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Advances in the Use of Butorphanol Tartrate in Postoperative Analgesia after Cesarean Section

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Abstract: *As an agonist-antagonist opioid with good analgesic effect and few side effects, butorphanol tartrate has been widely used as a postoperative analgesic in clinical practice, and its special affinity for κ-opioid receptors makes Butorphanol particularly effective in postoperative analgesia after caesarean section. Meanwhile, with its unique characteristics, Butorphanol tartrate can be stably paired with other drugs alone or in combination with other drugs, and applied to post-cesarean section patients through different modes of administration to produce safe and highly effective analgesia and help the mothers to recover quickly after the operation.*

Keywords: *Butorphanol tartrate; Cesarean section; Analgesia*

1. Introduction

In recent years, with the increase in population and the development of medical technology, as well as in order to safeguard the lives of mothers and infants, more and more pregnant women choose to undergo cesarean section during labour, and cesarean section has become one of the most common inpatient procedures worldwide [1]. Studies have reported that the rate of cesarean section in China increased from 28.8% in 2008 to 36.7% in 2018 [2], with a consequent dramatic increase in the demand for postoperative analgesia. Opioids have stable and efficient analgesic effects and are widely used in postoperative analgesia after caesarean section, but routinely used opioids, including morphine, fentanyl and sufentanil, are prone to adverse reactions such as nausea and vomiting, itching and respiratory depression, which can affect the maternal postoperative recovery [3]. Butorphanol tartrate, as a new agonist-antagonist opioid, is well suited for the management of visceral pain after caesarean section because of its analgesic effect with fewer side effects and its high affinity for κ-opioid receptors compared with conventionally used opioids [3]. This review explores the safety and efficacy of Butorphanol tartrate in post-cesarean section analgesia with different modes of administration based on existing studies to provide a basis for a multimodal analgesic regimen after cesarean section.

2. Post-caesarean section pain

Due to the enormous trauma to internal organs during caesarean section, postoperative pain management may be very severe. In addition, the routine use of hysterotonin treatment for mothers after cesarean section promotes uterine recovery and reduces postoperative bleeding, yet produces very painful uterine spasmodic pain [4]. Therefore, postoperative pain after caesarean section has become one of the most important maternal concerns. Severe postoperative uterine cramping pain may interfere with early ambulation, resulting in prolonged bed rest, which may lead to increased incidence of serious adverse events such as thromboembolism, uterine insufficiency, and postpartum haemorrhage [5,6]. It has been found that the incidence of postoperative pain and consequent anxiety and depression after caesarean section is higher than in vaginal deliveries, and that these factors increase the release of dopamine and prednisolone in the body, leading to suppression of lactogen secretion and release, which reduces breast milk production and delays breastfeeding and early mother-infant bonding [7]. Inadequate postoperative analgesia also increases the need for opioids, and relevant studies have shown a strong association between the level of pain after labour and the incidence of postnatal depression and the development of chronic pain, thereby delaying maternal recovery after surgery [8,9]. Therefore, failure to provide safe and efficient pain management for women after cesarean section will significantly increase the risk and incidence of adverse events for mothers and babies in the perinatal

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period.

In 2019, the Obstetric Anaesthesia and Perinatal Society proposed the concept of enhanced recovery after cesarean section (ERAC) and its related elements, and efficient and safe pain management strategies are an important part of rapid recovery [10]. Good postoperative analgesia can reduce maternal pain, improve maternal quality of life and health, reduce the incidence of postoperative complications and maternal mortality, and at the same time reduce opioid overdose, shorten hospital stay, reduce hospital costs, and alleviate the burden on society and families [11]. Therefore, the management of postoperative pain after cesarean section, especially the effective relief of contraction pain, is an important challenge for clinical anaesthesiologists at a time when the ERAC concept has been proposed. It is urgent to improve the analgesic regimen after cesarean section and find a safe and effective drug with few side effects.

