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七氟烷复合麻醉对老年骨科患者术后早期认知功能的影响 *

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摘要 目的：探讨七氟烷复合麻醉对老年骨科患者术后早期认知功能的影响。**方法：**选择 2017 年 12 月 ~2019 年 6 月在西安医学院第二附属医院（本院）骨科诊治单侧老年全膝关节置换手术患者 112 例，随机数字表法分为七氟烷组与对照组，各 56 例。对照组给予常规静脉注射全身麻醉，在此基础上七氟烷组给予七氟烷吸入麻醉，记录与调查两组术后早期认知功能。**结果：**经过对比，两组手术时间、术中出血量对比差异无统计学意义（*P*>0.05），而七氟烷组的术后苏醒时间（7.10± 0.22）min、拔管时间（8.65± 0.46）min 等都显著短于对照组（14.09± 1.09）min、（18.76± 1.44）min，两组对比有统计学意义（*P*<0.05）。所有患者在 T1、T2、T3 与 T4 时间点的心率和血氧饱和度均表现正常，对比均无统计学意义（*P*>0.05）。七氟烷组术后 1 d、术后 14 d 的血清白介素（Interleukin，IL）-6、肿瘤坏死因子（Tumor necrosis factor，TNF）-α 值显著低于对照组，对比有统计学意义（*P*<0.05），且两组术后 14 d 的血清 IL-6 与 TNF-α 值均显著低于术后 1 d（*P*<0.05）。术后 1 个月七氟烷组的认知功能障碍发生率为 1.8 %（1/56），显著低于对照组的 12.5 %（7/56），两组间对比有统计学意义（x^2=4.846，*P*=0.028）。**结论：**七氟烷复合麻醉在老年骨科患者中的应用能促进患者康复，安全性比较好，能抑制炎症因子的释放，从而减少术后早期认知功能障碍的发生。

关键词：七氟烷；麻醉；全膝关节置换手术；认知功能；老年人

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Effects of Sevoflurane Anesthesia on Early Cognitive Function in Elderly Patients with Orthopedics*

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ABSTRACT Objective: To explore the effects of sevoflurane anesthesia on early cognitive function in elderly patients with orthopedics. **Methods:** From December 2017 to June 2019, 112 cases of patients with unilateral elderly total knee arthroplasty were selected as patients in the orthopedics department of our hospital and were equally divided into sevoflurane group and the control group accorded to random number table. The control group were given general intravenous anesthesia, and the sevoflurane group were given sevoflurane inhalation anesthesia. The early cognitive function of the two groups were recorded and investigated. **Results:** There were no significant difference in the operation time and intraoperative blood loss compared between the two groups (*P*>0.05). The postoperative wake-up time (7.10.22) min and extubation time (8.65± 0.46) min in the sevoflurane group were significantly shorter than those of the control group(14.09± 1.09) min and (18.76± 1.44) min. The comparison between the two groups was statistically significant (*P*<0.05). The heart rate and blood oxygen saturation of all patients at time points T1, T2, T3 and T4 were normal, and there were no statistically significant difference compared between the groups (*P*>0.05). The serum interleukin (IL) -6 and Tumor necrosis factor (TNF) -α values in the sevoflurane group were significantly lower control group at 1 and 14 days after surgery(*P*<0.05), and the serum IL-6 and TNF-α values of the two groups were significantly lower than that of the 1 day after the operation (*P*<0.05). The incidence of cognitive dysfunction in the sevoflurane group at 1 month after operation was 1.8 % (1/56), which was significantly lower than that of the control group at 12.5 % (7/56) (*P*<0.05), the comparison between the two groups was statistically significant (x^2=4.846, *P*=0.028). **Conclusion:** The application of sevoflurane anesthesia in elderly orthopedic patients can promote the rehabilitation of patients, has better safety, can inhibit the release of inflammatory factors, and reduce the incidence of early postoperative cognitive dysfunction.

Key words: Sevoflurane; Anesthesia; Total knee arthroplasty; Cognitive function; Elderly

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前言

膝骨关节病变是一类常见的退行性疾病,以中老年患者居多[1]。全膝关节置换是一种根治终末期膝骨关节病变的手术治疗方法,能恢复膝关节结构和功能、能解除膝关节疼痛[2,3]。由于该类手术在围手术期需要使用抗凝药物预防血栓形成,且患者常合并有各种基础疾病,在手术中多需要采用全身麻醉[4]。全身麻醉可在保障手术效果的基础上,可引发机体产生强烈的应激反应,导致机体内环境的严重紊乱,使机体代谢和免疫功能紊乱,从而增加围术期的不良反应的发生率[5,6]。七氟烷为一种挥发性麻醉药,化学名为氟甲基 - 六氟 - 异内基醚,具有不刺激上呼吸道、血气分配系数低、起效速度快等优点[7,8]。术后早期认知功能障碍(postoperative cognitive dysfunction, POCD)是骨科术后常见的神经系统并发症,严重影响患者的生活质量,同时也是家庭和社会的负担[9,10]。认知功能障碍发生的危险因素有手术、麻醉、基础疾病等,炎症反应也可参与认知功能障碍的发生与发展[11,12]。本文具体探讨了七氟烷复合麻醉对老年骨科患者术后早期认知功能的影响,以明确七氟烷的应用价值。

