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Research Article

Effects of Dexmedetomidine on Oxidative Stress, Inflammatory Response, Coagulation Function and Hemodynamics in Patients Undergoing Hysterectomy

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Abstract

Objective To investigate the effects of dexmedetomidine on oxidative stress, inflammatory response, coagulation function and hemodynamics in patients undergoing hysterectomy. *Methods* 92 patients who underwent hysterectomy in our hospital from January to September 2023 were selected as subjects. According to the difference in anesthesia, 46 patients were in the control group and 46 in the dexmedetomidine group. Patients in the control group received midazolam anesthesia, and patients in the dexmedetomidine group received dexmedetomidine anesthesia. The changes of oxidative stress, inflammatory response, coagulation function and hemodynamics were compared between T0 (before anesthesia), T1 (10 min after anesthesia), T2 (after extubation) and T3 (24 h after surgery). *Results* At T0, there was no significant difference in T-AOC, GSH-Px, MBP, MCP-1, AT III, FDP, MAP and SpO_2 between the two groups ($P>0.05$). At the time of T1, T2 and T3, the two groups of patients T-AOC, GSH-Px were all lower than T0 ($P<0.05$), MBP and MCP-1 were all higher than T0 ($P<0.05$). The levels of T-AOC and GSH-Px in the dexmedetomidine group were significantly higher than those in the control group ($P<0.05$). The levels of MCP-1 was significantly lower than that of the control group ($P<0.05$). At the T1 and T2, ATIII levels was lower than T0 ($P<0.05$), and FDP levels was higher than T0 ($P<0.05$). At the time of T3, the levels of ATIII and FDP in the dexmedetomidine group recovered to the normal level of T0. There was no significant change in MAP and SpO_2 at each time in the dexmedetomidine group ($P>0.05$). *Conclusion* Dexmedetomidine can more effectively alleviate the oxidative stress response in patients with hysterectomy, reduce the symptoms of inflammation in patients, improve the coagulation status of patients and have less influence on hemodynamics, and have high clinical value.

Keywords

Dexmedetomidine, Total Hysterectomy, Oxidative Stress, Inflammatory Response, Coagulation, Hemodynamics

1. Introduction

Hysterectomy is common in obstetrics and gynaecology. But patients often have more inflammation and blood clotting after surgery. This is because of pain and tug reflexes from the operation. It can lead to problems like blood clotting issues, thrombosis after surgery, and bleeding. It also makes it harder for the body to recover after surgery [1, 2]. Relevant studies

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have indicated that anaesthesia mode is closely related to postoperative recovery [3]. Dexmedetomidine is a new type of α2 adrenergic receptor agonist with high selectivity, analgesia, anxiolysis and other effects, which may have advantages in improving the stress response and hypercoagulability in total hysterectomy patients [4]. Therefore, this study will investigate the effects of dexmedetomidine on oxidative stress, inflammatory response, coagulation and haemodynamics in total hysterectomy patients.

2. Patients and Methods

This randomized controlled study was conducted in Deyang people's hospital from January to September 2023. The study was approved by the Hospital's Ethics Committee and written informed consent was obtained from all subjects participating in the trial.

In the study, patients who were treated with total hysterectomy in our hospital, aged 30-62 years old, with ASA grading of I-II, and had not taken hormonal drugs recently were included. Exclusion criteria: patients with combined neurological, endocrine system and coagulation diseases, patients with cardiovascular diseases such as concomitant hypertension, bradycardia, atrioventricular block, hypovolemia, patients with severe hepatic and renal insufficiency, patients with contraindications or allergies to the drugs used in this study.

