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Meta-analysis of Acupuncture Combined with Non-general Anesthesia in Anorectal Surgery

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Abstract: *To provide a meta-analysis protocol that synthesizes the existing evidence on the effect of acupuncture combined with non-general anesthesia versus simple non-general anesthesia when used in anorectal surgery can reduce the occurrence of adverse reactions associated with anorectal surgery. To evaluate the efficacy and safety of acupuncture combined with non-general anesthesia and simple non-general anesthesia in anorectal surgery. Meta-analysis of randomized controlled trials of acupuncture combined with non-general anesthesia were evaluated using the Cochrane systematic evaluation method. The search was conducted on CNKI, Wanfang Data, VIP Full-Text e-Journals Database, Pubmed and Embase, and the search concluded in August 2022. Randomized controlled trials of spinal anesthesia with or without supplemental acupuncture that met inclusion criteria were selected. Seven RCTs comprising 625 patients were included. Display after analysis showed high heterogeneity in the rate of significant efficacy of acupuncture combined with non-general anesthesia, with results showing RR = 1.12, 95% CI (0.88, 1.42), combined effect size test Z = 0.90, P = 0.37, suggesting no statistically significant difference. However, the homogeneity of the adverse reaction analysis was good, and results showed RR = 0.45, 95% CI (0.35, 0.57), with a combined effect size Z = 6.58, P < 0.0001. This statistically significant result indicated that the rate of adverse reactions was lower when acupuncture was combined with non-general anesthesia compared to alone with non-general anesthesia. Supplementation of spinal anesthesia with acupuncture can reduce the occurrence of adverse reactions associated with anorectal surgery.*

Keywords: *Acupuncture; non-general anesthesia; anorectal surgery; Meta-analysis; Combined anesthesia*

1. Introduction

Benign anorectal disease encompasses such pathology as anal fissures, fistulas, hemorrhoids, abscesses, and pilonidal cysts, with up to 90% being amenable to ambulatory surgery. Most anorectal surgery has the advantages of a relatively short duration, definitive treatment, and reasonably prompt recovery [1-2]. Although anorectal surgical procedures are often short, a profound, localized depth of anesthesia is necessary. There are several anesthetic options, such as perianal nerve block, direct infiltration of local anesthetic, spinal anesthesia, sacral anesthesia, intravenous anesthesia (conscious sedation or monitored anesthesia), and general anesthesia. Traditional local anesthesia may be variably effective and initially uncomfortable for the patient. General anesthesia may be associated with postoperative nausea and vomiting, prolonged stay, more expensive, and awkward management if the prone position is preferred. Therefore, a non-general anesthetic option is most often preferred at present. The application of acupuncture in perioperative period has a long history, and gradually expanded to all aspects of perioperative period, involving preoperative sedation, intraoperative auxiliary anesthesia, postoperative analgesia and other perioperative whole process, which can promote the recovery of physiological function of patients, protect organ function, and achieve ideal results [3-5]. The purpose of this study was to comprehensively evaluate the role of acupuncture combined with non-general anesthesia in anorectal surgery through Meta-analysis of relevant RCTS.

1.1 Literature sources

The literature was retrieved from CNKI, Wanfang Data, VIP Full-Text e-Journals Database, PubMed and Embase through November 2022. The Chinese search terms included: "acupuncture anesthesia", "acupuncture", "electro-acupuncture ", "intraspinal anesthesia", and "anorectal surgery". The English search terms included: "acupuncture anesthesia", "acupuncture", "electro-acupuncture ", "intraspinal

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anesthesia", and "anorectal surgery".

1.2 Inclusion criteria

Inclusion criteria included the following: (1) randomized controlled trials applying acupuncture anesthesia to anorectal surgery; (2) acupuncture combined with spinal anesthesia or other non-general anesthetics as the experimental group, and spinal anesthesia alone or combined with other non-general anesthetic as the control group, provided that the other anesthetics in both groups were the same; and (3)a clear and recognized anorectal disease diagnosis.

