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右美托咪定对老年骨质疏松合并股骨颈骨折患者术后苏醒质量、定量脑电图和谵妄的影响*

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摘要 目的:探讨右美托咪定(Dex)对老年骨质疏松合并股骨颈骨折患者术后苏醒质量、定量脑电图和谵妄的影响。方法:选择2016年1月-2021年3月期间我院收治的老年骨质疏松合并股骨颈骨折患者97例,将其根据随机数字表法分为对照组(48例)和Dex组(49例),两组均行全髋关节置换术治疗,Dex组麻醉诱导前给予0.5 μg/kg Dex,对照组予以等量生理盐水,观察两组术后苏醒质量、血流动力学变化、定量脑电图频率,记录两组谵妄和麻醉不良反应发生情况。结果:与对照组相比,Dex组呼吸恢复时间、拔管时间、睁眼时间更短($P<0.05$)。两组手术切皮时(T2)~术毕时(T4)时间点心率(HR)均低于麻醉前(T1)时间点,平均动脉压(MAP)均高于T1时间点,组内对比差异有统计学意义($P<0.05$)。Dex组T2~T4时间点HR高于对照组对应时间点,MAP低于对照组对应时间点($P<0.05$)。Dex组术后1d左/右颞区、左/右额区δ波频率低于对照组($P<0.05$)。Dex组术后1d左/右颞区、左/右额区α1波频率高于对照组($P<0.05$)。Dex组术后谵妄发生率低于对照组($P<0.05$)。两组间麻醉不良反应发生率无统计学差异($P>0.05$)。结论:老年骨质疏松合并股骨颈骨折患者手术期间予以Dex,可改善患者术后苏醒质量,且对血流动力学影响较小,可减轻对患者大脑额叶δ、α1波频率的影响,同时降低谵妄的发生率。

关键词: 右美托咪定;老年;骨质疏松;股骨颈骨折;苏醒质量;定量脑电图;谵妄

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Effect of Dexmedetomidine on Postoperative Recovery Quality, Quantitative Electroencephalogram and Delirium in Elderly Patients with Osteoporosis Complicated with Femoral Neck Fracture*

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ABSTRACT Objective: To investigate the effect of dexmedetomidine (Dex) on postoperative recovery quality, quantitative electroencephalogram and delirium in elderly patients with osteoporosis complicated with femoral neck fracture. **Methods:** 97 elderly patients with osteoporosis complicated with femoral neck fracture who were treated in our hospital from January 2016 to March 2021 were selected, they were randomly divided into control group (48 cases) and Dex group (49 cases) by the random number table method. Total hip arthroplasty was performed in both groups, and Dex group was given 0.5 μg/kg Dex before anesthesia induction, and the control group was given the same amount of normal saline. The wake-up quality, hemodynamic changes and quantitative electroencephalogram frequency of the two groups were observed, and the occurrence of delirium and adverse anesthetic reactions were recorded. **Results:** Compared with the control group, the respiratory recovery time, extubation time and eye-opening time in Dex group were earlier ($P<0.05$). The heart rate (HR) at surgical excision of skin (T2)~finish the operation (T4) time point in both groups was lower than that at before anesthesia (T1) time point, and the mean arterial pressure (MAP) was higher than that at T1 time point, the intra-group comparison difference was statistically significant ($P<0.05$). HR at T2~T4 time point in Dex group was higher than that in control group, MAP was lower than that in control group at corresponding time points ($P<0.05$). δ wave frequencies of left frontal region, right frontal region, left temporal region and right temporal region in both groups at 1d after operation were increased compared with those before operation, and the Dex group was lower than the control group ($P<0.05$). The α1 wave frequencies of left frontal region, right frontal region, left temporal region and right temporal region in both groups at 1d after operation decreased compared with those before operation, and Dex group was higher than control group ($P<0.05$). The incidence of postoperative delirium in Dex group was lower than

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that in control group ($P<0.05$). There was no statistical difference in the incidence of adverse anesthetic reactions between the two groups ($P>0.05$). **Conclusion:** Dex is given to elderly patients with osteoporosis complicated with femoral neck fracture during operation, can improve the quality of postoperative recovery without aggravating blood flow fluctuation, alleviate the influence on the δ , $\alpha 1$ wave frequency of the frontal lobe of the patient, and it can reduce the incidence of delirium.