3. Butorphanol tartrate

Opioid is a generic term for a large class of analgesic drugs whose structure is related to the natural plant alkaloids found in opium. Opioids act by binding to specific cell-surface receptors, which include three main categories: μ-receptors, δ-receptors and κ-receptors. These receptors are mainly found in the central nervous system, brain and spine, and activation of the relevant receptors produces a series of intracellular signals including inhibition of adenylate cyclase, reduction of calcium channel opening, increase in potassium current and activation of protein kinase C (PKC), which reduces cellular excitability and inhibits neurotransmitter transmission, resulting in an analgesic effect [12]. Butorphanol tartrate is a typical agonist-antagonist opioid analgesic drug, with an analgesic potency 5-7 times that of morphine, and its in vitro affinity for each of the three major opioid receptors is 1:4:25 (μ:δ:κ) [13,14]. Numerous studies have shown that butorphanol has partial agonist and partial antagonist effects on μ-opioid receptors, agonist and partial antagonist effects on κ-opioid receptors, and dominant antagonist activity on δ-opioid receptors, thus, Butorphanol tartrate is effective in relieving both mechanical and visceral pain, as well as decreasing the incidence of adverse events, such as drug dependence, constipation, respiratory depression, and agitated anxiety, which may be associated with opioid medications [15,16].

Since its introduction to the market in 1978, Butorphanol tartrate has been used in a large number of applications for perioperative pain management, and has been widely recognised for its safety and reliability, and has become even more favoured by clinicians and patients due to its relatively few side effects. A meta-analysis showed that butorphanol tartrate was compared with other opioids, including morphine, fentanyl and sufentanil, in terms of postoperative pain management and the incidence of adverse events, and found that butorphanol was comparable to the other drugs in terms of postoperative analgesia, with a significant advantage in terms of sedative effect, and that it was associated with a significantly lower incidence of adverse events such as nausea, vomiting, itching and dizziness [17]. Nowadays, butorphanol is not limited to intraoperative applications, but its use in extra-operative anaesthesia and analgesia has also matured. In painless gastrointestinal endoscopy, the use of butorphanol tartrate not only reduces the incidence of physical movement and coughing in patients, which is conducive to the smooth operation of endoscopy, but also reduces the amount of propofol used, reduces the pain of propofol injections, and reduces the incidence of adverse reactions, such as dizziness, drowsiness, and respiratory depression, and shortens the recovery time of patients [18,19]. The analgesic effect of using Butorphanol for mandibular third molar extraction is significantly better than Tramadol in the dental clinic [20]. The use of Butorphanol tartrate in painless abortion, with its longer sedative-analgesic effect, can effectively relieve the pain of postoperative uterine contractions, lower incidence of nausea and vomiting and respiratory depression, also improves the intraoperative and postoperative safety and comfort of patients [21].

4. Multimodal analgesic programme with bupropion tartrate

Butorphanol tartrate has evolved from intravenous and intramuscular administration to a variety of delivery modes, including patient controlled intravenous analgesia (PCIA), epidural administration, intrathecal injection, and transnasal administration, which have demonstrated their unique advantages in perioperative pain management. Its effectiveness and safety have been clinically proven over a long period of time. Continuous infusion of butorphanol tartrate by PCIA after total hysterectomy in a caval tunnel resulted in satisfactory analgesia without serious adverse events, including respiratory depression, hypotension, bradycardia, and somnolence, when compared with the control group [22]. In

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orthopaedic surgeries with high injury irritation and severe postoperative pain, postoperative intravenous self-administered analgesia with bupropion compared with sufentanil has shown good analgesic effects and reduced opioid use, improving the quality of patients' postoperative recovery [23].

When administered intrathecally, butorphanol tartrate is used as an adjuvant in combination with local anaesthetics to provide satisfactory analgesia, reduce the adverse effects of local anaesthetic drugs, and prolong the duration of postoperative analgesia [24]. Intrathecal local anaesthetics interfere with afferent and efferent sensory and motor impulse conduction by inhibiting voltage-gated sodium channels in the spinal cord, whereas intrathecal injection of butorphanol activates opioid receptors in the dorsal grey matter of the spinal cord and blocks calcium channels to regulate the function of afferent pain fibres, producing a synergistic effect when the two are used in combination, i.e., local anaesthetic drugs blocking the Na+ channels and butorphanol blocking Ca+ channels, which improves both the analgesic quality, as well as reducing sympathetic inhibition and obtaining more stable haemodynamics, which is very beneficial for cardiac patients undergoing non-cardiac surgery [25,26]. At the same time, intrathecal injection of Butorphanol combined with local anaesthetic drugs can also reduce the intensity of motor block, which is conducive to the early walking of patients, and can reduce the occurrence of itching and other complications [27].