1.3 Exclusion criteria

Exclusion criteria were as follows: (1) review articles, animal experiments, basic studies, case reports, non-clinical randomized controlled trials, and short theoretical articles; (2) significant data duplication in publications; and (3) obvious errors in the original text.

1.4 Literature screening and data extraction

Two evaluators independently read the abstracts of all downloaded literature to initially exclude those that did not meet the inclusion criteria. The full text of the studies that conform to the criteria was carefully reviewed, and any disagreements were decided through discussion with a third evaluator. The included literature was then subjected to data extraction according to the content of the collection form, which included general information about the literature, such as basic information, study population, number of cases, interventions, outcome indicators, efficacy, as well as methodological features like randomization method, blinded setting, and baseline equilibrium.

1.5 Literature quality evaluation

In terms of quality evaluation, the Cochrane tool was applied to evaluate the risk of bias in 6 domains of the literature, and the risk of bias was judged as "low risk of bias", "unclear risk of bias", and "high risk of bias". It included selection bias: (1) whether the random sequence generation was detailed; (2) allocation concealment: whether the concealment method was specified; implementation bias: whether the intervention to administer the blinding was specified and the effect of the blinding was judged; measurement bias: whether the study results were described specifically and whether the blinding implementation was effective; follow-up bias: whether the relevant results and data were fully counted, including the number of missed cases and dropouts as well as the reasons for missing cases and dropouts, so that relevant treatment could be performed; reporting bias: selective reporting of study results; other bias: in addition to the bias mentioned above, bias due to other causes was evaluated. Any questions raised in the article will be addressed in the text accordingly.

1.6 Statistical processing

Meta-analysis was performed using RevMan 5.4 software. Risk ratio (*RR*) was used as an effect indicator for dichotomous variable data, and mean difference (MD) was used to count the change values of continuous variable data. All effect sizes were expressed as 95%*CI*. When I^2<50% and *P*>0.1, there was no statistical heterogeneity and fixed-effects model analysis was used; conversely, statistical heterogeneity was suggested, and the heterogeneity was dealt with by random-effects model analysis, sensitivity analysis, or abandonment of Meta-analysis. When the number of studies containing an outcome indicator exceeded 10, funnel plots were applied to analyze publication bias. A difference of *P*<0.05 was considered statistically significant.

2. Results

2.1 Search and inclusion

The initial wide literature search retrieved 461 relevant studies, of which 23 were retained through an initial screening by reading the titles and abstracts. Ultimately, 7 studies met the inclusion criteria after reviewing the full text and included 625 patients; 312 cases were managed with non-general anesthesia supplemented with acupuncture, and 313 cases of non-general anesthesia alone (Figure 1).