Key words: Dexmedetomidine; Elderly; Osteoporosis; Femoral neck fracture; Recovery quality; Quantitative electroencephalogram; Delirium

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前言

骨质疏松是老年患者常见的骨骼疾病,是以骨组织微结构破坏、骨量低、骨脆性增加为特征的全身性骨病^[1]。股骨颈骨折是老年骨质疏松患者常见的并发症之一,可导致下肢功能障碍^[2]。全髋关节置换术是治疗老年骨质疏松合并股骨颈骨折患者的常用方案之一,但鉴于老年患者多伴有多种原发疾病,且免疫力下降,致使其对手术及麻醉的要求更为严格^[3]。围术期强烈的应激反应可导致循环波动,提高脑损害发生几率^[4]。同时,已有报道表明年龄是术后谵妄发生的危险因素^[5]。因此,合理的选择麻醉药物是老年患者手术顺利进行的前提。右美托咪定(Dex)是近年来各类外科手术中常用的麻醉药物,镇静、镇痛效果确切^[6]。本研究通过观察 Dex 在老年骨质疏松合并股骨颈骨折患者中的应用价值,以期为此类患者麻醉药物的选择提供数据参考。

1 资料与方法

1.1 一般资料

选择 2016 年 1 月 -2021 年 3 月期间我院收治的 97 例老年骨质疏松合并股骨颈骨折患者。纳入标准:① 骨质疏松诊断标准参考《原发性骨质疏松症诊治指南(2011 年)》^[7];② 年龄 ≥ 60 岁;③ 经影像学检查证实为单侧股骨颈骨折;④ 择期拟行全髋关节置换手术;⑤ 意识清晰、可清楚地交流和配合治疗;⑥ 美国麻醉医师协会(ASA)^[8]分级 I-III 级。排除标准:① 术前合并急慢性感染;② 近期服用免疫抑制剂、抗生素等药物者;③ 存在凝血功能障碍者;④ 存在手术禁忌者;⑤ 合并精神疾病者,精神性药物滥用者;⑥ 对麻醉药物存在严重过敏者。研究方案获得我院伦理学委员会批准进行,经患者及其家属知情,且签署了同意书。将其根据随机数字表法分为对照组(48 例)和 Dex 组(49 例),对照组男性 28 例,女性 20 例,年龄 60~74 岁,平均年龄(71.43 ± 1.17)岁;骨折部位:左肢 27 例,右肢 21 例;体质量指数(BMI)17~29 kg/m²,平均(22.08 ± 1.43)kg/m²;ASA 分级:I 级、II 级、III 级例数分别为 19 例、16 例、13 例。Dex 组男性 30 例,女性 19 例,年龄 61~75 岁,平均年龄(71.62 ± 1.38)岁;骨折部位:左肢 27 例,右肢 22 例;BMI 18~31 kg/m²,平均(22.14 ± 1.51)kg/m²;ASA 分级:I 级、II 级、III 级例数分别为 21 例、17 例、11 例。两组性别、年龄、骨折部位、BMI、ASA 分级对比无差异($P>0.05$),具有可比性。

1.2 方法

两组术前 6 h 禁食,3 h 禁饮,患者入室后去枕平卧,常规建立静脉通道,监测生命体征。术前 0.5 h 肌内注射硫酸阿托品注射液(国药准字 H32022466,规格:1 mL:5 mg,厂家:江苏悦

