Efficacy and Safety of Acetaminophen Mannitol Injection in Postoperative Analgesia in Spinal Surgery

Jinfeng Wang, Bowen Chen, Xingyu Chen, Weilian Wang, Jiapeng Dan, Kun Zhang^{*}

Department of Anesthesiology, Jingzhou Hospital Affiliated to Yangtze University, Jingzhou, 434020, China

zhangkunyangtzeu@163.com

*Corresponding author

Abstract: How to effectively relieve pain and reduce adverse reactions after spinal surgery has become an urgent problem to be solved. To solve this problem, the study evaluated the efficacy of acetaminophen mannitol injection in postoperative analgesia after spinal surgery through the use of sufentanil, pain rating and adverse reaction statistics. The results showed that the probability of adverse reactions in the experimental group was 9.86%, while the probability of adverse reactions in the control group was 15.07%. It is proved that acetaminophen mannitol injection not only has significant analgesic effect, but also can greatly shorten the postoperative recovery time of spinal surgery patients, and effectively reduce the risk of various complications. It provides a safer and more effective analgesic program for the postoperative recovery of spinal surgery patients. It is of great practical significance to improve the quality of life of patients after operation and reduce their physical and mental burden.

Keywords: Acetaminophen Mannitol; Spinal Surgery; Postoperative Analgesia; Clinical Trial; Analgesics

1. Introduction

Spinal surgery is a complex and delicate surgical procedure, and postoperative pain management has always been the focus of clinical attention. Postoperative pain not only affects the patient's recovery process but may also lead to a series of complications, such as deep vein thrombosis and lung infection, which in turn prolongs hospitalization and increases medical costs[1]. Traditional analgesic regimens mostly rely on opioids. Although they have definite analgesic effects, long-term or high-dose use can easily cause adverse reactions such as drug tolerance, respiratory depression, nausea and vomiting, and addiction, limiting their clinical application. Therefore, exploring a postoperative analgesia solution that can provide both effective analgesia and good safety has become a key issue that needs to be urgently addressed in the current field of spinal surgery. In response to this challenge, previous literature has extensively explored the potential application of a variety of non-opioid analgesics, among which acetaminophen has attracted much attention due to its good analgesic effect and low risk of side effects [2]. However, the analgesic effect of acetaminophen alone is limited and cannot meet the demand for high-intensity analgesia after spinal surgery. In order to improve the analgesic effect and reduce adverse reactions, researchers have begun to explore the combined use of acetaminophen with other drugs and the development of new preparations.

Therefore, a clinical trial is conducted to evaluate the performance of acetaminophen mannitol injection for analgesia and safety after spinal surgery. The patients enrolled in the study are randomly assigned to experimental and control groups. This paper measures the analgesic efficacy of using different analgesic methods by comparing the differences in sufentanil dosage, pain scores, and postoperative adverse effects between the two study groups. The study also delves into the overall impact of acetaminophen mannitol on patients' postoperative recovery, with the expectation that it will provide new insights and strategies for analgesic treatment after spinal surgery and open up new pathways for future related research.

2. Related Works

In recent years, the exploration of analgesia for spinal surgery has become increasingly extensive and in-depth, bringing many innovative solutions to postoperative care. A comprehensive analysis by Sun et al., through a rigorous summary of 11 randomized controlled trials, revealed the excellent performance of vertical facet block in lumbar surgery analgesia[3]. In a further study, Zhang et al. compared the analgesic effects of bilateral erector spinae plane block and local wound infiltration and found that erector spinae plane block can more effectively reduce the need for opioids in the early stage after spinal fusion surgery, providing a new idea for postoperative analgesia [4]. In terms of technique exploration, Mirkheshti et al. compared the application of ultrasound guidance and traditional techniques in erector spinae plane block in a randomized non-inferiority study. The results showed that ultrasound-guided blockade technology showed more positive potential in reducing the use of opioids[5]. In addition, Jelodar et al. conducted a double-blind randomized clinical trial to explore the effects of dexmedetomidine, ketamine, and morphine as analgesic adjuvants and found that the combination of dexmedetomidine and morphine had the best effect in relieving pain[6]. Mahmoud et al. conducted a double-blind prospective comparative study to compare the analgesic effects of erector spinae plane block and intrathecal morphine[7].

Although the above studies have achieved valuable results in exploring the application of various analgesic techniques after lumbar spine surgery, there are still certain limitations. Some studies lacked direct comparison of non-opioid analgesics and did not fully consider the matching of preoperative pain scores and the assessment of patient satisfaction, which limited the comprehensiveness of the conclusions. Therefore, this paper integrates the advantages of the above-mentioned analgesic techniques and makes up for their shortcomings to provide more precise and practical clinical guidance for analgesia management after lumbar surgery. As a commonly used analgesic drug, the efficacy and safety of acetaminophen mannitol injection in postoperative analgesia of spinal surgery need further in-depth exploration, in order to provide new directions and ideas for clinical practice and optimize patients' postoperative recovery experience.

