Dexmedetomidine Added to Ropivacaine for Transversus Abdominis Plane Block Reduces the Incidence of Perioperative Neurocognitive Disorders:a single centre randomized controlled trial

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Research

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Abstract

Background Perioperative Neurocognitive Disorders is a common neurological complication with no effective treatments after surgery. This research aims to evaluate the effect of transversus abdominis plane block with dexmedetomidine added to ropivacaine on the incidence of perioperative neurocognitive disorders in patients undergoing abdominal surgery and provides a new way to prevent it.

Methods 180 patients submitted to radical laparoscopic colorectal cancer surgery were randomly divided into Control Group（n=90） and Dex Group(n=90). Ultrasound guided transversus abdominis plane block was performed after anesthesia induction: 0.5% ropivacaine 20ml was injected into each transversus abdominis plane in Control Group, 0.5% ropivacaine + 1μg/kg dexmedetomidine (add up to 20ml) in Dex Group. Primary indicators were the incidence of perioperative neurocognitive disorders within 30days after surgery. Secondary indicators were the duration of operation and anesthesia, consumption of general anesthetics, fluid intake, urine and blood loss during operation, visual analog pain scores.

Results 169 cases were finally analyzed, including 84 in Control Group and 85 in Dex Group. The consumption of propofol and remifentanil in Dex Group was lower than that in Control Group ((0.82±0.33) g vs. (1.22±0.42) g，(1.17±0.40) mg vs. (1.48±0.60) mg, P<0.05). There was no significant difference in visual analog pain scores between the two groups at 3days and 7days after surgery (P>0.05), while lower than Control Group at 6 hours and 24 hours after surgery. In terms of the incidence of perioperative neurocognitive disorders, compared with Control Group, there was no significant differences at 3days and 7days (P>0.05), but significantly decreased at 6hours, 24days and 30days after surgery (7.1% vs.17.9%，4.7% vs.14.3%，3.5% vs. 11.9%，P<0.05) in Dex Group.

Conclusion While conducting transversus abdominis plane block after general anesthesia induction, dexmedetomidine added to ropivacaine for it can reduce the incidence of perioperative neurocognitive disorders within 30days after surgery，which may be related to reduce the consumption of general anesthetics and provide satisfactory postoperative analgesia.

Trial registration: Dexmedetomidine Added to Ropivacaine for Transversus Abdominis Plane Block Reduces the Incidence of Perioperative Neurocognitive Disorders：a single centre randomized controlled trial, ChiCTR2100046876. Registered 29 May 2021, https://www.chictr.org.cn/edit.aspx?pid=125579&htm=4.

Background

Perioperative neurocognitive disorders(PND), which was known as postoperative cognitive dysfunction (POCD) previously (Evered et al. 2018), is a common neurological complication after surgery and anesthesia with a incidence about 53%-80% in normal subjects(Telugu et al. 2013; Kok et al. 2017). At present, there is no effective treatment for PND, so our purpose of this study is to provide a new way to prevent the occurrence of PND. Transversus Abdominis Plane Block (TAPB) is a new regional nerve block which is beneficial to the analgesia of abdominal surgery(Hsiao-Chien et al. 2017; Petersen et al. 2010).

In our clinical study, we accidentally found that dexmedetomidine added to ropivacaine for TAPB could reduce delirium within 3 days after abdominal surgery. Thus, we wonder that whether this method could reduce the incidence of PND.

Methods

Participants

This research was approved by the Ethics Committee of The Second People's Hospital of Yibin City. 180 patients submitted to laparoscopic radical resection of colorectal cancer were randomly divided into Control Group (n = 90) and DEX Group (n = 90) before surgery. All patients signed informed consent. Briefly, We enrolled patients 60 years of age or older who had 95 activity daily living (ADL) scales or higher. We excluded patients if they were drug users, regular binge drinking, diagnosed with cognitive dysfunction or mental disabilities. We also rejected participants if they were diagnosed with coagulation dysfunction and diabetes. All eligible patients were performed bilateral TAPB with ultrasound guided after induction by the same anesthesiologist who didn't participate in data collection. We announced the withdrawal of participants who were operated less than 2 hours, turned to laparotomy operation or transferred to intensive care unit (ICU) after surgery.