兴药业有限公司)0.01 mg/kg。Dex 组患者于麻醉诱导前经静脉泵注盐酸右美托咪定注射液[国药准字 H20090248,规格:2 mL:200 μ g(按右美托咪定计),厂家:江苏恒瑞医药股份有限公司]0.5 μ g/kg,15 min 注射完毕;对照组给予等剂量生理盐水。注射完毕后,若无明显不良反应,则依次静脉注射 0.2 mg/kg 依托咪酯(国药准字 H32022992,规格:10 mL:20 mg,厂家:江苏恩华药业股份有限公司)、0.8 mg/kg 罗库溴铵注射液(国药准字 H20183106,规格:5 mL:50 mg,厂家:福安药业集团庆余堂制药有限公司)、3 μ g/kg 枸橼酸芬太尼注射液[国药准字 H20123297,规格:2 mL:0.1 mg(以芬太尼计),厂家:国药集团工业有限公司廊坊分公司]行麻醉诱导,气管插管后连接麻醉机行间歇正压通气。术中静脉输液泵注射吸入 1.5%七氟烷(批准文号 HJ20160431,规格:250 mL,厂家:Baxter Healthcare Corporation)、丙泊酚中/长链脂肪乳注射液(批准文号 HJ20171120,规格:10 mL:0.1 g,厂家:Fresenius Kabi Deutschland GmbH)维持麻醉,罗库溴铵 0.3 mg/(kgoh)、芬太尼 0.3 μ g/(kgoh)间断静脉输注。

1.3 评价指标

(1)以停用静脉麻醉药为计时起点,记录两组患者呼吸恢复时间、拔管时间、睁眼时间。(2)观察两组患者麻醉前(T1)、手术切皮时(T2)、植入假体时(T3)、术毕时(T4)的血流动力学[平均动脉压(MAP)、心率(HR)]变化。(3)比较两组患者术前、术后 1 d 的左额区、右额区、左颞区、右颞区 δ 和 $\alpha 1$ 波频率。佩戴电极帽,将电极分别放置在额、颞区,佩戴电极帽脑电图机连接,通过广州三瑞公司生产的 LQWY-N8 数字化脑电图机进行信号采集,记录患者脑电图情况。(4)采用意识模糊评估法(CAM-ICU)^[9]评估术后谵妄情况,每天评估 1 次,连测 3 天,综合 3 次结果进行评估。具体标准:① 思维混乱;② 意识状态改变;③ 注意力障碍;④ 意识水平改变。同时符合①、②、③项或只要符合④项可定义为谵妄。(5)记录两组不良反应情况。

1.4 统计学方法

以 SPSS25.0 处理数据。计数资料包括不良反应发生率、谵妄发生率以率表示,采用 χ^2 检验。用($\bar{x} \pm s$)表示呼吸恢复时间、拔管时间、睁眼时间等计量资料,比较采用配对 t 检验和成组 t 检验。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 苏醒质量对比

与对照组相比,Dex 组呼吸恢复时间、拔管时间、睁眼时间更短($P<0.05$),见表 1。

2.2 血流动力学指标对比

两组 T2~T4 时间点 HR 均低于 T1 时间点,MAP 均高于 T1 时间点, 组内对比差异有统计学意义 ($P<0.05$)。Dex 组 T2~T4 时间点 HR 高于对照组对应时间点,MAP 低于对照组对应时间点($P<0.05$)。见表 2。

2.3 两组定量脑电图指标对比

两组术后 1 d 左 / 右额区、左 / 右额区 δ 波频率均较术前升高,但 Dex 组低于对照组($P<0.05$)。两组术后 1 d 左 / 右额区、左 / 右额区 $\alpha 1$ 波频率均较术前下降,但 Dex 组高于对照组

($P<0.05$)。详见表 3。

2.4 两组患者谵妄发生率及不良反应发生率对比

Dex 组术后发生谵妄 2 例,谵妄发生率为 4.08%;对照组术后发生谵妄 11 例,谵妄发生率为 22.92%;Dex 组术后谵妄发生率低于对照组($\chi^2=7.412, P=0.006$)。Dex 组出现不良反应 2 例,包括低血压 1 例、恶心 1 例,对照组出现低血压 1 例,两组不良反应发生率对比无统计学差异($\chi^2=0.366, P=0.545$)。