Compared with intermittent parenteral application of opioids, epidural administration acts on specific opioid receptors that are abundantly distributed in the posterior horn of the spinal cord, resulting in a more rapid onset of analgesic action and a lower incidence of adverse effects such as nausea, vomiting, and pruritus [28]. Due to its high lipid solubility, bupropion tartrate diffuses in the spinal cord after epidural administration, reducing the transfer of residual drug in the cerebrospinal fluid from the lumbar region to the brainstem, avoiding inhibition of the medullary respiratory centre and reducing the incidence of respiratory depression [29]. As with intrathecal injection, butorphanol, as an epidural adjuvant, provides high quality intraoperative analgesia and longer lasting postoperative analgesia along with more stable haemodynamics [30].

Intravenous, intrathecal and epidural administration of Butorphanol tartrate has demonstrated its good analgesic advantages and safety, but these modes of administration have the first-off effect and the inconvenience and danger of invasive manipulation, so researchers want to seek an alternative route of administration. Butorphanol, with its small molecular weight and high lipid solubility, is easily absorbed through the nasal mucosa to exert its pharmacological effects, and has a natural advantage of transnasal administration [31]. In 1991, the FDA formally approved that Butorphanol tartrate could be administered nasally, and intranasal administration has multiple significant advantages, (1) transnasal Butorphanol can avoid degradation in gastrointestinal fluids and hepatic first-pass elimination, with higher bioavailability of about 48%-70%, up to 80% [32]; (2) nasal mucosa is rich in blood vessels, and the local absorption of the drug is fast after transnasal administration, and the effects take place rapidly, and it is generally considered that the analgesic effect can be achieved in 15 minutes, and the peak time of blood concentration is about 20 minutes on average. It is generally believed that the analgesic effect can be achieved in 15 minutes, and the average time for the blood concentration to reach the peak is about 20 minutes. Compared with intravenous administration, transnasal Butorphanol is also able to provide postoperative analgesia of higher quality and longer duration [33,34]; (3) Compared with other modalities, intranasal administration is simple and convenient, requires no invasive manipulation, and reduces the additional pain, with better patient compliance, which makes it easier to implement postoperative pain management.

The safety and efficacy of Butorphanol Tartrate Nasal Spray in analgesia have also been confirmed by a large number of clinical studies. Zhao YQ et al. observed the analgesic effect of butorphanol tartrate nasal spray in patients with moderate-to-severe cancer pain, and found that the effective rate of pain relief in these patients reached more than 80%, the rate of sleep improvement reached 55.6%, and the quality of life of 76.2% of the patients was improved [35]. In short outpatient procedures, the use of butorphanol nasal spray can provide reliable analgesia for patients with extraction of blocked third molars, but high doses may cause adverse effects such as dizziness [36]. Yash et al. further studied and found that when buttorphanol nasal spray was used continuously at intervals of 6 hours, it was safely tolerated by patients and the analgesic effect was higher than that of oral analgesic drugs, providing strong evidence for the effectiveness and safety of buttorphanol nasal spray [37]. Compared with morphine in painless fibrinoscopy applications, the incidence of intraoperative patient choking was significantly lower in the bupropion nasal spray group, and the incidence of postoperative nausea and vomiting was also significantly lower [38]. Butorphanol nasal spray also showed superiority in perioperative analgesia. After the use of Butorphanol nasal spray in patients undergoing low-level laparoscopic surgery, the pain of this group of patients could be effectively relieved within 30 min, and

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the haemodynamic indexes were stable [39]. In the postoperative analgesia of gynaecological open laparotomy, nasal spray of 1 mg of Butorphanol tartrate was able to achieve satisfactory analgesic and sedative effects, and at the same time reduce the occurrence of adverse events such as over-sedation and drowsiness [40].

