

· 临床研究 ·

艾司氯胺酮对老年人全髋置换术后疲劳综合征的影响[△]

陈军, 谢芳, 邹锋, 张南南*

(上海交通大学医学院附属第六人民医院麻醉科, 上海 200233)

摘要: [目的] 探讨艾司氯胺酮对老年全髋置换术患者术后疲劳综合征的影响。[方法] 183例全髋置换术老年患者, 随机分为给药组(92例)和对照组(91例)。比较两组临床与检验结果。[结果] 给药组术中低血压发生率(8.7% vs 19.8%, $P=0.039$)显著低于对照组。术后随时间推移, 两组术后疲劳综合征(postoperative fatigue syndrome, POFS)发生率、疼痛NRS评分均显著改善($P<0.05$)。给药组在术后1 d(13.0% vs 28.6%, $P=0.008$)、3 d(8.7% vs 19.6%, $P=0.026$)的POFS发生率, 术后下地行走时间[(7.6±1.3) h vs (8.2±1.6) h, $P=0.006$]、术后7 d内觉醒次数[(82.6±9.2)次 vs (90.2±9.3)次, $P<0.001$]显著优于对照组。检验方面, 与术前相比, 术后即刻、术后1、3 d, 两组白介素-1 β (interleukin-1 β , IL-1 β)、超敏C反应蛋白(hypersensitive C-reactive protein, hs-CRP)、皮质醇、血清白介素-6(interleukin-6, IL-6)浓度均显著升高($P<0.05$), 术前两组间上述检验指标的差异均无统计学意义($P>0.05$), 术后相应时间点, 给药组上述检验指标均显著低于对照组($P<0.05$)。[结论] 艾司氯胺酮降低老年全髋置换术患者早期POFS发生率, 可能与抑制炎症反应、减少术中低血压、缩短下地行走时间、改善睡眠质量有关。

关键词: 老年人, 全髋关节置换术, 艾司氯胺酮, 术后疲劳综合征, 炎症因子

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Effect of esketamine on fatigue syndrome after total hip arthroplasty in elderly // CHEN Jun, XIE Fang, ZOU Feng, ZHANG Nan-nan*. Department of Anesthesiology, Shanghai Sixth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200233, China

Abstract: [Objective] To investigate the effect of esketamine (ESK) on fatigue syndrome after total hip arthroplasty (THA) in the elderly. [Methods] A total of 183 elderly patients who were undergoing THA were randomly divided into ESK group (92 cases) and control group (91 cases). The clinical and laboratory results of the two groups were compared. [Results] The ESK group proved significantly lower incidence of intraoperative hypotension than the control group (8.7% vs 19.8%, $P=0.039$). The occurrence of postoperative fatigue syndrome (POFS) and pain NRS score in both groups were significantly improved over time postoperatively ($P<0.05$). The ESK group was significantly superior to the control group in terms of incidence of POFS 1 day (13.0% vs 28.6%, $P=0.008$) and 3 days postoperatively (8.7% vs 19.6%, $P=0.026$), as well as bed rest time [(7.6±1.3) hours vs (8.2±1.6) hours, $P=0.006$] and the number of awakening within 7 days after the operation [(82.6±9.2) times vs (90.2±9.3) times, $P<0.001$]. As for blood test, the interleukin-1 β (IL-1 β), hypersensitive C-reactive protein (hs-CRP), cortisol, serum interleukin-6 (IL-6) were significantly increased in both groups immediately after surgery, 1 and 3 days after surgery compared with those preoperatively ($P<0.05$). There were no statistical significances in the above test indexes between the two groups before surgery ($P>0.05$). However, the ESK group had significantly lower levels of the aforesaid test parameters than the control group at all corresponding time points after surgery ($P<0.05$). [Conclusion] Esketamine reduces the incidence of POFS after THA in the elderly, which may be related to inhibiting inflammatory response, reducing intraoperative hypotension, shortening bed rest time and improving sleep quality.