表 1 苏醒质量对比($\bar{x} \pm s, \text{min}$)

Table 1 Comparison of recovery quality($\bar{x} \pm s, \text{min}$)

Groups	Respiratory recovery time	Extubation time	Eye-opening time
Control group(n=48)	13.02 $\pm$ 2.58	17.95 $\pm$ 2.18	13.27 $\pm$ 1.31
Dex group(n=49)	8.84 $\pm$ 1.79	12.67 $\pm$ 2.23	7.91 $\pm$ 1.08
t	9.287	11.789	22.007
P	0.000	0.000	0.000

表 2 血流动力学指标对比($\bar{x} \pm s$)

Table 2 Comparison of hemodynamic indexes($\bar{x} \pm s$)

Groups	Time points	HR(beats/min)	MAP(mmHg)
Control group(n=48)	T1	76.59 $\pm$ 5.32	81.27 $\pm$ 7.84
	T2	61.55 $\pm$ 4.29 [°]	97.84 $\pm$ 6.42 [°]
	T3	64.96 $\pm$ 5.43 [°]	93.27 $\pm$ 7.66 [°]
	T4	68.14 $\pm$ 6.17 [°]	89.79 $\pm$ 9.45 [°]
Dex group(n=49)	T1	76.73 $\pm$ 6.14	81.83 $\pm$ 10.73
	T2	67.81 $\pm$ 5.46 [°]	93.29 $\pm$ 8.61 [°]
	T3	70.07 $\pm$ 6.05 [°]	88.85 $\pm$ 7.38 [°]
	T4	73.29 $\pm$ 5.71 [°]	85.73 $\pm$ 6.46 [°]

Note: compared with T1 time point, [°] $P<0.05$. Compared with the control group at corresponding time points, [°] $P<0.05$.

表 3 两组定量脑电图指标对比($\bar{x} \pm s$)

Table 3 Comparison of quantitative electroencephalogram indexes between the two groups($\bar{x} \pm s$)

Groups	Time points	δ wave band				$\alpha 1$ wave band			
		Left frontal region	Right frontal region	Left temporal region	Right temporal region	Left frontal region	Right frontal region	Left temporal region	Right temporal region
Control group(n=48)	Before operation	7.58 $\pm$ 0.61	7.43 $\pm$ 0.56	7.42 $\pm$ 0.61	7.48 $\pm$ 0.64	11.46 $\pm$ 0.55	11.35 $\pm$ 0.76	12.13 $\pm$ 0.81	11.58 $\pm$ 0.72
	1 d after operation	9.84 $\pm$ 0.82 [°]	9.42 $\pm$ 0.63 [°]	9.26 $\pm$ 0.53 [°]	9.61 $\pm$ 0.57 [°]	7.40 $\pm$ 0.67 [°]	7.27 $\pm$ 0.79 [°]	7.64 $\pm$ 0.85 [°]	7.45 $\pm$ 0.69 [°]
Dex group(n=49)	Before operation	7.52 $\pm$ 0.57	7.36 $\pm$ 0.44	7.46 $\pm$ 0.48	7.53 $\pm$ 0.52	11.27 $\pm$ 0.53	11.46 $\pm$ 0.84	11.96 $\pm$ 0.73	11.25 $\pm$ 0.81
	1 d after operation	8.76 $\pm$ 0.73 [°]	8.38 $\pm$ 0.59 [°]	8.23 $\pm$ 0.52 [°]	8.56 $\pm$ 0.48 [°]	8.64 $\pm$ 0.72 [°]	9.02 $\pm$ 0.87 [°]	8.84 $\pm$ 0.95 [°]	8.67 $\pm$ 0.63 [°]

Note: compared with the same group before operation, [°] $P<0.05$. Compared with the control group 1d after operation, [°] $P<0.05$.