In summary, butorphanol tartrate has become one of the first choices of perioperative analgesic drugs with its good sedative-analgesic effect and few side effects. And its various modes of administration also have their own advantages, with precise effects, safety and reliability, providing more ideas for multimodal analgesic solutions and greatly improving the quality of postoperative pain management.

5. Butorphanol tartrate in post-cesarean section analgesia

Uterine contraction pain is intermittent spasmodic pain associated with uterine contractions, which belongs to a type of visceral pain and is mainly triggered by prostaglandins [41]. Studies have shown that butorphanol tartrate, as a κ-opioid receptor agonist, is effective in relieving visceral pain [42]. κ-opioid receptors are G-protein-coupled receptors, and stimulation of κ-receptors inhibits the cyclic adenosine monophosfate (cAMP) signalling pathway, and when butorphanol tartrate activates κ-receptors, it is effective in relieving visceral pain by down-regulating spinal cord dorsal horn cAMP-dependent protein kinase A (PKA) expression, inhibiting the cAMP-PKA-cyclophosphoadenosine effector-binding protein signalling pathway, thereby relieving contraction pain [43]. Meanwhile, it was found that women were more sensitive to κ opioid receptors and had a more significant analgesic effect compared with male patients, so the use of Butorphanol tartrate as an analgesic drug for post-cesarean section uterine contraction pain has a unique advantage [44].

The application principle of PCIA is to inject the drug into the patient's body continuously and slowly through the vein according to the set dose, so that the drug can maintain a stable blood concentration in the body and can be self-regulated by the patient to obtain the best analgesic effect with the smallest dosage, which avoids the drawbacks of excessive fluctuation of blood concentration caused by intravenous and intramuscular pushes [45]. The effect and side effects of Butorphanol tartrate are both dose-related and dose-dependent, with the increase of dose, the sedative and analgesic effect is obviously improved, but the incidence of nausea and vomiting, etc. also increases, so the use of PCIA pumped Butorphanol application in post-cesarean section will be very beneficial [45]. Liu H et al. found that continuous pumping of butorphanol tartrate was effective in relieving uterine contraction pain in primary caesarean section, and its reliable sedation could avoid postoperative pain hypersensitivity due to sleep deprivation [46]. Mothers with scarred uterus are more sensitive to pain, and the pain caused by postoperative uterine contractions is more intense, PCIA continuous infusion of Butorphanol can also achieve satisfactory analgesic and sedative effects for mothers with second cesarean section, and when used in combination with other opioids, it can also reduce the total opioid dosage and lower the incidence of adverse effects [47,48].Qin C et al. also demonstrated that for repeat intolerable postoperative uterine spasmodic pain in women undergoing cesarean section, the application of Butorphanol tartrate in PCIA provided better analgesia and accelerated postoperative recovery [48].

The pain impulses caused by uterine contractions are transmitted through visceral afferent nerve fibres, accompanied by sympathetic nerve fibres and enter the spinal cord at the T10-L1 spinal cord segment. When the relevant pathway can be successfully blocked by epidural administration, the pain of uterine contractions can be effectively relieved, and the epidural drugs are rarely transferred to breast milk, so the epidural administration of drugs can be safely and effectively applied to analgesia after cesarean section [49]. Satisfactory analgesia after caesarean section can be obtained with epidural administration of butorphanol tartrate alone, which has a rapid onset of action and is more analgesic than morphine, although the duration of action is limited [50]. When buprenorphine is used as an epidural adjuvant in combination with bupivacaine, the onset of analgesia is significantly shorter, duration and quality of analgesia are significantly improved, and the incidence of adverse events such as respiratory depression, nausea and vomiting, and itching is low, as compared to the drug alone [51. Butorphanol tartrate, when used as a continuous epidural pumping drug in post-caesarean section and labour analgesia, not only obtains a more stable and long-lasting analgesic effect, but also does not produce motor blockade, which can be safely and effectively applied to maternal post-caesarean section analgesia [52,53].