Computer generated sequence was used for randomization at 1:1 ratio. Group assignment was concealed inside sequentially numbered opaque envelopes which were opened before anaesthesia. Patients in both groups underwent epidural anaesthesia, and 30 min before anaesthesia, patients were injected with 100mg of sodium phenobarbital (Tianjin Jin Yao Pharmaceutical Co., Ltd., China Pharmaceutical License H12020381) and 0.3mg of scopolamine (Shandong Weifang Pharmaceutical Factory Co., Ltd., China Pharmaceutical License H20058488) intramuscularly, and patients were monitored for their heart rates, blood pressures, oxygen saturation and other vital indications; patients were placed in internal jugular veins, and patients received 10mL/kg of compound sodium chloride (Zhejiang Maoyuan Pharmaceutical Co., Ltd.) using conventional nasal catheters. Vital signs; patients were placed in the internal jugular vein, patients received compound sodium chloride (Zhejiang Maoyuan Pharmaceutical Co., Ltd., State Drug Permit H33021931) 10mL/kg, and conventional nasal catheter was used for oxygen inhalation; patients were placed in the left position, and the doctor chose the L2-3 vertebral space for the epidural puncture. After a successful puncture, the lumbar needle was put in through the epidural needle and pierced the arachnoid membrane. After some fluid flowed out, the patient got cerebrospinal fluid injected. Then, more fluid from the brain was given to the patient. After the cerebrospinal fluid flowed out, the patient was injected with 2mL of a mixture of 2mL of 0.75% bupivacaine (Shanghai Hefeng Pharmaceutical Co., Ltd., State Pharmaceutical Permit H31022840) + 1mL of 10.0% glucose solution; an epidural catheter was placed at the head end of the patient for 3~4cm, and the speed of infusion, the patient's position, or the amount of epidural anaesthesia drugs were adjusted according to the patient's blood pressure level, so as to make the patient's anaesthesia level controlled at the $T_{5\sim6}$ level. Fifteen minutes before skin cutting, patients in the control group were injected with midazolam (Yichang Renfu Pharmaceutical Co., Ltd., State Drug Permit H20067040) 0.03 mg/kg, and patients in the dexmedetomidine group were injected with dexmedetomidine (Jiangsu Hengrui Medicine Co., Ltd., State Drug Permit H20090248) at a constant speed (200 μg/2mL dexmedetomidine + 48mL 0.9% sodium chloride solution), which was formulated as 4 μg/mL of dexmedetomidine and 0.9% sodium chloride solution (200μg/2mL dexmedetomidine + 48mL 0.9% sodium chloride solution), ensuring that the injection was completed within 10min.

The changes of oxidative stress, inflammatory response, coagulation function and haemodynamics in T0 (before anaesthesia), T1 (10min after anaesthesia), T2 (after extubation) and T3 (24 h after surgery) were compared and analysed between the two groups. 2mL of peripheral venous blood was drawn from patients at each moment, centrifuged (3000r/min, 15min, centrifugation radius 10cm), and the supernatant was removed and placed in the refrigerator at -80 ℃ for measurement. Oxidative stress: total antioxidant capacity (T-AOC) and glutathione peroxidase (GSH-Px) of the patients were detected using a fully automated biochemical analyser (Beckman Coulter, USA, model AU5800). Inflammatory factors: patients' fluid myelin basic protein (MBP) and monocyte chemotactic protein-1 (MCP-1) were detected by immunosorbent assay; MBP and MCP-1 kits were provided by Shanghai Research and Development Biochemical Reagent Company Limited, and the detection steps were carried out in strict accordance with the instructions. Coagulation function: Antithrombin (AT) III and fibrin degradation product (FDP) levels were measured by enzyme-linked immunosorbent assay in both groups. Haemodynamics: mean arterial pressure (MAP) and oxygen saturation (SpO_2) levels were detected with the aid of a non-invasive haemodynamic monitor (Myriad, China, model PM-9000) in both groups.

Statistical package for social science (SPSS) software, version 26 for Microsoft Windows (IBM Corp., Armonk, NY) was used for data analysis. Categorical data were presented as frequency (%) and were analysed by the Chi-square test. Continuous data were checked for normality using the Shapiro-Wilk test and were presented as mean ± standard deviation or median (quartiles) as appropriate. Continuous data were analysed using the unpaired t-test or the Mann Whitney test according to normality of the data. A *P*-value less than 0.05 was considered statistically significant.

3. Results

100 patients were assessed for eligibility, 8 patients were excluded for not fulfilling the inclusion criteria, and 92 patients were included and were available for the final analysis (Figure 1).