3 讨论

骨质疏松合并股骨颈骨折患者在实施手术时,需进行扩髓

腔、置入假体等多项牵拉、扯动操作,可诱发机体释放炎症因子,导致不同程度的应激状态,造成肾上腺皮质激素、儿茶酚胺大量释放,可引起各脏器及脑部功能损伤^[10-12]。老年患者由于身

体机能下降,肺储备功能较差,手术耐受性较差,受麻醉诱导、气管插管、手术操作可引起血流动力学波动^[13,14]。此外,谵妄是老年患者术后的常见并发症之一,可表现出广泛的认知功能障碍、注意力障碍、睡眠觉醒周期障碍、情感障碍等;围术期应激反应的持续存在,可诱发更强的中枢神经系统炎症反应,进一步促进谵妄的发生^[15,16]。因此,选用可减轻老年患者围术期应激反应的麻醉药物具有重要意义。

Dex 是新型 $\alpha 2$ 肾上腺素能受体激动剂,可产生近似自然睡眠的镇静作用,且具备一定的镇痛效果^[17]。以往研究证实其用于老年患者中安全有效^[18]。本研究中,Dex 组可有效缩短呼吸恢复时间、拔管时间、睁眼时间,说明应用 Dex 可改善患者苏醒质量。主要可能是辅助应用 Dex 能够在一定程度上减少术中麻醉药物用量,有助于患者术后快速苏醒。同时也有研究证实^[19],外科手术中 Dex 的应用有利于维持血流动力学稳定。基于 Dex 的多种药物特性,本研究将其用于老年骨质疏松合并股骨颈骨折患者的麻醉方案中,结果显示,两组均产生一定程度的血流波动,但 Dex 组波动较对照组更轻微,可见 Dex 有利于维持血流动力学稳定。Dex 主要通过激动内源性促睡眠通路和作用于蓝斑核的 $\alpha 2$ 受体这 2 个机制产生类似于镇静催眠的效果,促使患者进入自然睡眠状态,且在这一过程中,Dex 不会产生呼吸抑制,可稳定术中的血氧供给,有效缓解手术带来的各种应激反应,从而维持血流动力学稳定^[20-22]。定量脑电图可敏感的反映药物对中枢神经系统的影响,其可依据脑电波频率不同分为 β 、 θ 、 α 、 δ 4 个频段,其中 α 波属于高幅快波,反映大脑皮层处于兴奋状态, δ 波属于低幅慢波,反映大脑皮层处于抑制状态^[23]。以往相关研究证实^[24],机体 $\alpha 1$ 波频率下降, δ 波频率升高,提示机体认知功能下降。本次研究中,两组患者 δ 波频率升高、 $\alpha 1$ 波频率下降,提示两组患者均有一定的脑功能损伤,存在不同程度的认知功能下降。但 Dex 组术后的 δ 波频率低于对照组, $\alpha 1$ 波频率高于对照组,同时研究结果还显示 Dex 组术后谵妄发生率低于对照组,提示 Dex 应用于围术期麻醉,可有效减轻对患者大脑额叶 δ 、 $\alpha 1$ 波频率的影响,降低术后谵妄发生率。Dex 的脑保护作用机制可能与其具有较强的镇静、降低局部血流供应的功能有关^[25-27]。相关研究结果显示^[28],Dex 可通过激动软脑膜动脉平滑肌和小动脉上的 α 受体促进血管收缩,降低局部血流供应,维持脑氧供需平衡,继而保护脑组织。也有研究结果认为^[29],Dex 可通过抑制炎症反应,进而抑制中枢海马区的炎症反应,发挥神经保护作用。王伟等人^[30]的研究则显示右美托咪定可通过使机体产生接近生理状态的睡眠-觉醒周期,增强镇痛、镇静效果,从而减少由疼痛诱发的认知功能障碍,降低术后谵妄的发生率。

综上所述,老年骨质疏松合并股骨颈骨折患者手术期间予以 Dex,可改善患者术后苏醒质量,减轻对患者大脑额叶 δ 、 $\alpha 1$ 波频率的影响,还可降低术后谵妄的发生率,稳定机体血流动力学水平。

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(上接第 2156 页)

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