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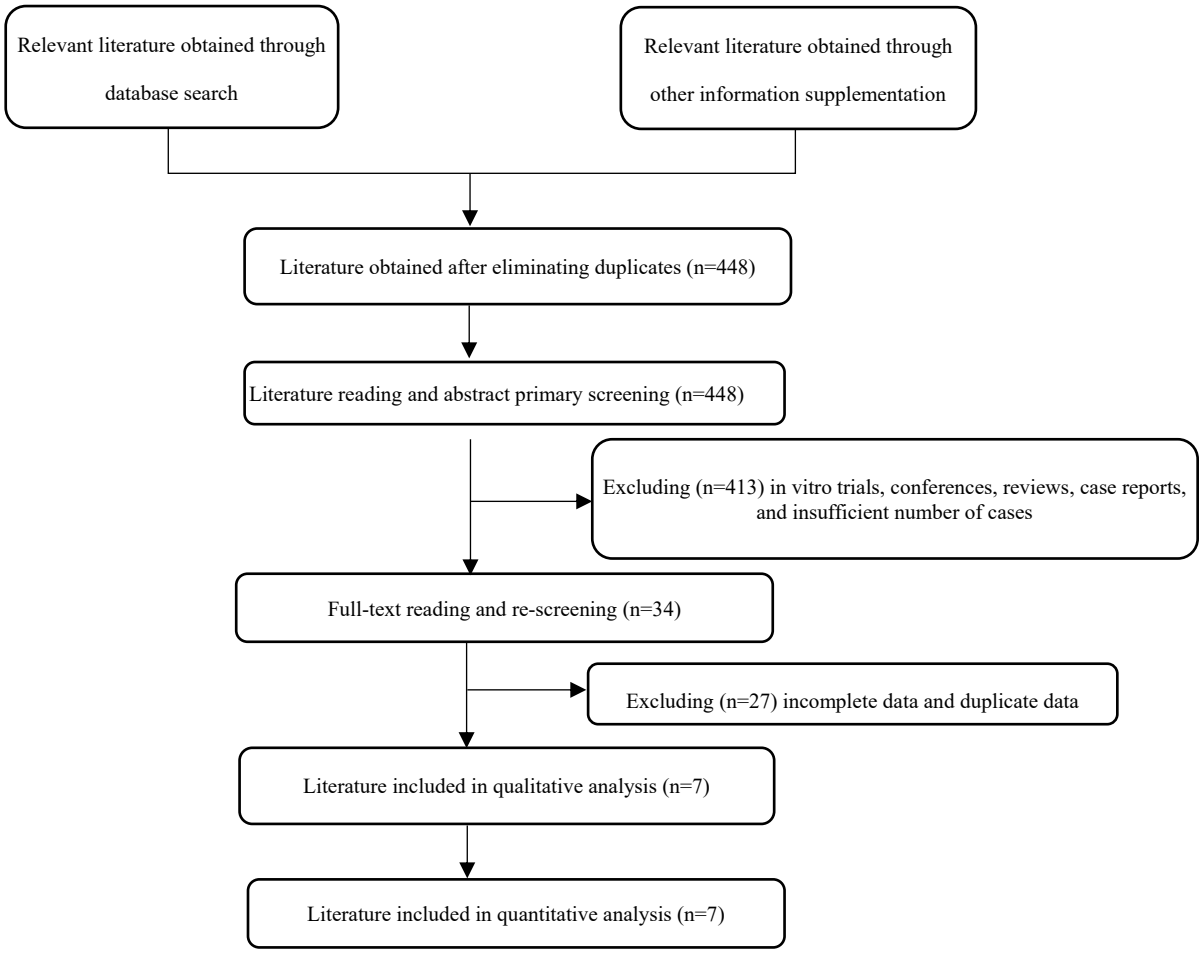

Figure 1: The process of literature selection and inclusion

2.2 Basic characteristics of the included literature studies

The basic information, measurement indicators and relevant acupoints of the literature were included, as shown in Table 1.

Table 1: Basic characteristics of included research studies

Investigators	Gender (male/ female)	Age (years)	Number of cases (*n*)		Drug used for anesthesia	Frequency of electro-acupuncture (Hz)	Outcome indicator	Acupoint
			Trial	Control				
Zhao Yingchun	73/29	20~70	51	51	Lidocaine	20	Analgesic effect, adverse reactions	Changqiang, Yaoyu
Fan Weicong	51/49	23~71	50	50	Lidocaine	40~100	Analgesic effect, adverse reactions	Neiguan, Hegu, Changqiang
Xu Tianshu	23/17	19~72	20	20	Lidocaine	2/100	Analgesic effect, adverse reactions	Changqiang, Yaoyu
Jin Shengli	31/29	19~65	30	30	Lidocaine, levobupivacaine	-	Pain condition, degree of anal relaxation during operation	Neiguan, Hegu, Zusanli, Zongmai
Liu Yong	110/89	25~60	100	99	Lidocaine	50	Anesthesia effect, adverse reactions, patient satisfaction	Baliao, Chengshan, Hegu
Dai Lingying	20/10	19~60	15	15	Lidocaine	2/100	Anesthesia effect and complications	Changqiang, Yaoyu
Yang Jun	51/43	24~69	47	47	Bupivacaine, fentanyl, dezocine	–	Anesthesia onset time, recovery time, adverse reactions	Neiguan, Hegu, Zusanli

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2.3 Quality evaluation of the included literature

Randomization method: One study [12] used the random number table for grouping; the remaining six [6-11] only mentioned random grouping without mentioning the specific method.