1 资料与方法

1.1 研究对象

选择 2017 年 12 月 ~2019 年 6 月选择在本院骨科诊治单侧老年全膝关节置换手术患者 112 例,纳入标准:因退行性关节炎、类风湿性关节等需行单侧膝关节置换;年龄 60-75 岁;术中均未输血;ASA 分级Ⅰ或Ⅱ级;肝肾功能均未见异常;患者或家属知情同意;经医院伦理委员会批准。排除标准:长期服用镇静药物者; 术前简易智能精神状态检查量表(mini-mental state examination,MMSE)评分 <23 分;既往有药物滥用史、麻醉药品的依赖者;患者家属不同意参加本研究;过敏体质者;合并感染性疾病、凝血功能异常者。根据随机数字表法把所有患者分为七氟烷组与对照组各 56 例, 两组的一般资料无差异(P>0.05)。见表 1。

表 1 两组的一般资料对比

Table 1 Comparison of two groups of general information between the two groups

Groups	n	ASA rating (Ⅰ/Ⅱ)	Gender (male / female)	Age (years)	BMI(kg/m^2)	Location of onset (left / right)
Sevoflurane group	56	30/26	28/28	66.20± 4.14	22.19± 2.17	28/28
Control group	56	28/28	29/27	66.98± 3.33	22.09± 1.74	29/27

1.2 麻醉方法

所有患者都给予全身麻醉, 麻醉诱导前 30 min 肌肉注射盐酸戊乙奎醚 0.01 mg/kg, 在 1 %利多卡因局部浸润麻醉下行桡动脉穿刺置管术并监测生命体征。麻醉诱导采用静脉注射依托咪酯 0.15-0.3 mg/kg、苯磺顺阿曲库铵 0.3-0.4 mg/kg、瑞芬太尼 0.5-1 μg/kg、咪达唑仑 0.05-0.1 mg/kg。采用呼吸通气气管插管, 均呼吸参数: 潮气量 6-8 mL/kg, 维持呼气末二氧化碳在 35-45 mmHg,呼吸频率 10-12 次 /min。在此基础上七氟烷组给予七氟烷吸入麻醉,采用面罩吸入 8.0 %的七氟烷。待患者意识清楚、肌力恢复满意后拔除气管导管,送麻醉恢复室。

1.3 观察指标

(1)记录两组的手术时间、术中出血量、术后苏醒时间、拔管时间。(2)记录麻醉诱导后(T1)、手术开始时(T2)、手术开始后 5 min(T3)、手术结束时(T4)的心率和血氧饱和度。(3)在术后 1 d 与术后 14 d 采集患者的静脉血 2-3 mL,30 min 静置,3000 rpm 离心, 取血清 -80℃保存待测, 酶联免疫法检测血清 IL-6、TNF-α 等含量。(4)在术后 1 个月采用 MMSE 量表对患者的认知功能进行测定,包括地点向力、延迟记忆等方面,得分 <27 分判定为认知功能障碍。

1.4 统计方法

应用 SPSS 21.00,计量资料用 ($\bar{x}$± s)表示,计数数据用%表示,对比分别利用 t 检验与 x^2 分析,P<0.05 有统计学意义。

2 结果

2.1 两组围手术指标对比

经过对比,两组手术时间、术中出血量对比无统计学意义(P>0.05),而七氟烷组的术后苏醒时间(7.10± 0.22)min、拔管时间 (8.65± 0.46)min 等都显著短于对照组 (14.09± 1.09)min、(18.76± 1.44)min,两组对比有统计学意义(P<0.05)。见表 2。

表 2 两组术后复苏等情况对比($\bar{x}$± s)

Table 2 Comparison of postoperative resuscitation between the two groups ($\bar{x}$± s)

Groups	n	Operation time (min)	Intraoperative blood loss (mL)	Postoperative wake-up time (min)	Extubation time (min)
Sevoflurane group	56	122.15± 22.99	300.87± 34.65	7.10± 0.22*	8.65± 0.46*
Control group	56	121.76± 18.33	301.76± 41.84	14.09± 1.09	18.76± 1.44

Note: Compared to the control group, *P<0.05.