Data Collection

Baselines: age, body weight, body mass index (BMI), sex, education background, ASA score physical status, preoperative surgical history, the mini-mental state examination (MMSE) score were obtained before surgery. Primary indicators: the incidence of PND, which was assessed by MMSE at 6 hours, 24 hours, 3 days, 7 days and 30 days after surgery. Comparing with the MMSE score before operation, if the figure decreases by more than 2 points, the patient shall be diagnosed with PND (Li et al.2015). Secondary indicators: Intraoperative informations (duration of operation and anesthesia, consumption of general anesthetics, fluid intake, urine and blood loss), visual analog pain scores (VAS) in the rest at 6 hours, 24 hours, 3 days and 7 days after surgery.

Intervention

All participants, prepared preoperative fasting, were randomly divided into Control Group and Dex Group by digit table. Both two groups participants were performed anaesthesia induction with a same proposal before performed TAPB : sufentanil 0.30μg·kg^{-1}, midazolam 0.04 mg·kg^{-1}, cisatracurium 0.15mg·kg^{-1} and etomidate 0.20 mg·kg^{-1}. We used classical method (Hebbard et al.2007) with ultrasound technology to implement bilateral TAPB. The only difference between the two groups was the local anesthetics of TAPB：0.5% ropivacaine 20ml was injected into each transversus abdominis plane in Control Group, while 0.5% ropivacaine + 1μg/kg dexmedetomidine (add up to 20ml) in Dex Group. The

remifentanil(0.05–0.3μg·kg^{-1}·min^{-1}) and propofol (2–6 mg·kg^{-1}·min^{-1}) was continuously intravenous pumped to maintain anesthesia depth (Bispectral Index 40–60). Cisatracurium was administered (0.10 ~ 0.15 mg·kg^{-1}·h^{-1}) to maintain satisfactory muscle relaxation. Vasoactive drugs were used to maintain intraoperative blood pressure and heart rate fluctuations at about 20% of the participants' baseline. The patients were sent back to the ward after surgery and given tramadol 100mg intravenously for analgesia on time according to the degree of postoperative pain.

Statistical analysis

Statistical software SPSS 19.0 and Graphpad Prism7.0 were used to describe and analyze the statistical results with significance determined at a value of $P < 0.05$.

Results

Baseline characteristics

180 patients were enrolled in this trial, 4 cases had the surgical process converted to open laparotomy, 2 cases were discontinued due to the tumor extensive abdominal metastasis, and 5 cases were sent to intensive care unit. So, 169 cases (84 cases in Control Group and 85 cases in Dex Group) were finally completed in this study. There were no significant baseline differences between those two groups (Table 1).

Table 1
Comparison of basic conditions. Chi-square test / T test.

	Control Group (n = 84)	Dex Group (n = 85)	t/χ2	*P*
Patient characteristics Age(yr)	63.61 ± 7.08	62.16 ± 6.68	1.37	0.171
Weight (kg)	59.65 ± 10.22	62.00 ± 10.29	− 1.49	0.139
BMI ($kg.m^{-2}$)	23.00 ± 3.62	23.16 ± 3.33	− 0.312	0.755
MMSE(min)	25.77 ± 1.31	25.88 ± 2.522	0.253	0.80
Sex (female/male)	34/50	27/58	1.39	0.238
Education Background			1.92	0.383
illiteracy	5(6.0)	8(9.4)		
primary	51(60.7)	56(65.9)		
≥ junior	28(33.3)	21(24.7)		
ASA Score Physical Status (I/II/III)	9/56/19	6/50/29	3.017	0.221
Operation history(yes/no)	16/68	24/61	1.97	0.16

Intra-operative Findings

There were no significant differences in operation type, surgery and anesthesia time, consumption of sufentanil, fluid intake, urine volume and blood loss between the two groups (P > 0.05). However, the consumption of propofol and remifentanil in Dex Group was significantly lower than that in Control Group ((0.82 ± 0.33) g vs. (1.22 ± 0.42) g, (1.17 ± 0.40)mg vs. (1.48 ± 0.60)mg, P < 0.05) (Table 2).