Allocation concealment: Not all the literature specified the concealment method.

Blinding: Not all the literature specified the blinding method.

Study quality evaluation: Literature studies were evaluated using the Cochrane tool, as shown in (Figure 2).

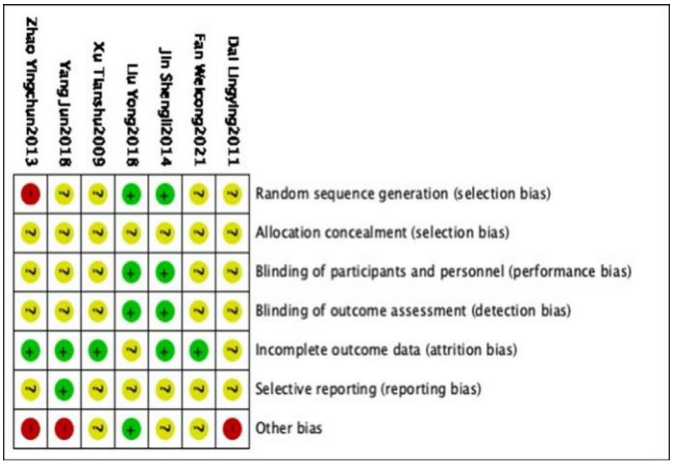

Figure 2: Quality evaluation of included studies

2.4 Characteristics of included literature studies

1) Acupoint selection: Among the 7 [6-12] literature studies, 4 [7,10-11,12] selected Changqiang and Yaoyu, 4 [6-9] selected Hegu, 2 [7-8] selected Baliao and Chengshan, and 2 [6,9] selected Neiguan and Zusanli.

2) Inclusion of outcomes Six [6,8-12] of the seven [6-12] studies classified the efficacy of analgesia into three classes: significantly effective, effective, and ineffective. The significant efficacy rate was calculated as the number of cases with significant efficacy divided by the total number of cases in the group. Six [7-12] of the seven [6-12] literature studies counted related adverse reactions.

2.5 Analysis of outcome indicators

Six [6,8-12] of the seven studies described the significant efficacy rate of acupuncture anesthesia combined with non-general anesthesia, and their analysis is shown in (Figure 3). As shown, for the heterogeneity test, chi^2=30.38, P<0.0001, and I^2=84%>50%, indicating high heterogeneity among studies. A random effects model was selected for Meta-analysis, and the results showed that the *RR* = 1.12, 95% *CI* (0.88, 1.42) and the combined effect size test Z = 0.90, P = 0.37, with no statistically significant difference.

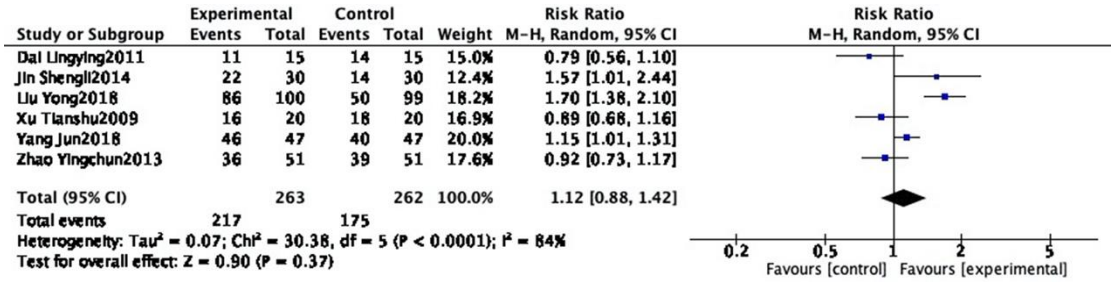

Figure 3: Meta-analysis forest plot of the significant efficacy rates for acupuncture combined with non-general anesthesia

Adverse reactions were described in 6 [7-12] of the 7 included literature studies, and the analysis is

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shown in Figure 4. The heterogeneity test, chi^2 = 4.20, P = 0.52, I^2 = 0% < 50%, indicated a low heterogeneity among studies. A fixed effects model was selected for Meta-analysis, which showed a statistically significant result with RR = 0.45, 95% CI (0.35, 0.57) and a combined effect size test Z = 6.58, P<0.0001, It indicates that the adverse reaction rate of acupuncture combined with non-general anesthesia is lower than that of simple non-general anesthesia.