3. Methods

3.1 The Necessity of Postoperative Analgesia in Spinal Surgery

Spinal surgery, as an important therapeutic tool in the field of modern medicine, is widely used in the treatment of various spinal disorders including spinal fractures, degenerative spinal diseases, scoliosis, and spinal tumours. These diseases not only bring great physical pain to patients but may also seriously affect their quality of life and working ability [8-9]. With the continuous progress of medical technology and the deepening of the concept of minimally invasive, the way of spinal surgery has been constantly innovated and optimized, striving to achieve the therapeutic effect while minimizing the trauma of surgery to patients. Minimally invasive techniques use small incisions or puncture paths to access the spine, and high-definition imaging systems and special surgical instruments to complete the surgical operation, significantly reducing the tissue damage, bleeding, and post-operative recovery time associated with traditional open surgery. However, although minimally invasive surgery has significantly reduced the size and depth of surgical incisions, any form of surgery can cause some degree of damage to the surrounding tissues, triggering inflammatory and painful reactions. At the same time, during surgery, the surrounding tissues can become oedematous as a result of the irritation, and the oedematous areas may compress the nerves in the spine, causing the patient to feel pain in the lower back. Therefore, doctors need to formulate a personalised pain management plan according to the patient's specific situation, including a combination of medication, physiotherapy, psychological support and other means, in order to reduce the patient's pain level and promote post-operative recovery.

Hormones are important regulatory substances in the human body, and fluctuations in their levels can have a wide range of effects on multiple systems in the human body. After spinal surgery, hormone levels in patients may change significantly due to stimulation from factors such as pain. Such changes may lead to a decline in the patient's immune function, making them more susceptible to infection and other diseases. At the same time, the imbalance of hormone levels may also cause metabolic disorders and other problems, further disrupting the balance of the body's internal environment. More seriously, pain itself, as a strong stressor, can cause overactivation of the sympathetic nervous system. Activation of the sympathetic nervous system leads to an increase in the release of a series of stress hormones, of

which norepinephrine and cortisol are the most critical [10]. Excessive release of these stress hormones will further increase the body's metabolic burden and suppress immune function, thus forming a vicious cycle and causing the patient's physical condition to deteriorate.

Therefore, analgesia and sedation treatment are required after surgery[11]. Effective analgesia can not only quickly relieve patients' pain and improve their quality of life but also reduce the occurrence of stress reactions and avoid a series of adverse consequences such as hormone imbalance and decreased immune function. Through reasonable analgesic treatment, patients can better survive the postoperative recovery period and promote early recovery of the body.

3.2 Application of Acetaminophen Mannitol in Postoperative Analgesia of Spinal Surgery

Acetaminophen mannitol is a drug developed as an adjunct to opioids, designed to effectively relieve moderate to severe pain in adult patients following surgery. The mechanism of action of the main active ingredient, acetaminophen, focuses on the inhibition of pain signalling pathways in the central nervous system, specifically targeting pain receptors in the spinal cord and cerebral cortex [12]. This mechanism of action enables the drug to quickly relieve postoperative pain and alleviate the patient's suffering.

The safety of acetaminophen mannitol in postoperative analgesia for spinal surgery has been widely recognized. The drug has few adverse reactions, most of which are mild and transient. In addition, since the drug has little effect on liver and kidney function, it is suitable for patients with liver and kidney damage. At the same time, acetaminophen mannitol is well tolerated and will not produce obvious drug resistance even with long-term use[13]. However, it is unstable in aqueous solution and easily hydrolyzed, and its physical and chemical properties are unstable, making it difficult to make an injection solution, which limits its use in the perioperative period. Acetaminophen mannitol injection is China's first intravenous aminophenol drug. It is easy to administer, has a rapid onset of action, is excreted through the kidneys, and is widely used in postoperative pain management. At present, there is no research on the analgesic effect of this drug on postoperative pain in China. Flurbiprofen axetil, as a commonly used nonsteroidal anti-inflammatory drug, has a definite perioperative analgesic effect. Therefore, this study compared the analgesic effects of acetaminophen mannitol injection and flurbiprofen axetil after thoracoscopic radical resection of lung cancer to provide options for clinical medication.

4. Results and Discussion

4.1 General Information

Between March and May 2023, 120 patients who underwent spinal surgery at one hospital were selected as the sample for this study. These 120 patients were divided equally into a control group (60 patients) and an observation group (60 patients). Patients in both groups were classified experimentally according to the classification criteria of the American Society of Anaesthesiologists (ASA). The results showed no statistically significant differences between the two groups (P > 0.05), ensuring comparability between the two groups. The specific data information is shown in Table 1.

