for the treatment of perioperative myocardial injury in Chinese medicine diagnosis and treatment expert consensus. *Chinese Journal of Integrated Traditional and Western Medicine*, 10, 6-10.

Ming, H. (2018). Effects of long distance brisk walking on hemodynamics related indexes and cardiopulmonary function in elderly patients with coronary heart disease complicated with hypertension. *Zhongguo Laonianxue Zazhi*, 12, 55-58.

Mostafa, H. S., Ali, M. R., & Mohamed, R. M. (2021). Production of a novel probiotic date juice with anti-proliferative activity against Hep-2 cancer cells. *Food Science and Technology*, 41(Suppl. 1), 105-115. http://dx.doi.org/10.1590/fst.09920.

Oprescu, D. N., Bacalbasa, N., Balescu, I., & Filipescu, A. (2017). Urinary tract resections in advanced-stage cervical cancer: a series of eight cases. *Anticancer Research*, 37(6), 3271-3276. PMid:28551675.

Price, B. A., Bednarski, B. K., You, Y. N., Manandhar, M., Dean, E. M., Alawadi, Z. M., Bryce Speer, B., Gottumukkala, V., Weldon, M., Massey, R. L., Wang, X., Qiao, W., & Chang, G. J. (2017). Accelerated enhanced Recovery following Minimally Invasive colorectal cancer surgery (RecoverMI): a study protocol for a novel randomised controlled trial. *BMJ Open*, 7(7), e015960. http://dx.doi.org/10.1136/bmjopen-2017-015960. PMid:28729319.

Rafiq, S., Gulzar, N., Huma, N., Hussain, I., & Murtaza, M. S. (2020). Evaluation of anti-proliferative activity of Cheddar cheeses using colon adenocarcinoma (HCT-116) cell line. *International Journal of Dairy Technology*, 73(1), 255-260. http://dx.doi.org/10.1111/1471-0307.12665.

Shao, Z., & Sun, W. (2018). USCOM monitoring of CO and FTC for the treatment of volumetric treatment of patients undergoing laparoscopic radical colon cancer surgery. *Chinese Journal of Anesthesiology*, 38, 985-988.

Shen, G., & Yu, X. (2019). Application value of laparoscopy in radical mastectomy and omental breast reconstruction. *Oncology Letters*, 18(1), 645-650. http://dx.doi.org/10.3892/ol.2019.10339. PMid:31289537.

Sun, J., Guo, X., & Wang, H. (2018). Effect of Shenfu injection combined with low-dose hydrocortisone on myocardial injury in patients with severe pneumonia. *Zhongguo Laonianxue Zazhi*, 38, 69-71.

Wang, N., Zheng, B., Wu, T., Qiao, Q., Zhai, Y., Zhang, B., Zhou, S., Shi, W., & He, X. (2018). Application of Overlap method to digestive tract reconstruction of totally laparoscopic left colectomy. *Zhonghua Wei Chang Wai Ke Za Zhi*, 21(3), 299-304. PMid:29577218.

Yuan, F., Zhang, Y., & Qiu, L. (2018). Application value of fusiform tubular stomach in thoracic laparoscopic combined with esophageal cancer radical resection for digestive tract reconstruction. *Zhonghua Xiaohua Waike Zazhi*, 17, 810-816.

Yuwa-Amornpitak, T., Butkhup, L., & Yeunyaw, P.-N. (2020). Amino acids and antioxidant activities of extracts from wild edible mushrooms from a community forest in the Nasrinual District, Maha Sarakham, Thailand. *Food Science and Technology*, 40(3), 712-720. http://dx.doi.org/10.1590/fst.18519.

Zhang, Q., Li, C., Shao, F., Zhao, L., Wang, M., & Fang, Y. (2017). Efficacy and safety of combination therapy of shenfu injection and postresuscitation bundle in patients with return of spontaneous circulation after in-hospital cardiac arrest: a randomized, assessor-blinded, controlled trial. *Critical Care Medicine*, 45(10), 1587-1595. http://dx.doi.org/10.1097/CCM.0000000000002570. PMid:28661970.

Zhao, Y., Sun, J., & Wu, Y. (2017). Correlation and clinical significance of Survivin, Caspase9 and Ki-67 expression in colorectal cancer. *Journal of Clinical & Experimental Pathology*, 8, 85-88.