Key words: elderly, total hip arthroplasty, esketamine, postoperative fatigue syndrome, inflammatory factors

术后疲劳综合征(postoperative fatigue syndrome, POFS)是指患者在手术后出现乏力、抑郁、焦虑、

失眠、认知功能障碍等一系列症状, 严重损害患者生活质量和术后康复过程^[1]。老年人行全髋关节置换术

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作者简介:陈军,副主任医师,研究方向:麻醉与器官保护,(电子信箱)mazui5433@sina.com

*通信作者:张南南,(电子信箱)330770970@qq.com

创伤较大,疼痛剧烈^[2],是POFS发生的高危人群,POFS的发生阻碍患者的术后快速康复,增加住院时间、并发症发生风险^[3]。POFS的发生与手术应激反应导致炎症反应失控有关^[4],有效预防POFS具有重要的临床意义。艾司氯胺酮是N-甲基-D-天冬氨酸受体(N-methyl-D-aspartic acid, NMDA)拮抗剂^[5],髋关节置换手术中应用具有抑制炎症因子水平、促进术后康复作用^[6]。目前,艾司氯胺酮对老年全髋关节置换术后患者POFS发生的影响,尚未见报道。本研究探讨老年全髋关节置换术中应用艾司氯胺酮对术后POFS发生的影响,现报道如下。

1 临床资料

1.1 一般资料

纳入2023年10月—2024年6月收治的髋部骨折患者183例,均具有全髋关节置换术的指征,均无严重心脏、肾或肝脏疾病、认知功能障碍、精神疾病、恶性肿瘤。根据随机数字表法分为两组,给药组92例和对照组91例。两组患者年龄、性别、BMI、ASA分级的差异均无统计学意义($P>0.05$)。本研究为随机双盲对照研究,手术由同一组骨科医生进行,骨科医生和病房护士都不知晓研究方案的细节,所有患者均保持同等条件的病房,光照、噪音控制条件相等,晚上9点熄灯休息,早上6点开灯,允许患者家属1人下午4点探视1次,每次1h。术前研究者详细解释研究内容、目的、可能的风险和益处。本研究已获本院伦理委员会批准[伦理编号:2023-133-(1)],患者或家属均已签署知情同意书。

1.2 治疗方法

给药组:麻醉诱导时静脉注射艾司氯胺酮0.5 mg/kg(用生理盐水配成5 mL),术中静脉持续泵注艾司氯胺酮每小时0.5 mg/kg(设置泵注速率为25 mL/h)。

对照组:麻醉诱导时静脉注射生理盐水5 mL,术中持续泵注生理盐水25 mL/h。

麻醉与手术方法:患者入室后,进行常规监测,包括心率、血压、血氧饱和度、鼻咽温度,行有创桡动脉监测和颈内静脉置管穿刺。静脉输注聚明胶肽5 mL/kg,并进行超声引导下腰丛阻滞+骶丛阻滞,各注入0.25%罗哌卡因20 mL。连接脑电麻醉深度多参数监护仪,依次静脉注射丙泊酚1~2 mg/kg、舒芬太尼0.4 μ g/kg、罗库溴铵0.6 mg/kg,进行气管插管。麻醉维持:靶控输注丙泊酚3~5 μ g/mL,调整丙泊酚

靶控浓度维持意识指数(IOC1):40~60、间断静脉注射舒芬太尼维持脑电伤害敏感指数(IOC2):35~45。术后镇痛:布托啡诺3 mg+舒芬太尼50 μ g+昂丹司琼8 mg使用生理盐水稀释至120 mL,负荷剂量4 mL,背景速率2 mL/h,按压剂量2 mL/次,锁定时间30 min,持续镇痛48 h。术后若患者连续2次有效按压镇痛泵自控给药按钮后NRS评分仍然 >3 分,肌注氨丁三醇30 mg进行补救镇痛。

1.3 评价指标

记录临床结果,包括手术时间、总失血量、术后早期不良事件、下地时间、术后7 d内总觉醒次数。术后疲劳综合征发生率,采用围术期疲劳评定量表(identity-consequence fatigue scale, ICFS-10)进行判断,ICFS-10得分 >24 分定义为发生POFS^[7]。检验结果:记录术前、术后即刻、术后1、3 d血清白介素-1 β (interleukin-1 β , IL-1 β)、超敏C反应蛋白(hypersensitive C-reactive protein, hs-CRP)、血清白介素-6(interleukin-6, IL-6)、皮质醇水平。

1.4 统计学方法

采用SPSS 22.0软件进行统计学分析。计量数据以 $\bar{x} \pm s$ 表示,资料呈正态分布时,两组间比较采用独立样本 t 检验,组内行单因素方差分析;资料不符合正态分布时,采用秩和检验。计数资料采用 χ^2 检验或Fisher精确检验。等级资料两组比较采用Mann-whitney U 检验。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 临床结果