	Number of people				Asa classification	
Group	Male	Female	Weight (kg)	Average age	I 34	II
Control group	33	27	55-88	57.34±3.24	34	26
Experimental group	31	29	57-83	61.03±1.57	31	29

Table 1. Basic information of the research subjects

Subsequent analysis of the surgical status of the study participants showed no statistically significant differences between the two patient groups in terms of blood loss and duration of surgery (P > 0.05). No significant differences were also found in the surgical status of the study participants. Specific information on the data can be found in Table 2.

Project	Control group	Experimental group	P-value
Intraoperative bleeding volume (ml)	173±1.17	169±2.11	>0.05
Surgical duration (h)	5.34±2.34	6.12±1.08	>0.05

Table 2. Analysis of surgical conditions of subjects

Afterwards, the patients in the experimental group received 50 ml of acetaminophen-mannitol solution by intravenous drip after endotracheal intubation and before surgical skin incision. For 2 consecutive days after surgery, this dose was infused twice a day, with an interval of 12 hours. Patients in the control group received continuous intravenous infusion at the same time point at a rate of $0.51~\mu g$ per kg of patient body weight.

 6.39 ± 1.93

>0.05

 6.57 ± 1.68

4.2 Analgesic Effect of Acetaminophen Mannitol Injection

Hospitalization time (d)

This study examined the analgesic effects of two study groups using different analgesic methods by counting the difference in sufentanil dose between the experimental and control groups at 6-12 hours post-operatively. The data are shown in Figure 1.

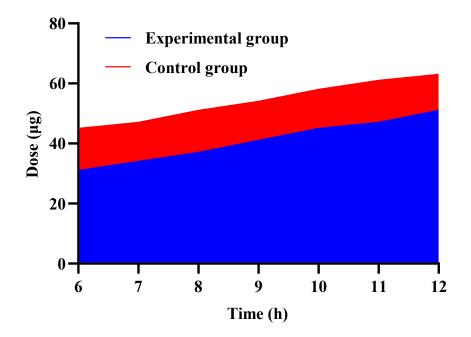


Figure 1. Sufentanil dosage

As shown in Figure 1, at various time periods after surgery, the amount of sufentanil used in both groups increases over time, but the increase in the control group significantly exceeds that in the experimental group. This indicates that the acetaminophen group shows a better effect in reducing the postoperative sufentanil dosage, which may mean that acetaminophen mannitol injection can reduce patients' dependence on opioids while providing effective analgesia, thereby helping to reduce related adverse reactions and complications.

In order to more comprehensively evaluate the analgesic effect, the study used the Visual Analogue Score (VAS) and the Budd-Chiari Syndrome Score (BCS) to assess the pain level and comfort of the patients, as shown in Figure 2.

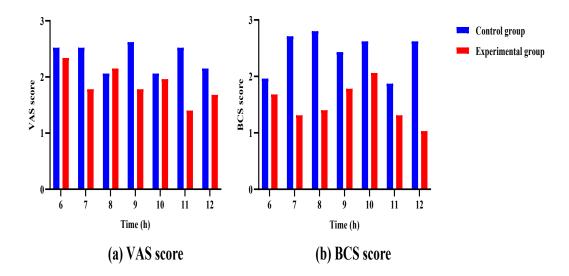


Figure 2. Comparison of VAS and BCS scores

According to Figure 2, it is found that within 6 to 12 hours after surgery, the VAS scores of the experimental group are lower than those of the control group, while the BCS scores are always higher than those of the control group. These differences reach statistical significance, further verifying the excellent effect of acetaminophen mannitol injection in postoperative analgesia after spinal surgery.

In addition to evaluating analgesic efficacy, the occurrence of side effects was also investigated in detail in the present study. In this study, the occurrence of four possible side effects after spinal surgery - nausea, vomiting, dizziness and drowsiness - was analyzed in both groups. The detailed statistical results are shown in Figure 3.

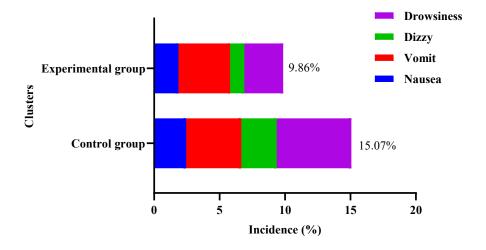


Figure 3. Incidence of adverse reactions

As can be seen in Figure 3, the experimental group shows a lower incidence rate than the control group. The overall statistical results show that the probability of occurrence is 9.86% in the experimental group and 15.07% in the control group. Combined with the experimental results above, it can be proved that acetaminophen mannitol can reduce the occurrence of adverse reactions while providing effective analgesia, creating a more favourable environment for patients' postoperative recovery.