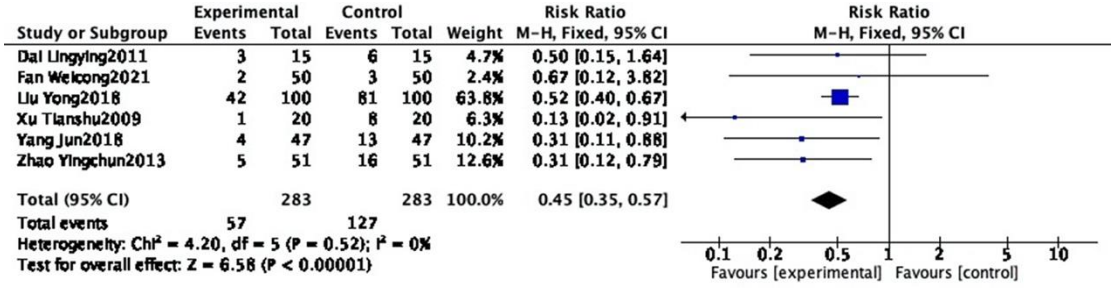

Figure 4: Meta-analysis forest plot of the adverse reaction rate of acupuncture combined with non-general anesthesia

3. Discussion

Acupuncture therapy is an important treatment method in traditional Chinese medicine. It is a non-pharmacological treatment approach [13-14]. Acupuncture is one of the commonly used natural therapies in the history of Chinese medicine. It can stimulate the meridians of the whole body, regulate the functions of the zang-fu organs, smooth the qi and blood, and balance Yin and Yang [15]. In recent years, the scope of application of acupuncture has been expanding. In 1996, the World Health Organization pointed out the relevant diseases or clinical symptoms suitable for acupuncture treatment, which is suitable for various diseases mainly pain. Especially for perioperative sedation and analgesia, has become the focus of clinical research. The advantages of acupuncture anesthesia include being economical, safe, simple, and easy to perform, allowing patients to remain awake during surgery and experience better postoperative recovery with fewer side effects. Acupuncture assisted anesthesia during operation not only has the effect of anesthesia and analgesia, but also can reduce the experimental dose of anesthetic drugs and reduce the adverse reactions caused by anesthetic drugs. Sun Qing et al. [16] used acupuncture stimulation of pain points combined with ultrasound-guided cervical nerve root block treatment for patients with radiculopathy. The pain score of the patients after treatment was significantly lower than that of simple nerve block therapy, and no adverse reactions such as dizziness, nausea, vomiting, local anesthetic poisoning, infection, nerve injury and pneumothorax were reported. Yan Fenghong et al. [17] used acupuncture anesthesia for patients undergoing hemorrhoid surgery. The postoperative pain score of the acupuncture anesthesia group was (1.78±0.68), which was significantly lower than that of the control group (2.95±0.96), and the anesthetic effective rate was 94.00%, which was significantly higher than that of the control group (69.00%), with statistical significance (P < 0.05). Therefore,it can also promote tissue metabolism and enhance the functionality of the reticular endothelial system. Acupuncture not only stimulates the release of endogenous opioid substances but also alleviates pain by regulating the hypothalamus-limbic system. Biella et al. [18] used positron emission tomography to study local cerebral blood flow in response to acupuncture at Stomach 36 and Pericardium 6, demonstrating that acupuncture can increase blood flow in the left anterior cingulate gyrus, bilateral insula, bilateral cerebellum, left superior frontal gyrus, and frontal gyrus. The brain regions activated by acupuncture are closely related to those stimulated by pain. Biella et al. believe that acupuncture can regulate imbalances in pain neural information, correct pain sensation, and thus increase the pain threshold.