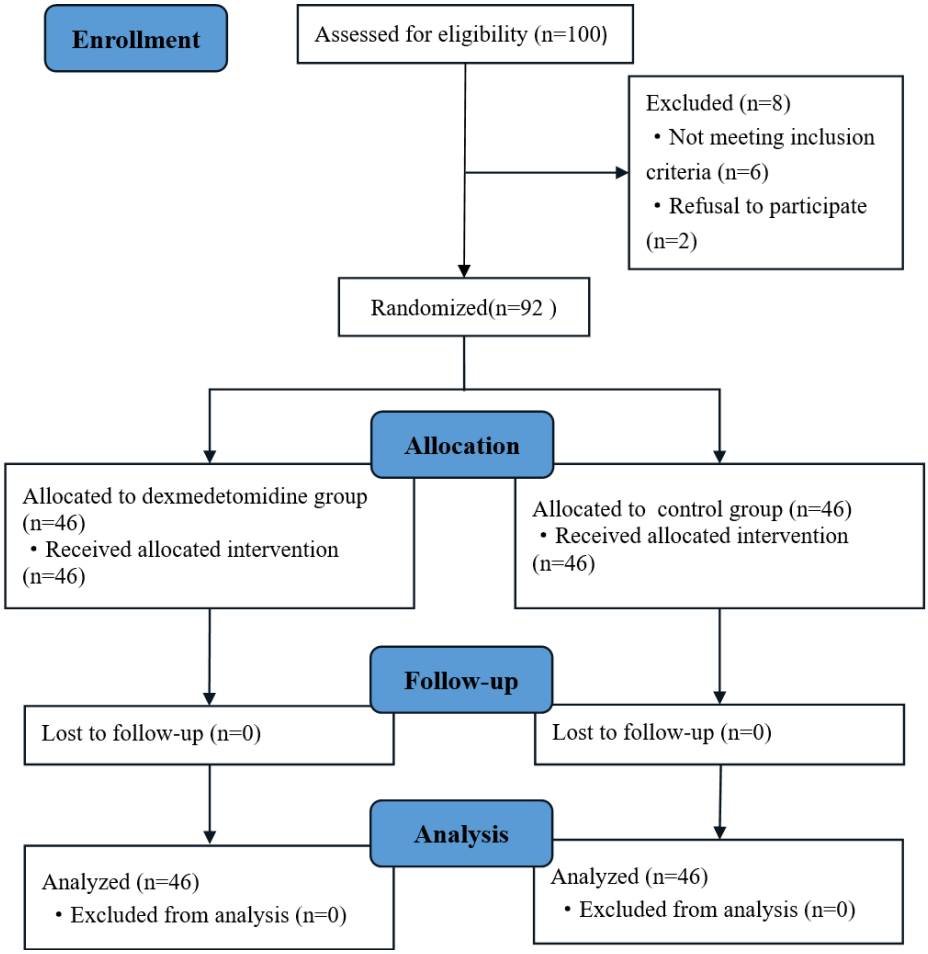

Figure 1. *Consort's flow chart.*

Control group age 30~60 years old; weight 45~65kg, height 155.5~168.2cm, operation time 50~68min; including 26 cases of ASA grade I, 20 cases of ASA grade II. Dexmedetomidine group Age 31~62 years old; weight 45.5~64kg, height 156~167.5cm, operation time 51~70min; of which 25 cases of ASA Grade I, 21 cases of ASA Grade II. There was no significant difference between the two groups of total hysterectomy patients in terms of age, height, weight, operation time, and ASA grade ($P > 0.05$).

At the moment of T0, there was no statistically significant difference in the comparison of T-AOC and GSH-Px between the two groups ($P>0.05$); at the moments of T1, T2, and T3, T-AOC and GSH-Px were lower than that at the moment of T0 in both groups ($P<0.05$), in which the patients in the dexmedetomidine group had T-AOC and GSH-Px [T1: (5.26±0.56) U/mL, (26.44±3.11) U/mL; T2: (7.14±0.82) U/mL, (36.87±3.32) U/mL; T3: (8.24±0.81) U/mL, (45.22±5.53) U/mL] were significantly higher than those in the control group [T1: (3.89±0.47) U/mL, (22.26± 2.18) U/mL; T2: (5.11±0.64) U/mL, (32.86±2.57) U/mL; T3: (6.18±0.69) U/mL, (38.26±3.87) U/mL] ($P<0.05$), Table 1.