Intrathecal opioids also act on the spinal cord to produce analgesia and are administered in small doses with high efficiency, but their incidence of adverse effects is equally elevated, therefore highly

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lipid soluble opioids are safer for intrathecal use [54]. Butorphanol tartrate has high lipid solubility and has fewer side effects as an intrathecal agent in caesarean section, which can ensure the safety of mother and baby, and Abbi P et al. found that butorphanol as an adjuvant combined with bupivacaine for intrathecal injection in caesarean section resulted in safe and longer lasting analgesia compared to fentanyl [55]. However, the current study is limited to a single intrathecal injection for analgesia, and the safety and efficacy of continuous intrathecal pumping in postoperative cesarean section need to be further investigated.

Butorphanol tartrate administered intranasally has a rapid onset of action, precise analgesic effect, high bioavailability and ease of use, and is well suited for self-controlled analgesia in women after caesarean section. Studies have shown that intranasal administration of Butorphanol provides better analgesia and longer duration of analgesia in post-caesarean section analgesia compared to intravenous administration, but the incidence of adverse effects such as dizziness and drowsiness is dose-dependent, and the dose of a single dose of the drug should be administered cautiously during drug use [56]. Shang Yu et al. also found that small-dose intranasal administration of Butorphanol tartrate significantly reduced severe visceral pain during dilatation and stretching of the uterus, and also had a significant effect on the relief of postoperative uterine contraction pain, and reduced the incidence of respiratory depression [57]. The use of Butorphanol nasal spray 1 mg during caesarean section not only compensates for the incomplete block of combined lumbar and rigid anaesthesia for visceral and detrusor pain, but also reduces the pain of contractions after the planes have subsided and does not affect the neonatal Apgar score [58]. Therefore, low-dose butorphanol tartrate nasal spray is safe and reliable for intraoperative and postoperative analgesia in cesarean section.

6. Summary

The analgesic efficacy of Butorphanol tartrate, whether administered by PCIA, intrathecal injection, epidural or transnasal administration, for post-caesarean section pain as well as its safety and harmlessness to mother and baby have been widely demonstrated. Different modes of administration have their advantages and disadvantages; is it possible to sustain intrathecal pumping of Butorphanol tartrate? Can the optimal dose for a single intranasal dose and the optimal duration of intermittent administration be determined? All relevant questions need to be further investigated. We will continue to improve the current delivery method and explore other simpler and more efficient delivery modes to improve the post-caesarean pain management programme and reduce the pain of post-caesarean patients to a greater extent, so as to achieve the expectation of rapid recovery of mothers in the postoperative period.

References

[1] Eisenach JC, Pan PH, Smiley R, et al. Severity of acute pain after childbirth, but not type of delivery, predicts persistent pain and postpartum depression[J]. Pain, 2008, 140(1): 87-94.
[2] Li HT, Hellerstein S, Zhou YB, et al. Trends in cesarean delivery rates in China, 2008-2018[J]. JAMA, 2020 Jan 7, 323(1): 89-91.
[3] QIN Chunyu, FENG Xuewei, WANG Chengrong, et al. Effectiveness and safety of opioids for postoperative analgesia after caesarean section[J]. Journal of Clinical Pharmacotherapy, 2020, 18(11): 67-71.
[4] Lavand'homme P. Postcesarean analgesia: effective strategies and association with chronic pain[J]. Curr Opin Anaesthesiol, 2006, 19(3): 244-248.
[5] Dualé C, Frey C, Bolandard F, et al. Epidural versus intrathecal morphine for postoperative analgesia after Caesarean section[J]. Br J Anaesth, 2003, 91(5): 690–694.
[6] Loane H, Preston R, Douglas MJ, et al. A randomized controlled trial comparing intrathecal morphine with transversus abdominis plane block for post-cesarean delivery analgesia[J]. Int J Obstet Anesth, 2012, 21(2): 112–118.
[7] Wang Y, Fang X, Liu C, et al. Impact of intraoperative infusion and postoperative PCIA of dexmedetomidine on early breastfeeding after elective cesarean section:a randomized double-blind controlled trial[J]. Drug Des Devel Ther, 2020, 14: 1083-1093.
[8] Kainu JP, Halmesmäki E, Korttila KT, et al. Persistent pain after cesarean delivery and vaginal delivery: a prospective cohort study[J]. Anesth Analg, 2016, 123(6): 1535–1545.
[9] Eisenach JC, Pan PH, Smiley R, et al. Severity of acute pain after childbirth, but not type of delivery,predicts persistent pain and postpartum depression[J]. Pain, 2008, 140(1): 87–94.
[10] Bollag L, Lim G, Sultan P, et al. Society for obstetric anesthesia and perinatology: consensus statement and recommendations for enhanced recovery after cesarean[J]. Anesth Analg, 2021, 132(5):