Studies have shown that with acupuncture at Large Intestine 4 and Stomach 36, increased activity in the hypothalamus and ventral nucleus can be observed on functional MRI images. In contrast, activity in the anterior rostral part of the cingulate gyrus, amygdala, and hippocampus is weakened. Therefore, the analgesic effect achieved by acupuncture at Large Intestine 4 and Stomach 36 may be related to stimulating descending antinociceptive neurons and attenuating pain-related limbic system activity. [19-21]

Numerous studies indicate that central endogenous morphine-like substances, dopamine, norepinephrine, 5-hydroxytryptamine, nitric oxide, γ-aminobutyric acid, and acetylcholine, among other neurotransmitters or active substances, are involved in acupuncture analgesia to varying degrees. [22]. Tu Lifang et al. [23] applied balance acupuncture combined with five-tone method to patients after

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gynecological laparoscopic surgery. Compared with acupuncture alone, it could significantly relieve the postoperative pain of patients and reduce their anxiety and depression, and the difference was statistically significant ($P < 0.05$). Quan Longfang et al. [24] completely randomly divided in patients undergoing anorectal hemorrhoidal surgery into 3 groups. Within 24 h after surgery, simple acupuncture therapy (group A), oral tramadol hydrochloride sustained-release tablets (group B) and oral loxoprofen sodium tablets (group C) were used for analgesia, respectively. The pain score of group A 30 min and 2 h after operation was significantly lower than that of group B and C [(3.4±1.7) score ratio (4.5±1.7), (4.6±1.8) score, (2.3±1.5) score ratio (3.2±1.8), (3.2±1.8) score]. The total effective rate of 87.1% was significantly higher than that of 67.1% in group B and 65.7% in group C, and the levels of interleukin 8, tumor necrosis factor α and high-sensitive C-reactive protein were significantly higher in groups B and C, the difference was statistically significant ($P < 0.05$).Jiao Yini et al. [25] conducted a study of perioperative hip replacement patients undergoing iliac fascia block anesthesia, combined with wrist and ankle needle acupuncture and acupuncture in the lower 1, 4 and 5 areas of the operative side, and the pain scores at 6, 12 and 24 h after surgery were significantly reduced, and the incidence of postoperative adverse reactions was 13.33% significantly lower than that of the control group (53.33%), with statistical significance ($P < 0.05$).Therefore, the analgesic effect of acupuncture therapy should not be ignored. It can activate its own analgesic system, regulate the human neurohumoral system and automatic regulation mechanism, relieve muscle spasm, promote blood circulation of the affected limb, and finally achieve significant analgesic effect. At the same time, it can release the analgesic factors and play the analgesic role.

Current research on the mechanisms of acupuncture analgesia has developed from the cellular level to the molecular level, including techniques such as mRNA probes, gene knock-in, gene knockout, and injection of neurotransmitter cDNA liposomes, as well as the regulation of the expression of proto-oncogenes (c-fos, c-jun) by acupuncture.

Some limitations remain in this study: (1) Only 1 of the 7 included papers described the randomized grouping method, i.e., the randomized number table method was used; however, none of the 7 papers described whether patients or performers were blinded and whether allocation concealment was used. The quality of this Meta-analysis was compromised by the poor strength of the concluding arguments in each literature. (2) The included literature was all in Chinese and none in English, which may have resulted in bias due to the incomplete inclusion of literature. In the process of literature screening, some of the observed indicators in the literature were clinically significant, but there was a lack of RCT studies observing the same indicator. The requirements of Meta-analysis could not be met, and some valuable literature might be excluded. (3) The sample size of the included studies was small, and some of them were heterogeneous, which may also affect the study results. (4) The type, frequency, length of intervention of the acupuncture as well as the specific type of nerve block were ignored, which may also affect the reliability of the results.

According to the results of the Meta-analysis, acupuncture combined with non-general anesthesia may reduce the incidence of postoperative adverse reactions. However, the quality of the included literature was not perfect this time, and some of them included a small sample size. In the future, large-scale, high-quality randomized controlled trials are still needed to provide more support for the results of this study.

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