两组患者均顺利完成手术,两组临床资料比较见表1,两组手术时间、术中失血量、术中输液量、术后恶心呕吐、苏醒期躁动、苏醒延迟、谵妄的差异均无统计学意义($P>0.05$)。给药组术中低血压发生率显著低于对照组($P<0.05$)。术后随时间推移,两组POFS发生率、疼痛NRS评分均显著改善($P<0.05$)。给药组术后1、3 d的POFS发生率显著低于对照组($P<0.05$),给药组术后下地行走时间显著早于对照组($P<0.05$),术后7 d内觉醒次数显著低于对照组($P<0.05$)。两组术后7 d POFS发生率及术后1、3、7 d疼痛NRS评分差异均无统计学意义($P>0.05$)。

2.2 检验结果

两组患者检验结果见表2,与术前相比,两组术后即刻、术后1、3 d, IL-1 β 、Hs-CRP、皮质

醇、IL-6 浓度均显著升高 ($P<0.05$)，术前，两组间上述检验指标的差异均无统计学意义 ($P>0.05$)，术后相应时间点，给药组的 IL-1 β 、hs-CRP、皮质醇浓度和 IL-6 浓度均显著低于对照组 ($P<0.05$)。

表 1. 两组临床资料比较			
Table 1. Comparison of clinical data between the two groups			
指标	给药组 (<i>n</i> =92)	对照组 (<i>n</i> =91)	<i>P</i> 值
年龄 (岁, $\bar{x} \pm s$)	72.4 $\pm$ 5.6	72.6 $\pm$ 5.8	0.813
性别 (例, 男/女)	52/40	50/41	0.474
BMI (kg/m ² , $\bar{x} \pm s$)	25.2 $\pm$ 2.1	25.4 $\pm$ 2.3	0.540
ASA 分级 (例, II/III)	76/16	75/17	0.486
手术时间 (min, $\bar{x} \pm s$)	99.3 $\pm$ 13.6	98.2 $\pm$ 13.9	0.589
术中失血量 (mL, $\bar{x} \pm s$)	198.5 $\pm$ 42.6	195.9 $\pm$ 43.2	0.682
术中输液量 (mL, $\bar{x} \pm s$)	1 307.4 $\pm$ 230.8	1 350.9 $\pm$ 231.9	0.205
总不良反应 [例 (%)]	23 (5.0)	37 (8.1)	<0.001
术中低血压	8 (8.7)	18 (19.8)	0.039
恶心呕吐	7 (7.6)	9 (9.9)	0.388
苏醒期躁动	1 (1.0)	2 (2.2)	0.496
苏醒延迟	1 (1.0)	3 (3.3)	0.306
谵妄	6 (6.5)	5 (5.5)	0.288
POFS 发生率 [例 (%)]			
术后 1 d	12 (13.0)	26 (28.6)	0.008
术后 3 d	8 (8.7)	18 (19.6)	0.026
术后 7 d	5 (5.4)	9 (9.9)	0.197
<i>P</i> 值	0.028	<0.001	
疼痛 NRS 评分 (分, $\bar{x} \pm s$)			
术后 1 d	3.1 $\pm$ 0.6	3.2 $\pm$ 0.7	0.301
术后 3 d	2.2 $\pm$ 0.3	2.3 $\pm$ 0.4	0.057
术后 7 d	1.5 $\pm$ 0.2	1.5 $\pm$ 0.3	>0.999
<i>P</i> 值	<0.001	<0.001	
术后下地行走时间 (h, $\bar{x} \pm s$)	7.6 $\pm$ 1.3	8.2 $\pm$ 1.6	0.006
觉醒次数 (次, $\bar{x} \pm s$)	82.6 $\pm$ 9.2	90.2 $\pm$ 9.3	<0.001

3 讨 论

本研究结果表明，术中应用艾司氯胺酮可降低老年全髋关节置换术患者术后 1、3 d POFS 的发生率，证实艾司氯胺酮具有预防 POFS 发生的作用。POFS 的成因复杂，主要与手术创伤导致的应激反应、炎症反应失控、骨骼肌收缩力下降有关^[8]。本研究结果表明，艾司氯胺酮降低老年全髋关节置换术患者炎症因子 IL-1 β 、hs-CRP、皮质醇和 IL-6 水平，表明其具有显著的抗炎、抗应激反应作用。炎症因子在手术创