2.2 两组不同时间点的生命体征变化对比

经过比较, 两组患者在 T1、T2、T3、T4 时间心率和血氧饱和度均在正常范围变化,患者均表现正常,两组对比均无统计学意义(P>0.05)。见表 3。

表 3 两组不同时间点的生命体征变化对比($\bar{x}\pm s$)

Table 3 Comparison of changes in vital signs at two different time points($\bar{x}\pm s$)

Index	Group	T1	T2	T3	T4
Blood oxygen saturation (%)	Sevoflurane group	98.44± 2.49	98.21± 3.14	96.73± 1.94	94.78± 1.43
	Control group	98.78± 4.20	98.09± 2.94	97.24± 2.44	95.67± 4.09
Heart rate (times / min)	Sevoflurane group	132.00± 18.29	123.40± 24.87	126.40± 20.59	125.30± 17.89
	Control group	133.09± 11.98	131.40± 19.49	131.99± 18.93	126.53± 8.92

2.3 两组术后不同时间点的血清 IL-6 与 TNF-α 表达对比

两组术后 14 d 的血清 IL-6 与 TNF-α 值均显著低于术后 1 d (P<0.05)；七氟烷组术后 1 d、术后 14 d 的血清 IL-6 与 TNF-α 值显著低于对照组，对比有统计学意义(P<0.05)。见表4。

表 4 两组术后不同时间点的血清 IL-6 与 TNF-α 表达对比 (ng/L，$\bar{x}\pm s$)

Table 4 Comparison of serum IL-6 and TNF-α expression at different time points between the two groups (ng/L, $\bar{x}\pm s$)

Groups	n	Postoperative 1 d		Postoperative 14 d	
		IL-6	TNF-α	IL-6	TNF-α
Sevoflurane group	56	89.29± 9.48*	34.11± 3.99*	11.45± 2.10#*	13.02± 1.84#*
Control group	56	127.29± 18.42	43.20± 4.58	24.68± 1.49#	28.00± 2.15#

Note: Compared with the same group 1 day before surgery, #P<0.05, compared with the control group at the same time, *P<0.05,

2.4 两组术后 1 个月认知功能障碍发生情况对比

术后 1 个月七氟烷组的认知功能障碍发生率为 1.8 %（1/56），显著低于对照组的 12.5 %（7/56），对比有统计学意义(x^2=4.846，P=0.028)。

3 讨论

随着医疗科学技术的提高，接受手术治疗的老年骨科患者增多，在延长患者的生存时间取得了很好的效果，但是对患者有一定的负面影响，比如可造成认知功能障碍的发生，从而影响患者的生活质量[13,14]。特别是很多老年人由于血管动脉粥样硬化、调节功能衰退等因素的影响，在手术与麻醉等刺激下，可导致患者血管阻力和心脏负荷增强，从而影响麻醉与术后恢复效果[15,16]。

七氟烷是一种吸入麻醉药，在血液中的溶解度较低，也就是说血 / 气的分配系数较小，具有对气道刺激小等诸多优点[17]。本研究显示七氟烷组的术后苏醒时间、拔管时间等都显著短于对照组；所有患者在不同时间点的心率和血氧饱和度均表现正常，表明七氟烷复合麻醉的应用能促进患者术后康复，且应用安全性比较好。Birch S[18]等人和 Choi S[19]等人与本研究一致，表明七氟烷能使患者迅速进入麻醉状态，对呼吸循环功能影响小。因此七氟烷在老年骨科患者中的应用具有一定的价值。

随着医学技术的发展与人口老龄化进程的加快，当前全膝关节置换手术患者逐年增加[20]。不过任何手术都有一定应激因素，特别是关节置换术后体内某些成分释放进行入血液可导致持续性应激反应的发生，可造成中枢敏化，造成术后患者持续疼痛[21,22]。机体的慢性炎症是以 IL-6 及 TNF-α 等血清炎症因子增加为特征，IL-6 及 TNF-α 也是机体炎症反应的敏感指标[23]。大量炎症因子的可释放产生神经细胞毒性作用，影响神经突触部位的连接功能，导致神经纤维退行性改变，认识功能损伤，影响神经信号的传导[24,25]。本研究显示七氟烷组术后 1 d、术后 14 d 的血清 IL-6 与 TNF-α 值显著低于对照组，Shi CX[26]等人研究发现七氟烷的后处理降低了缺血再灌注大鼠脑梗死区域的炎症反应水平，并降低了缺血再灌注损伤大鼠的促炎细胞因子如 TNF-α，IL-1β，IL-6 的水平，与本研究结果类似。表明七氟烷的应用能抑制炎症因子的释放。主要原因可能是七氟烷对呼吸道刺激小，有芳香味，患者易接受[27]。

认知功能障碍是手术后并发的神经系统障碍性疾病，选择最佳的麻醉方法与药物可逆转患者的认知功能障碍，对预防认知功能减退具有重要意义[28,29]。静脉麻醉是当前全身麻醉的主要方法之一，但是在麻醉苏醒期，可使得患者出现躁动、无理性言语、妄想思维等情况，导致出现认知功能障碍[30,31]。本研究显示术后 1 个月七氟烷组的认知功能障碍发生率为 1.8 %，显著低于对照组的 12.5 %，表明七氟烷复合麻醉的应用能减少术后认知功能障碍的发生。Xihua Lu[32]等人的研究也显示七氟烷麻醉后对大鼠认知功能障碍的神经有保护作用，提示七氟烷刺激小，对患者的神经系统的损伤小，降低了患者术后认知障碍。本研究也存在一定的不足，观察时间比较短，且没有进行剂量分析，将在后续研究中深入探讨。

总之，七氟烷复合麻醉在老年骨科患者中的应用能促进患者康复，安全性比较好，能抑制炎症因子的释放，从而减少术后早期认知功能障碍的发生。

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