5. Conclusion

In this paper, the performance of acetaminophen mannitol injection in analgesia was systematically evaluated by observing the actual effect of the use of the drug in spinal surgery patients in the

postoperative period. It was found that the application of acetaminophen mannitol could substantially shorten the postoperative recovery time of spinal surgery patients and effectively reduce the risk of various complications. This is of great significance in improving the quality of life of patients and reducing their physical and psychological burdens. However, there are some limitations in this study that cannot be ignored. The relatively limited sample size and short follow-up period may limit the applicability of the study results and the accurate assessment of long-term effects. Therefore, it is necessary for future studies to further expand the sample size and extend the follow-up period in order to more comprehensively investigate the actual benefits of this formulation in clinical practice.

Acknowledgement

This work was supported by Chen Xiao-Ping Foundation For The Development Of Science And Technology Of Hubei Province (No.CXPJJH12000005-07-63).

References

- [1] Wang Yin, Wen Chuanyun, Man Jinyu. Comparison of the effects of hydromorphone and sufentanil in postoperative analysis and delirium control in elderly orthopedic patients[J]. Chinese and Foreign Medical Treatment, 2024, 43(34): 21-24+37.
- [2] Zhang Tingyu, Zhang Wei, Xu Xiaqing, et al. Analysis of 78 cases of adverse drug reactions of propacetamol hydrochloride injection for postoperative analgesia[J]. Journal of Henan Surgery, 2024, 30(06): 121-123.
- [3] Sun Q, Zhang C, Liu S, et al. Efficacy of erector spinae plane block for postoperative analgesia lumbar surgery: a systematic review and meta-analysis[J]. BMC anesthesiology, 2023, 23(1): 54-55.
- [4] Zhang Z, Zhu R L, Yue L, et al. Bilateral ultrasound-guided erector spinae plane block versus wound infiltration for postoperative analysis in lumbar spinal fusion surgery: a randomized controlled trial[J]. European Spine Journal, 2023, 32(1): 301-312.
- [5] Mirkheshti A, Raji P, Komlakh K, et al. The efficacy of ultrasound-guided erector spinae plane block (ESPB) versus freehand ESPB in postoperative pain management after lumbar spinal fusion surgery: a randomized, non-inferiority trial[J]. European Spine Journal, 2024, 33(3): 1081-1088.
- [6] Jelodar A G, Makrani N F, Shafizad M, et al. Comparison of dexmedetomidine and ketamine in adjuvant with morphine for postoperative pain management following lumbar fusion surgery[J]. Interdisciplinary Neurosurgery, 2023, 33(1): 101767-101771.
- [7] Mahmoud A M, Ragab S G, Shawky M A, et al. The efficacy of erector spinae plane block compared with intrathecal morphine in postoperative analgesia in patients undergoing lumbar spine surgery: a double-blind prospective comparative study[J]. Pain Physician, 2023, 26(2): 149.
- [8] Zhu Qingxin, Tian Lei, Wen Kaixuan. Effects of dexmedetomidine combined with different doses of sufentanil on postoperative analysis in patients undergoing spinal surgery[J]. Chinese Health Care, 2024, 42(14): 39-42.
- [9] Xiang Yun, Xu Qiaomin, Ai Mengting. Effects of esketamine combined with sufentanil on perioperative indicators and postoperative analysesic and sedative effects of spinal surgery[J]. Chinese Journal of Drugs and Clinics, 2024, 24(11): 696-699.
- [10] Zhou Y, Yuan P, Xing Q, et al. Efficacy of postoperative analgesia with intravenous paracetamol and mannitol injection, combined with thoracic paravertebral nerve block in post video-assisted thoracoscopic surgery pain: a prospective, randomized, double-blind controlled trial[J]. BMC anesthesiology, 2024, 24(1): 14-15.
- [11] Lu X, Zhou J, Li X, et al. Efficacy of intravenous paracetamol and mannitol in managing chronic post-thoracotomy pain in patients with lung cancer: Study protocol for a single center prospective randomized double-blind controlled trial[J]. medRxiv, 2024: 2024, 27(8): 24312675-24312677.
- [12] Hadavi S M R, Panah A, Shamohammadi S, et al. The Prophylactic Effect of Acetaminophen and Caffeine on Post Dural Puncture Headache after Spinal Anesthesia for Cesarean Section: A Randomized Double-Blind Clinical Trial[J]. Iranian Journal of Medical Sciences, 2024, 49(9): 573-575.
- [13] Wu Ruiyang, Han Linglong. Effects of esketamine combined with sufentanil postoperative patient-controlled analgesia on pain, stress hormones and immune function in patients undergoing spinal surgery[J]. Chinese Journal of Rational Drug Use, 2024, 21(07): 81-88.