Table 1. *Comparison of oxidative stress indices.*

Outcomes	Group	T0	T1	T2	T3
T-AOC (U/mL)	Control group	8.79±0.29	3.89±0.47*	5.11±0.64*	6.18±0.69*
	Dex group	8.82±0.52	5.26±0.56*#	7.14±0.82*#	8.24±0.81*#

Outcomes	Group	T0	T1	T2	T3
GSH-Px (U/mL)	Control group	48.37±5.58	22.26±2.18*	32.86±2.57*	38.26±3.87*
	Dex group	48.30±4.62	26.44±3.11*#	36.87±3.32*#	45.22±5.53*#

Data presented as mean ± standard deviatio, n=46; Dex: Dexmedetomidine, T-AOC:, GSH-Px:, *P<0.05 compared to T0, #P<0.05 compared with control group.

At the moment of T0, there was no statistically significant difference in MBP and MCP-1 between the two groups (P>0.05); at the moments of T1, T2, and T3, MBP and MCP-1 were elevated in both groups compared with the moment of T0 (P<0.05), in which MBP and MCP-1 in patients in the dexmedetomidine group [T1: (1.62±0.31) μg/L, (198.64±28.91) pg/mL; T2: (2.11±0.46) μg/L, (215.64±28.77) pg/mL; T3: (1.92±0.18) μg/L, (233.66±30.14) pg/mL] were significantly lower than those in the control group [T1: (1.74±0.38) μg/L, (263.72±30.45) pg/mL; T2: (2.97±0.56) μg/L, (422.75±32.17) pg/mL; T3: (2.82±0.47) μg/L, (524.28±42.73) pg/mL] (P<0.05), Table 2.

Table 2. *Comparison of inflammatory index changes.*

Outcomes	Group	T0	T1	T2	T3
MBP (μg/L)	Control group	0.98±0.16	1.74±0.38*	2.97±0.56*	2.82±0.47*
	Dex group	0.95±0.17	1.62±0.31*#	2.11±0.46*#	1.92±0.18*#
MCP-1 (pg/mL)	Control group	145.87±25.92	263.72±30.45*	422.75±32.17*	524.28±42.73*
	Dex group	146.12±25.89	198.64±28.91*#	215.64±28.77*#	233.66±30.14*#

Data presented as mean ± standard deviation, n=46; Dex: Dexmedetomidine, MBP:, MCP-1:, *P<0.05 compared to T0, #P<0.05 compared with control group.

At the moment of T0, there was no statistically significant difference in AT III and FDP between the two groups of patients (P>0.05); at the moments of T1 and T2, AT III of the two groups of patients was lower than that at the moment of T0 (P<0.05), and FDP was higher than that at the moment of T0 (P<0.05); at the moment of T3, the patients in the dexmedetomidine group had their AT III and FDP restored to the normal level at the moment of T0, but AT III and FDP of patients in the control group still differed significantly from those at the moment of T0 (P<0.05); AT III of patients in the dexmedetomidine group was significantly higher than that of the control group at the moments of T1, T2, and T3 [T1: (93.14±7.88)%; T2: (80.21±7.26)%; and T3: (103.96±10.17)%] [T1: (82.03±7.26)%; T2: (64.13±7.09)%; T3: (85.44±8.20)%] (P<0.05), and FDP [T1: (5.93±1.44) μg/mL; T2: (21.22±3.49) μg/mL; T3: (4.08±1.18) μg/mL] were significantly lower than the control group [T1: (8.16±1.49) μg/mL; T2: (39.16±6.73) μg/mL; T3: (8.13±1.62) μg/mL] (P<0.05), Table 3.

Table 3. *Comparison of Coagulation function Indexes.*

Outcomes	Group	T0	T1	T2	T3
AT III (%)	Control group	105.57±9.08	82.03±7.26*	64.13±7.09*	85.44±8.20*
	Dex group	105.62±9.11	93.14±7.88*#	80.21±7.26*#	103.96±10.17#
FDP (μg/mL)	Control group	4.03±1.18	8.16±1.49*	39.16±6.73*	8.13±1.62*
	Dex group	4.04±1.19	5.93±1.44*#	21.22±3.49*#	4.08±1.18#

Data presented as mean ± standard deviation n=46; Dex: Dexmedetomidine, AT III:, FDP:, *P<0.05 compared to T0, #P<0.05 compared with control group.