ISSN 2706-6819 Vol.6, Issue 2: 9-15, DOI: 10.25236/IJFM.2024.060202

1362-1377.
[11] Liu ZQ, Du WJ, Yao SL. Enhanced recovery after cesarean delivery: a challenge for anesthesiologists [J]. Chin Med J (Engl), 2020, 133(5): 590-596.
[12] No authors listed. LiverTox: clinical and research information on drug-induced liver injury [DB/OL]. National Institute of Diabetes and Digestive and Kidney Diseases, 2012.
[13] Commiskey S, Fan LW, Ho IK, et al. Butorphanol: effects of a prototypical agonist-antagonist analgesic on kappa-opioid receptors[J]. J Pharmacol Sci, 2005, 98(2): 109-116.
[14] Ji J, Lin W, Vrudhula A, et al. Molecular interaction between butorphanol and κ-opioid receptor[J]. Anesth Analg, 2020, 131(3): 935-942.
[15] Ide S, Minami M, Ishihara K, et al. Abolished thermal and mechanical antinociception but retained visceral chemical antinociception induced by butorphanol in mu-opioid receptor knockout mice [J]. Neuropharmacology, 2008, 54(8): 1182-1188.
[16] Grechko OY, Litvinov RA, Spasov AA, et al. Study of μ- and δ-opioid activities in agents with various κ-receptor selectivity[J]. Bull Exp Biol Med, 2017, 162(5): 632-635.
[17] Zhu Z, Zhang W. Efficacy and safety of butorphanol use in patient-controlled analgesia:a meta-analysis[J]. Evid Based Complement Alternat Med, 2021, 2021: 5530441.
[18] Lv S, Sun D, Li J, et al. Anesthetic effect of different doses of butorphanol in patients undergoing gastroscopy and colonoscopy[J]. BMC Surg, 2021, 21(1): 266.
[19] Zhu X, Chen L, Zheng S, et al. Comparison of ED95 of butorphanol and sufentanil for gastrointestinal endoscopy sedation: a randomized controlled trial[J]. BMC Anesthesiol, 2020, 20(1): 101.
[20] Hassan SS, Ahmed A, Rai M, et al. Analgesic efficacy of tramadol and butorphanol in mandibular third molar surgery: a comparative study[J]. J Contemp Dent Pract, 2012, 13(3): 364-370.
[21] LU Ruibin, XU Xudong. Clinical observation of propofol and butorphanol in painless abortion[J]. Journal of Clinical Anaesthesiology, 2009, 25(7): 625-626.
[22] Du J, Li JW, Jin J, et al. Intraoperative and postoperative infusion of dexmedetomidine combined with intravenous butorphanol patient-controlled analgesia following total hysterectomy under laparoscopy[J]. Exp Ther Med, 2018, 16(5): 4063-4069.
[23] Zhou WG. Observation of the clinical effect of Butorphanol tartrate for intravenous self-controlled analgesia after orthopaedic surgery[J]. Jiangxi Medicine, 2022, 57(3): 267-269.