Table 2
Comparison of intra-operative findings. Chi-square test/T Test.

	Control Group (n = 84)	Dex Group (n = 85)	t/χ2	*P*
Operation type□/□	56/28	53/32	1.47	0.4793
Surgery time(h)	4.05 ± 1.09	4.27 ± 1.16	-1.318	0.189
Anesthesia time(h)	4.79 ± 1.11	4.99 ± 1.12	-1.196	0.233
Propofol (g)	1.22 ± 0.42	0.82 ± 0.33	6.77	0.000*
Sufentanil (μg)	26.23 ± 4.17	27.24 ± 4.67	-1.49	0.138
Remifentanil (mg)	1.48 ± 0.60	1.17 ± 0.40	3.87	0.001*
Fluid intake(ml)	2094.04 ± 533.87	2089.17 ± 545.16	0.058	0.95
Urine(ml)	429.52 ± 164.52	465.74 ± 208.48	-1.25	0.212
Blood loss(ml)	216.19 ± 138.04	244.23 ± 161.41	-1.21	0.22
□=Laparoscopic radical resection of colon cancer;□=Laparoscopic radical resection				

of rectal cancer ; *There was a statistically significant difference between the two

groups (P < 0.05).

Postoperative Situation

postoperative pain

There was no significant difference in VAS pain scores between the two groups at 3days and 7days after surgery (P > 0.05), while VAS pain scores of Dex Group at 6 hours and 24 hours after surgery were significantly lower than those of Control Group (P < 0.05) (Fig. 1).

Primary outcome: the incidence of PND

There were some patients in both groups suffered from PND within 30days after surgery. In terms of the incidence of PND, compared with the Control Group, there was no significant differences at 3days and 7days (P > 0.05), but significantly decreased at 6hours, 24days and 30days after surgery in Dex Group (7.1% vs.17.9%, 4.7% vs.14.3%, 3.5% vs. 11.9%, P < 0.05)(Table 3).

Table 3
The incidence of PND in different time after surgery.

	Control Group (n = 84)	Dex Group (n = 85)	χ2	*P*
6h	15(17.9)	6(7.1)	4.527	0.033*
24h	12(14.3)	4(4.7)	4.524	0.033*
3day	7(8.3)	3(3.5)	0.995	0.319
7day	6(7.1)	2 (2.4)	1.220	0.270
30day	10(11.9)	3(3.5)	4.170	0.041*
* There was a statistically significant difference between the two groups (P < 0.05).				

Discussion

Perioperative Neurocognitive Disorders (PND) is a common neurological complication after surgery and anesthesia, mainly manifests as cognitive impairment. Advanced age, education level, preoperative complications, duration of surgery/anesthesia, surgical stimulation and anesthesia drugs are high risk factors of PND (Daiello et al.2019; Sanders et al.2011; Olesen et al.2015; Zhen et al.2009; Nagai et al.2017). Some researches have found that intraoperative general anesthesia may impair neurocognitive function of patients. Therefore, it is our goal to reduce the consumption of general anesthetics as much as possible. Professor Brummett (Brummett et al.2011) found that dexmedetomidine added to ropivacaine for perineural nerve block can prolongs the duration of analgesia and enhance the analgesic efficacy of ropivacaine. So, we wondered whether this effect could reduce the consumption of general anesthesia during surgery and thus reduce the incidence of postoperative cognitive impairment.

The differences between the two groups were the consumption of general anesthetics (propofol and remifentanil) during operation, the degree of postoperative pain and the incidence of PND. Firstly, the consumption of propofol and remifentanil in the Dex Group was significantly lower than that in the Control Group (Table 2). We shared professor Brummett's view (Brummett et al.2011) that dexmedetomidine added to ropivacaine for TAPB before surgery enhanced the analgesic efficacy of ropivacaine which helped reduce the consumption of propofol and opioid. Another reason we speculated is that the dexmedetomidine in the Dex Group may be slowly absorbed into blood to produce analgesic and sedative effects, and those effects were likely to be more enduring than dexmedetomidine used continuously intravenous pumping. But it is just our guess, we require further dynamic monitoring of the concentration of dexmedetomidine in the blood and compare the effects of dexmedetomidine used in different ways on analgesia. Secondly, VAS pain scores of the Dex Group were significantly lower than those of the Control Group overall (Fig. 1). Several studies conclude that dexmedetomidine added to ropivacaine can block the hyperpolarization-activated cation current and mediate pain signal transduction pathway (Brummett et al.2011; Esmaoglu et al.2010). And finally, all in all, the incidence of