At the moment of T0, there was no difference in the comparison of MAP and SpO_2 between the two groups (P>0.05); at the moments of T1 and T2, the MAP of the control group patients was significantly higher than that at the moment of T0 (P<0.05), and the SpO_2 was significantly lower than that at the moment of T0 (P<0.05); and at the moments of T1 and T2, the MAP of the control group patients [T1: (96.32±11.89) mmHg; T2: (97.11±12.06) mmHg] was higher than the level of MAP [T1: (85.73±11.11) mmHg; T2: (85.92±11.04) mmHg] in the dexmedetomidine group during the same period (P<0.05); the patients' SpO_2 [T1: (92.44±1.41)%; T2: (92.24±1.37)%] was lower than the level of SpO_2 [T1: (95.52±1.38)%; T2: (96.02±1.43)%] in the dexmedetomidine group during the same period (P<0.05). At the moment of T3, MAP and SpO_2 of patients of the two groups were restored to the normal level at the moment of T0; the patients in the dexmedetomidine group did not have any difference of MAP and SpO_2 at each moment. MAP and SpO_2 did not change significantly (P > 0.05); Table 4.

Table 4. *Comparison of hemodynamic changes.*

Outcomes	Group	T0	T1	T2	T3
MAP (mmHg)	Control group	84.81±10.97	96.32±11.89*	97.11±12.06*	85.14±11.18
	Dex group	85.02±10.94	85.73±11.11#	85.92±11.04#	85.66±11.09
SpO_2 (%)	Control group	95.33±1.22	92.44±1.41*	92.24±1.37*	95.29±1.31
	Dex group	95.41±1.27	95.52±1.38#	96.02±1.43#	95.39±1.28

Data presented as mean ± standard deviation n=46; Dex: Dexmedetomidine, MAP:, SpO_2:, *P<0.05 compared to T0, #P<0.05 compared with control group.

4. Discussion

Since patients in gynaecological total hysterectomy often need to establish carbon dioxide (CO_2) pneumoperitoneum, patients are prone to sympathetic excitation after absorbing CO_2, which affects blood circulation and ultimately causes serious adverse effects on patients' physiological functions [5, 6]. Therefore, the stable condition of patients' vital signs during and after general anaesthesia for obstetrics and gynaecology surgery has received more and more attention from anaesthesia medical personnel. According to relevant studies [7, 8], adopting appropriate anaesthesia methods and selecting appropriate anaesthetic drugs are of great significance in reducing the stress response of patients during anaesthesia and surgery. Dexmedetomidine is a highly selective α2 adrenergic receptor agonist with strong analgesic, sedative, anxiolytic, and inhibitory sympathetic activity effects, and its advantages in stabilising haemodynamics and reducing oxidative stress during total hysterectomy are becoming more and more prominent [9].

Oxidative stress is a non-specific defence response of the patient's organism to external stimuli, and it is also one of the main causes of complications during anaesthesia, which has always been one of the most important concerns of medical personnel in surgery. Anaesthesia and surgery can cause increased stress response and damage to the patient's organism, and even increase the incidence of perioperative complications and the difficulty of postoperative recovery [10]. There are many factors in the serum that can visually reflect the degree of oxidative stress in patients, including GSH-Px, a peroxidative enzyme with a wide range of content in the body, which can convert toxic peroxides into non-toxic hydroxyl compounds, and has a protective effect on the structure of cell membranes [11], and T-AOC, which represents the total level of enzyme and non-enzymatic antioxidants in the body of the patient, whose level can directly show how active the patient's antioxidant system is and indirectly tell us about the activity of their body's antioxidant system. It also gives us a hint about the level of lipid peroxidation damage in patients. The results of this study showed that the T-AOC and GSH-Px of patients in both groups at T1, T2 and T3 were lower than those at T0, and the T-AOC and GSH-Px of patients in the dexmedetomidine group were significantly higher than those in the control group, suggesting that dexmedetomidine has a positive significance in alleviating the oxidative stress damage of patients. This is because dexmedetomidine can effectively reduce the secretion of stress hormones through effective sympathetic inhibition, which in turn effectively reduces the stress injury of patients and provides positive conditions for patients' postoperative recovery.