[24] Kumar A, Kumar R, Verma VK, et al. A randomized controlled study between fentanyl and Butorphanol with low dose intrathecal bupivacaine to facilitate early postoperative ambulation in urological procedures[J]. Anesth Essays Res, 2016, 10(3): 508-511.
[25] Gupta R, Arora D, Kaur S, et al. Comparative study of hemodynamic effects of intrathecal bupivacaine with butorphanol in cardiac and non-cardiac patients[J]. J Anaesthesiol Clin Pharmacol, 2020, 36(4): 511-517.
[26] Sharma A, Kumari A, Gupta R, et al. Comparison of intrathecal bupivacaine-fentanyl and bupivacaine-butorphanol combinations for joint replacement surgeries[J]. J Anaesthesiol Clin Pharmacol, 2022, 38(1): 79-83.
[27] Kaur M, Katyal S, Kathuria S, et al. A comparative evaluation of intrathecal bupivacaine alone, sufentanil or butorphanol in combination with bupivacaine for endoscopic urological surgery[J]. Saudi J Anaesth, 2011, 5(2): 202-207.
[28] Parikh GP, Veena SR, Vora K, et al. Comparison of epidural butorphanol versus epidural morphine in postoperative pain relief[J]. Middle East J Anaesthesiol, 2014, 22(4): 371-376.
[29] Swathi N, Ashwini N, Shukla MI. Comparative study of epidural bupivacaine with butorphanol and bupivacaine with tramadol for postoperative pain relief in abdominal surgeries[J]. Anesth Essays Res, 2016, 10(3): 462-467.
[30] Kaur J, Bajwa SJ. Comparison of epidural butorphanol and fentanyl as adjuvants in the lower abdominal surgery: A randomized clinical study[J]. Saudi J Anaesth, 2014, 8(2): 167-171.
[31] Gillis JC, Benfield P, Goa KL. Transnasal butorphanol. A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in acute pain management[J]. Drugs, 1995, 50(1): 157-175.
[32] Davis GA, Rudy AIa, Archer SM, et al. Bioavailability of intranasal butorphanol administered from a single-dose sprayer[J]. Am J Health Syst Pharm, 2005, 62(1): 48-53.
[33] Davis GA, Rudy AC, Archer SM, et al. Pharmacokinetics of butorphanol tartrate administered from single-dose intranasal sprayer[J]. Am J Health Syst Pharm, 2004, 61(3): 261-266.
[34] Dale O, Hjortkjaer R, Kharasch ED. Nasal administration of opioids for pain management in adults[J]. Acta Anaesthesiol Scand, 2002, 46(7): 759-770.
[35] Zhao Yuqing, Li Fang, Zhao Yunbo, et al. Clinical efficacy of butorphanol tartrate nasal spray in the treatment of 252 patients with cancer pain[J]. China Cancer Clinics, 2009, 36(9): 497-499.
[36] Wermeling DP, Grant GM, Lee A, et al. Analgesic effects of intranasal butorphanol tartrate administered via a unit-dose device in the dental impaction pain model: a randomized,double-blind,placebo-controlled,parallel-group study[J]. Clin Ther, 2005, 27(4): 430-440.