PND in the Dex Group was significantly lower than that in the Control Group. We analyze the possible reasons as follows: analgesic effect: Postoperative pain is an independent predictor of postoperative cognitive impairment (Vaurio et al. 2006), especially postoperative delirium. Some researches suggest that the release of various inflammatory factors is associated with postoperative pain, which may participate in the pathogenesis of neurocognitive impairment after surgery(Wick and Grant,2017; Ocalan et al. 2015). Reduce the consumption of propofol and remifentanil: At present, some scholars believe that opiates play an important role in the occurrence of PND (Pandharipande et al.2007; Alldred.2011). However, the mechanism is still unclear. While, the effect of propofol on postoperative cognitive function remains controversial: some researchers suggest that propofol can maintain natural sleep-wake cycle which may beneficial to reduce postoperative neurocognitive damage(Laalou et al.2010). But Another opinion is that propofol has the potential to induce postoperative neurocognitive damage (Goswami and Babbar. 2015). So, we need further researches to confirm these findings. The effect of dexmedetomidine: dexmedetomidine as a α_2-adrenergic agonist has a good analgesic and sedative activity. At present, a large number of reports have proved that dexmedetomidine, as a maintenance agent for general anesthesia, can reduce the incidence of postoperative cognitive POCD in patients undergoing cardiac surgery and non-cardiac surgery (Duan et al. 2018; Hilliard et al. 2015). Regrettably, however, a few studies have researched the effect of dexmedetomidine added to local anesthetic for peripheral nerve block on postoperative cognitive. In the end, we found that it is worth noting that the differences in the incidence of PND between the two groups were mainly shown at 6hours, 24hours and 30days after surgery. The differences in the incidence of PND in the early postoperative stage between the two groups were mainly related to the intensity of postoperative pain and the efficacy of TAPB analgesia. Postoperative pain in patients undergoing abdominal surgery mainly occurs in about 8h ~ 16h after surgery, while dexmedetomidine added to ropivacaine has sensory block durations about 613.34 ± 165.404 min (Wang et al. 2017). On the 30th day after surgery, the incidence of PND showed a difference again, indicating that the change of postoperative cognitive function was reversible. However, Whether this reversibility change influenced by other factors and the mechanism of this reversible change remains to be further studied.

Conclusions

Our single centre randomized controlled trial shows that dexmedetomidine added to ropivacaine for TAPB can reduce the incidence of PND within 30days after surgery, which may be related to reduce the consumption of general anesthetics and provide satisfactory postoperative analgesia.

Abbreviations

ADL Activity daily living

BMI Body mass index

ICU Intensive care unit

MMSE Mini-mental state examination

PND Perioperative neurocognitive disorders

POCD Postoperative cognitive dysfunction

TAPB Transversus abdominis plane block

VAS Visual analog pain scores

Declarations

Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

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DS Y was responsible for the review of the research process. XQ C and RF X completed the data collection and collation. ZL L and SW finished statistical analysis. LY was responsible for the writing of the manuscript. All authors read and approved the final manuscript.

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Ethics declarations

This research was approved by the Ethics Committee of The Second People's Hospital of Yibin City(ClinicalTrials.gov Identifier: 2019-015-01).

Consent for publication

Not applicable.

Competing interests

No competing interests.