Surgical trauma and anaesthesia not only cause patients to experience oxidative stress, but also easily cause a dramatic increase in the production of inflammatory factors, resulting in a state of microinflammation throughout the body, and a persistent microinflammatory state is very likely to cause patients to experience a persistent postoperative inflammatory

response, leading to infections and other complications, which have a negative impact on the patient's prognosis [12]. MCP-1 is a chemokine that binds to receptors, adsorbs and chemotaxis monocytes, regulates monocyte reorganisation, and regulates the production of inflammatory factors [13]. The results of this study found that the MBP and MCP-1 of both groups of patients at the moment of T1, T2 and T3 were significantly higher than at the moment of T0, and the MBP and MCP-1 of patients in the dexmedetomidine group were significantly lower than those in the control group. It is suggested that dexmedetomidine applied in total hysterectomy can effectively reduce the early postoperative inflammatory reaction of patients, which is more conducive to the early recovery of patients after surgery. The reason may be related to the inhibition of the release of catecholamines, cortisol and other mediators by dexmedetomidine.

In addition, due to the presence of more blocking fibrinogen activator in the uterus, when patients undergo total hysterectomy, it is easy to cause the release of tissue fibrinogen activator in the damaged tissues of the patients to the blood, which activates fibrinogen and causes the hypercoagulable state of the patient's blood; or due to the surgical operation to form a large area of tissue hypoxia, ischemia and injury, which leads to the release of tissue factors, destroys blood cells, and then releases the coagulant-promoting activity. FDP is the hallmark product of hyperfibrinolysis, and its expression in the patient's blood can directly reflect the severity of the patient's hyperfibrinolysis; AT III has a higher consumption in the patient's prolonged hyperfibrinolysis, which can reflect the patient's hyperfibrinolysis lifting situation [14-17]. Therefore, this study investigated the effects of dexmedetomidine on AT III and FDP levels in patients with total hysterectomy. The results of this study found that the AT III of patients in both groups at the moments of T1 and T2 were lower and the FDP was higher than that at the moment of T0, and the AT III and FDP of patients in the dexmedetomidine group at the moment of T3 were restored to the normal level at the moment of T0, and the patients' AT III at the moments of T1, T2, and T3 were significantly higher than that of the control group, and the FDP was significantly lower than that of the control group; The similarity with the findings of dexmedetomidine applied in total hysterectomy can effectively avoid the patients from developing hypercoagulable state of blood, which is more conducive to the recovery of patients' physiological functions after surgery. The reason for this may be that dexmedetomidine has the intervention effect of sympathetic nerve block during total hysterectomy anaesthesia, which can promote the blood flow of the patients, and is more conducive to avoiding hypercoagulability of blood.

In addition, in this study, during the observation of hemodynamic changes in patients, it was found that there were no significant changes in MAP and SpO_2 at all moments in patients in the dexmedetomidine group, but MAP in patients in the control group at the T1 and T2 moments was significantly higher than that at the T0 moment, and SpO_2 was significantly lower than that at the T0 moment, and it was higher/lower than that in the dexmedetomidine group at the same period [18]. It suggests that dexmedetomidine has less haemodynamic impact on patients during general anaesthesia in total hysterectomy patients compared to midazolam and is more helpful in maintaining normal vital signs and physiological functions of patients. The reason may be that dexmedetomidine can agonize the central postsynaptic α2 receptor, which can reduce the nerve tension and increase the activity of the vagus nerve, and can also effectively inhibit sympathetic overexcitability and effectively reduce the release of norepinephrine from sympathetic endings, which ultimately makes the patient's haemodynamics before and after anaesthesia to be able to maintain stability.

5. Conclusion

In conclusion, dexmedetomidine applied to patients undergoing total hysterectomy is conducive to ensuring the stability of patients' haemodynamics, better inhibiting the patients' oxidative stress response, reducing the patients' inflammatory symptoms, improving the patients' coagulation function status, and has a high value in clinical application.

Abbreviations

T-AOC: Total Antioxidant Capacity
GSH-Px: Glutathione Peroxi-Dase
MBP: Myelin Basic Protein
MCP-1: Monocyte Chemotactic Protein-1
ATIII: Antithrombin III
FDP: Fibrin Degradation Product
MAP: Mean Arterial Pressure
SpO2: Oxygen Saturation
CO_2: Carbon Dioxide

Conflicts of Interest

No potential conflict of interest was reported by these authors.

References

[1] Shen J, Li L, Jiang L, et al. Effect of dexmedetomidine hydrochloride on H_2O_2-induced oxidative stress and inflammatory response in Kupffer cells [J]. Journal of Central South University, 2016, 41(5): 477-481.