ISSN 2706-6819 Vol.6, Issue 2: 9-15, DOI: 10.25236/IJFM.2024.060202

[37] Merchant Y P, Halli R, Mograwala H. Comparative evaluation of intranasal butorphanol and oral diclofenac sodium for analgesia after surgical removal of impacted mandibular third molars: split-mouth prospective controlled clinical study[J]. J Maxillofac Oral Surg, 2019, 18(3): 395-399.
[38] Ai Q, Hu YP, Wang YJ, et al. Application of Butorphanol nasal spray in fibreoptic bronchoscopy[J]. Journal of Practical Medicine, 2009, 25(21): 3681-3682.
[39] Chu C C, Chen J Y, Chen C S, et al. The efficacy and safety of transnasal butorphanol for postoperative pain control following lower laparoscopic surgery[J]. Acta Anaesthesiol Taiwan, 2004, 42(4): 203-207.
[40] Zhang Xue, Chi Xiaohui, Tian Xueguang, et al. Clinical observation of Butorphanol tartrate nasal spray for postoperative analgesia in gynaecology[J]. Journal of Clinical Anaesthesiology, 2010, 26(5): 452-453.
[41] Hsu HW, Cheng YJ, Chen LK, et al. Differential analgesic effect of tenoxicam on the wound pain and uterine cramping pain after cesarean section[J]. Clin J Pain, 2003, 19(1): 55-58.
[42] Davis MP. Drug management of visceral pain:concepts from basic research[J]. Pain Res Treat, 2012, 2012: 265605.
[43] Wang Yueling, Ma Wenjuan, Yang Yong, et al. Effects of intrathecal injection of bupropion mixed with ketamine on cAMP-PKA-CREB signal transduction pathway in the dorsal horn of spinal cord of rats with inflammatory pain[J]. Chinese Journal of Anaesthesiology, 2009, 29(8): 712-715.
[44] Miller PL, Ernst AA. Sex differences in analgesia:a randomized trial of mu versus kappa opioid agonists[J]. South Med J, 2004, 97(1): 35-41.
[45] Liu Yusheng, Wang Wei, Cao Yan, et al. Clinical study of bupropion combined with flurbiprofenate for postoperative analgesia after caesarean section[J]. Journal of Clinical Anaesthesiology, 2013, 29(2): 113-116.
[46] Liu H, Wang Y, Li F, et al. Analgesic and sedative effects of different doses of dexmedetomidine combined with butorphanol in continuous analgesia after a cesarean section[J]. Front Surg, 2022, 9: 896536.
[47] Wang Chaohui, Mao Mao, Zhang Panpan, et al. Effect of continuous background infusion of different doses of butorphanol tartrate on postoperative pain after repeat caesarean section in women with scarred uterus[J]. Journal of Clinical Anaesthesiology, 2020, 36(7): 656-659.
[48] Cai Q, Gong H, Fan M, et al. The analgesic effect of tramadol combined with butorphanol on uterine cramping pain after repeat caesarean section: a randomized, controlled, double-blind study[J]. J Anesth, 2020, 34(6): 825-833.
[49] Mo X, Zhao T, Chen J, et al. Programmed intermittent epidural bolus in comparison with continuous epidural infusion for uterine contraction pain relief after cesarean section: a randomized, double-blind clinical trial[J]. Drug Des Devel Ther, 2022, 16: 999-1009.
[50] Palacios QT, Jones MM, Hawkins JL, et al. Post-caesarean section analgesia: a comparison of epidural butorphanol and morphine[J]. Can J Anaesth, 1991, 38(1): 24-30.
[51] Pokharel K, Rahman TR, Singh SN, et al. The efficacy and safety of low dose epidural butorphanol on postoperative analgesia following cesarean delivery[J]. JNMA J Nepal Med Assoc, 2008, 47(170): 57-61.
[52] Hu YM, Kong MJ. Butorphanol for epidural analgesia after caesarean section[J]. Journal of Clinical Anaesthesiology, 2007, 23(8): 691-692.
[53] Shankar K A, Puri R, Goel JK. Butorphanol-bupivacaine versus fentanyl-bupivacaine for extradural analgesia during labour[J]. Med J Armed Forces India, 2006, 62(3): 224-227.
[54] Escarment J, Clément HJ. Emploi des opiacés par voie périmédullaire en obstétrique. Use of epidural and intrathecal opiates in obstetrics[J]. Ann Fr Anesth Reanim, 1989, 8(6): 636-649. French.
[55] Abbi P, Gupta R, Kaur H, et al. Comparing duration of analgesia after intrathecal administration of opioids in primary paturients for lower segment cesarean section[J]. Anesth Essays Res, 2021, 15(3): 327-331.
[56] Abboud TK, Zhu J, Gangolly J, et al. Transnasal butorphanol: a new method for pain relief in post-cesarean section pain[J]. Acta Anaesthesiol Scand, 1991, 35(1): 14-18.
[57] Shang Yu, Gu Peifi. Observation on the anaesthetic effect of propofol reinforced by Butorphanol nasal spray on painless abortion[J]. Journal of Clinical Anaesthesiology, 2008, 24(11): 1000-1001.
[58] Du Jing, Sun Chuanliang. Effectiveness of butorphanol nasal drops for analgesia in women undergoing first caesarean section[J]. Journal of Clinical Anaesthesiology, 2021, 37(9): 977-978.