References

1. Evered L, Silbert B, Knopman DS, et al. Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery-2018[J].British journal of anaesthesia,2018,121(5):1005–1012.
2. Telugu SD, SriSha VD, PuniTh k, et al. Post-operative cognitive functions after general anesthesia with sevoflurane and desflurane in South Asian elderly [J]. Middle East J Anesthesiol. 2013;22(2):143–8.
3. Kok WF, Koerts J, Tucha O, et al. Neuronal damage biomarkers in the Identification of patients at risk of long-term postoperative cognitive dysfunction after cardiac surgery[J]. Anaesthesia. 2017;72(3):359.
4. Hsiao-Chien T, Takayuki Y, Tai-Yuan C, et al. Transversus Abdominis Plane Block:An Updated Review of Anatomy and Techniques[J]. Biomed Res Int. 2017;2017(01):1–12.
5. Petersen PL, Mathiesen O, Torup H, et al. The transversus abdominis plane block: a valuable option for postoperative analgesia? A topical review[J]. Acta Anaesthesiol Scand. 2010;54(5):529–35.
6. Li Y, He R, Chen S, et al. Effect of dexmedetomidine on early postoperative cognitive dysfunction and peri-operative inflammation in elderly patients undergoing laparoscopic cholecystectomy [J]. Exp Ther Med. 2015;10(5):1635–42.
7. Hebbard P, Fujiwara Y, Shibata Y, et al. Ultrasound-guided transversus abdominis plane (TAP) block [J]. Anaesth Intensive Care. 2007;35(4):616–7.

8. Daiello LA, Racine AM, Yun Gou R, et al. Postoperative delirium and postoperative cognitive dysfunction: Overlap and divergence. Anesthesiology. 2019;131:477–91.
9. Sanders RD, Pandharipande PP, Davidson AJ, et al.Anticipating and managing postoperative delirium and cognitive decline in adults.BMJ,2011,343(11): d4331.
10. Olesen SS, Khodayari-Rostamabad A, Graversen C, et al. Disruption of cortical connectivity during remifentanil administration is associated with cognitive impairment but not with analgesia[J]. Anesthesiology. 2015;122(1):140–9.
11. Zhen Y, Dong Y, Wu X, et al. Nitrous Oxide Plus Isoflurane Induces Apoptosis and Increases β-Amyloid Protein Levels[J]. Anesthesiology. 2009;111(4):741–52.
12. Nagai H, De VL, Bellesi M, et al. Sleep Consolidates Motor Learning of Complex Movement Sequences in Mice [J].Sleep,2017,40(2):1–15.
13. Brummett CM, Hong EK, Janda AM, et al. Perineural Dexmedetomidine Added to Ropivacaine for Sciatic Nerve Block in Rats Prolongs the Duration of Analgesia by Blocking the Hyperpolarization-activated. Cation Current[J] Anesthesiology. 2011;115(4):836–43.
14. Esmaoglu A, Yegenoglu F, Akin A, et al. Dexmedetomidine added to levobupivacaine prolongs axillary brachial plexus block[J]. Anesthesia & Analgesia, 2010, 111(6):pp. 1548–51.
15. Vaurio LE, Sands LP, Wang Y, et al. Postoperative Delirium: The Importance of Pain and Pain Management[J] Anesthesia & Analgesia. 2006;102(4):1267–73.
16. Wick EC, Grant MC, Wu CL. Postoperative multimodal analgesia pain management with nonopioid analgesics and techniques:A Review[J]. JAMA Surg. 2017;152(7):691–7.
17. Ocalan R, Akin C, Disli ZK, et al. Preoperative anxiety and postoperative pain in patients undergoing septoplasty[J]. BENT. 2015;11(1):19–23.
18. Pandharipande PP, Pun BT, Herr DL, et al. Effect of sedation with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients: the MENDS randomized controlled trial[J]. J Am Med Association. 2007;298(22):2644–53.
19. Alldred DP. Avoid benzodiazepines and opioids in people at risk of delirium [. J] Evidenc-Based Nursing. 2011;14(3):75–6.
20. Laalou FZ, Egard M, Guillot M, et al. Influence of preoperative cognitive status on propofol requirement to maintain hypnosis in the elderly[J]. British journal of anaesthesia,2010,105(3):342–346.
21. Goswami U, Babbar S, Tiwari S. Comparative evaluation of the effects of propofol and sevoflurane on cognitive function and memory in patients undergoing laparoscopic cholecystectomy:A randomised prospective study[J]. Indian J Anaesth. 2015;59(3):150–5.
22. Duan X, Coburn M, Rossaint R, et al. Efficacy of perioperative dexmedetomidine on postoperative delirium: systematic review and meta-analysis with trial sequential analysis of randomised controlled trials[J]. Br J Anaesth. 2018;121(2):384–97.