[2] Li Y, Wang B, Zhang L L, et al. Dexmedetomidine Combined with General Anesthesia Provides Similar Intraoperative Stress Response Reduction When Compared with a Combined General and Epidural Anesthetic Technique [J]. Anesthesia & Analgesia, 2016, 122(4): 1202-1210.

[3] Morley RL, Elliott L, Rees J, Rudd S, Mouton R, Hinchliffe RJ. Scoping review of mode of anaesthesia in emergency surgery. Br J Surg. 2020; 107: e17–25.

[4] Vorobeichik L, Brull R, Abdallah F W. Evidence basis for using perineural dexmedetomidine to enhance the quality of brachial plexus nerve blocks: a systematic review and meta-analysis of randomized controlled trials [J]. Br J Anaesth, 2017, 118(2): 167-181.

[5] Faisal M, Schäfer CN, Myrelid P, et al. Effects of analgesic and surgical modality on immune response in colorectal cancer surgery. Surg Oncol. 2021; 38: 101602.

[6] Nishida T, Hayashi T, Inamoto T, et al. Dual Gas Treatment With Hydrogen and Carbon Monoxide Attenuates Oxidative Stress and Protects From Renal Ischemia-Reperfusion Injury [J]. Transplant Proc, 2018, 50(1): 250-258.

[7] Li Y, Dong H, Tan S, et al. Effects of thoracic epidural anesthesia/analgesia on the stress response, pain relief, hospital stay, and treatment costs of patients with esophageal carcinoma undergoing thoracic surgery: a single-center, randomized controlled trial. Medicine (Baltimore) 2019; 98(7): e14362.

[8] Kim N S, Kang K S, Yoo S H, et al. A comparison of oxycodone and fentanyl in intravenous patient-controlled analgesia after laparoscopic hysterectomy [J]. Korean J Anesthesiol, 2015, 68(3): 261-266.

[9] Ülgey, A, Güneş I, Bayram A, et al. The analgesic effects of incisional levobupivacaine with dexmedetomidine after total abdominal hysterectomy. [J]. Erciyes Tip Dergisi, 2015, 37(2): 64-68.

[10] Geng R, Huang X, Li L, et al. Gene expression analysis in endometriosis: Immunopathology insights, transcription factors and therapeutic targets. Front Immunol. 2022; 13: 1037504.

[11] Shu A H, Wang Q, Chen X B. Effect of different depths of anesthesia on postoperative cognitive function in laparoscopic patients: a randomized clinical trial [J]. Curr Med Res Opin, 2015, 31(10): 1883-7.

[12] Takashima H., Maruyama T., Abe M. Significance of Levocarnitine Treatment in Dialysis Patients. Nutrients. 2021; 13: 1219.

[13] Vora K S, Baranda U, Shah V R, et al. The effects of dexmedetomidine on attenuation of hemodynamic changes and there effects as adjuvant in anesthesia during laparoscopic surgeries [J]. Saudi J Anaesth, 2015, 9(4): 386-392.

[14] Karanicolas P J, Lin Y, Tarshis J, et al. Major liver resection, systemic fibrinolytic activity, and the impact of tranexamic acid [J]. HPB, 2016, 18(12): 991-999.

[15] Sinha S K, Sachan M, Goel A, et al. Efficacy and Safety of Thrombolytic Therapy in Acute Submassive Pulmonary Embolism: Follow-Up Study [J]. J Clin Med Res, 2017, 9(2): 163-169.

[16] Acanfora D, Acanfora C, Scicchitano P, et al. Safety and Feasibility of Treatment with Rivaroxaban for Non-Canonical Indications: A Case Series Analysis [J]. Clin Drug Investig, 2016, 36(10): 857-862.

[17] Williams B, Mazzeffi M A, Sanchez P G, et al. Case Report of Severe Antithrombin Deficiency During Extracorporeal Membrane Oxygenation and Therapeutic Plasma Exchange for Double Lung Transplantation [J]. A A Case Rep, 2017, 8(1): 11-13.

[18] Reade M C. Low dose dexmedetomidine for the prophylaxis of perioperative ICU delirium—how much evidence is enough? [J]. J Thorac Dis, 2016, 8(11): 3020-3023.