伤后的全身炎症反应中起着关键作用，它们的升高加剧神经-内分泌失调和代谢状况下降，导致 POFS 的发生^[9]。研究发现，艾司氯胺酮可抑制老年髋关节置换术患者炎症因子和 NMDA 受体表达水平，不仅直接减轻手术创伤引起的炎症反应，还通过减少炎症对机体的持续刺激，加强神经内分泌系统的稳定性，促进术后代谢状态的恢复，减轻术后疼痛和认知功能障碍发生^[10]，有助于缓解术后疲劳。

表 2. 两组患者检验资料 ($\bar{x} \pm s$) 与比较			
Table 2. Comparison of anesthesia recovery data ($\bar{x} \pm s$) between the two groups			
指标	给药组 (<i>n</i> =92)	对照组 (<i>n</i> =91)	<i>P</i> 值
IL-1 β (pg/mL)			
术前	11.6 $\pm$ 1.5	11.2 $\pm$ 1.3	0.056
术后即刻	33.3 $\pm$ 3.8	38.2 $\pm$ 3.9	<0.001
术后 1 d	45.8 $\pm$ 4.7	56.2 $\pm$ 5.2	<0.001
术后 3 d	43.6 $\pm$ 4.6	52.4 $\pm$ 5.3	<0.001
<i>P</i> 值	<0.001	<0.001	
Hs-CRP (mg)			
术前	11.3 $\pm$ 2.7	10.9 $\pm$ 2.8	0.327
术后即刻	13.3 $\pm$ 3.3	15.2 $\pm$ 3.8	<0.001
术后 1 d	15.2 $\pm$ 3.6	17.5 $\pm$ 4.2	<0.001
术后 3 d	14.8 $\pm$ 3.4	16.6 $\pm$ 3.9	<0.001
<i>P</i> 值	<0.001	<0.001	
皮质醇 (nmol/L)			
术前	230.5 $\pm$ 20.2	232.4 $\pm$ 22.7	0.550
术后即刻	284.2 $\pm$ 26.7	312.4 $\pm$ 28.6	<0.001
术后 1 d	302.7 $\pm$ 27.8	326.9 $\pm$ 30.9	<0.001
术后 3 d	283.6 $\pm$ 25.4	308.3 $\pm$ 27.5	<0.001
<i>P</i> 值	<0.001	<0.001	
IL-6 (pg/mL)			
术前	22.5 $\pm$ 2.1	22.8 $\pm$ 2.2	0.347
术后即刻	25.2 $\pm$ 2.6	36.3 $\pm$ 2.9	<0.001
术后 1 d	32.7 $\pm$ 4.6	49.1 $\pm$ 5.3	<0.001
术后 3 d	31.6 $\pm$ 4.4	46.7 $\pm$ 4.8	<0.001
<i>P</i> 值	<0.001	<0.001	

本研究表明，用药组术中低血压发生率明显低于对照组，可能与艾司氯胺酮兴奋交感神经有关^[11]。术中低血压可导致术后谵妄、认知功能障碍、死亡率增加^[12]，减少术中低血压发生，能够保证重要脏器灌注，减少 POFS 发生^[13]。术后早期下地行走对老年全髋置换术患者快速康复意义重大，具有增强肌肉

力量、改善血液循环、预防血栓形成等作用。本研究表明,术中应用艾司氯胺酮能够缩短老年全髋置换术患者术后下地行走时间,可能与艾司氯胺酮降低术后疲劳感,提高术后恢复质量有关^[14]。艾司氯胺酮通过其抗炎和减轻术后疲劳作用,有利于患者肌力和精神状态的恢复,有助于患者更早地下地行走。术后恢复期间,睡眠质量对于患者的整体康复至关重要。本研究表明,用药组术后觉醒次数低于对照组,可能与艾司氯胺酮增加全脑血流量,改善颅内灌注,改善睡眠质量有关^[15]。睡眠质量改善能够减少 POFS 发生。

综上所述,艾司氯胺酮能够降低老年全髋置换术患者早期 POFS 的发生率,可能通过抑制炎症反应,减少术中低血压发生,缩短术后下地行走时间,改善睡眠质量有关。本研究的局限性:(1)为单中心研究,这可能限制了结果的外推性。不同医疗中心的患者群体、手术技术和术后护理可能影响研究结果;(2)未深入探讨不同剂量艾司氯胺酮对 POFS 发生的影响。

利益冲突声明 所有作者声明无利益冲突

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(同行评议专家: 付国建, 侯存强, 康鹏德, 周宗科)
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(同行评议专家: 黄长明, 袁普卫, 叶仙华, 巩文怡)
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