23. Hilliard N, Brown S, Mitchinson S. A case report of dexmedetomidine used to treat intractable pain and delirium in a tertiary palliative care unit[J]. Palliat Med. 2015;29(3):278–81.
24. Wang X, Yu F, Li K. Which is the better adjuvant to ropivacaine in brachial plexus block: Dexmedetomidine or morphine? A prospective, randomized, double-blinded, comparative study[J]. Int J Clin Exp Med. 2017;10(7):10813–9.

Figures

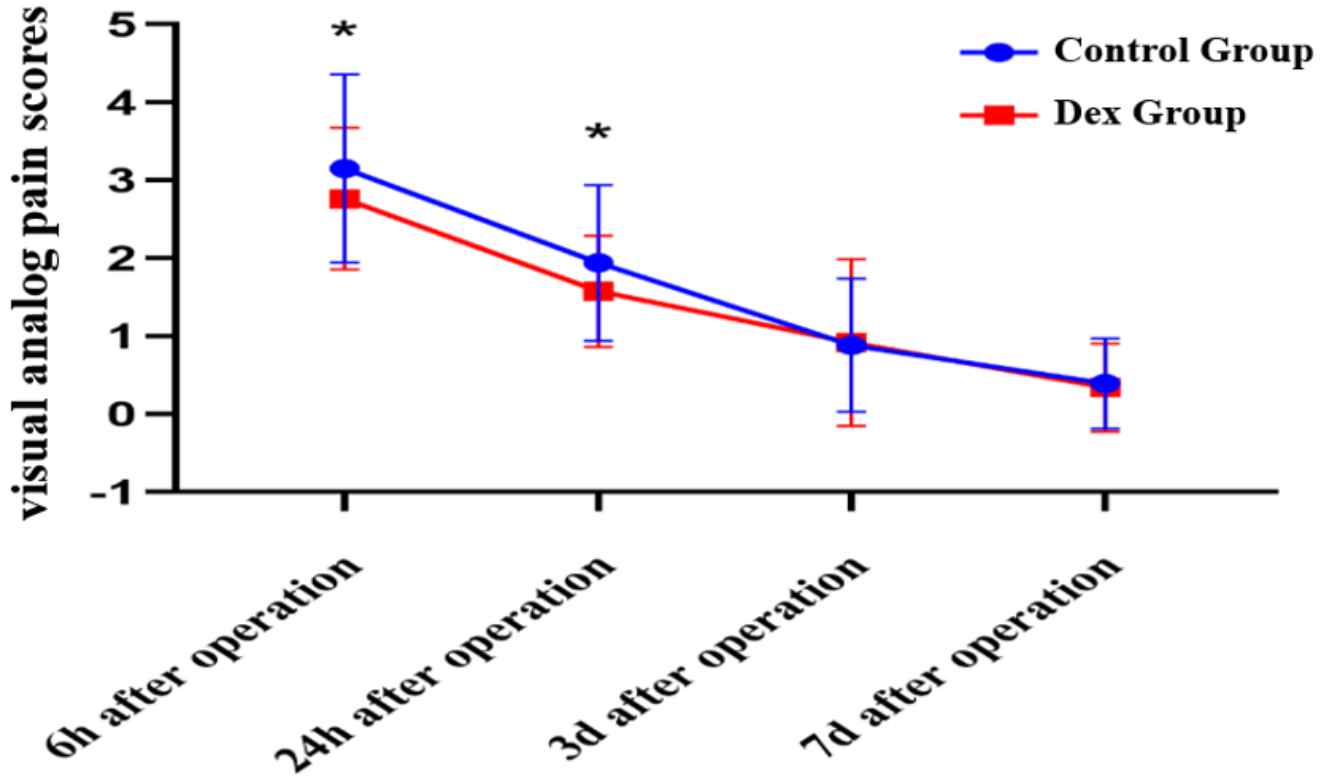

Figure 1

visual analog pain scores (VAS) at rest after surgery. Median VAS pain scores 0-10/10 with inter-quartile range (IQR). *****There was a statistically significant difference between the two groups (P<0.05).