

· 临床研究 ·

## 右美托咪定复合芬太尼对老年肱骨干骨折患者脑氧饱和度及术后早期认知功能的影响

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**【摘要】目的** 分析右美托咪定复合芬太尼用于老年肱骨干骨折患者麻醉后脑氧饱和度及早期术后认知功能的变化。**方法** 回顾性分析2013年3月至2016年12月期间深圳市龙岗区第二人民医院麻醉科因肱骨干骨折手术的老年患者272例,根据麻醉方式不同分为研究组(右美托咪定复合芬太尼全麻)和对照组(采用七氟醚-瑞芬太尼静吸复合麻醉),每组136例,比较2组患者入室(T1)、麻醉准备(T2)、手术30 min(T3)、手术结束(T4)4个时间点脑氧饱和度,以及治疗前1 d、治疗后1 d 和3 d 韦氏成人智力量表(WAIS-RC)各指标得分。应用SPSS 22.0统计软件对数据进行分析。组间比较采用t检验、方差分析或 $\chi^2$ 检验。**结果** 研究组患者的睁眼时间、苏醒评分、拔管时间、复苏室停留时间、心率、呼吸频率、平均动脉压以及疼痛程度评分均明显优于对照组患者,差异具有统计学意义( $P < 0.05$ )。对照组不同时点脑氧饱和度差异无统计学意义( $F = 2.04, P = 0.11$ ),研究组不同时点脑氧饱和度差异有统计学意义( $F = 41.57, P = 0.00$ )。研究组相比对照组患者T2[(64.82 ± 9.87)% vs (72.56 ± 9.80)%]、T3[(62.03 ± 11.05)% vs (70.23 ± 11.25)%]和T4[(69.20 ± 9.47)% vs (72.47 ± 9.88)%]时间点脑氧饱和度低,差异具有统计学意义( $P < 0.05$ )。研究组患者麻醉后1 d 和3 d 的常识、领悟、算术、相似、数字广度、填图、木块图、图片排列、图形拼凑得分低于对照组患者,差异具有统计学意义( $P < 0.05$ )。**结论** 右美托咪定复合芬太尼降低患者认知功能和脑氧饱和度的时限较短,具备一定的用药安全性,可用于老年肱骨干骨折患者,术中应密切观察并稳定患者的脑氧饱和度。

**【关键词】** 肱骨骨折;认知;芬太尼;脑氧饱和度

**【中图分类号】** R592;R971<sup>+2</sup>

**【文献标志码】** A

**【DOI】** 10.11915/j.issn.1671-5403.2018.11.194

## Effects of dexmedetomidine combined with fentanyl on cerebral oxygen saturation and early postoperative cognitive function in the elderly patients with humeral shaft fracture

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**【Abstract】Objective** To analyze the changes of cerebral oxygen saturation and cognitive function after anesthesia in the elderly patients with humeral shaft fracture treated with dexmetomidine and fentanyl. **Methods** A retrospective analysis was made of 272 elderly patients with humeral shaft fractures in the Department of Anesthesiology, the Second People's Hospital of Longgang District in Shenzhen from March 2013 to December 2016. According to the anesthesia type, they were divided into study group (dexmetomidine-fentanyl) and control group (sevoflurane-remifentanil) with 136 patients each. The 2 groups were compared in cerebral oxygen saturation at admission into operating room (T1), anesthesia preparation (T2), 30 min into the operation (T3) and the end of operation (T4) and in scores of Wechsler Adult Intelligence scale (WAIS-RC) at preoperative day 1 and postoperative day 1 and day 3. The data were analyzed with SPSS 22.0. Student's t test, ANOVA or  $\chi^2$  test was employed for intergroup comparison. **Results** The study group were significantly better than the control group in terms of blink time, awakening, extubation time, time in resuscitation room, heart rate, respiratory frequency, mean arterial pressure and pain. The difference was statistically significant ( $P < 0.05$ ). The control group had no significant difference in cerebral oxygen saturation at different time points ( $F = 2.04, P = 0.11$ ), but the study group had significant difference in the terms ( $F = 41.57, P = 0.00$ ). Compared with the control group, the study group had lower cerebral

oxygen saturation at T2 [ $(64.82 \pm 9.87)\%$  vs  $(72.56 \pm 9.80)\%$ ], T3 [ $(62.03 \pm 11.05)\%$  vs  $(70.23 \pm 11.25)\%$ ], and T4 [ $(69.20 \pm 9.47)\%$  vs  $(72.47 \pm 9.88)\%$ ], with statistically significant difference ( $P < 0.05$ )。The study group scored lower than the control group in common sense, understanding, arithmetics, similarity, digit span, filling in the chart, block diagram, picture arrangement and graphic patchwork at postoperative day 1 and day 3, the difference being statically significant ( $P < 0.05$ )。

**Conclusion** Dexmetomidine-fentanyl, with short-term reduction of cognitive function and cerebral oxygen saturation, can be a safe option for the treatment of humeral shaft fracture in the elderly patients, and it is necessary to observe and stabilize cerebral oxygen saturation in the procedure.

**[Key words]** humeral fracture; cognition; fentanyl; cerebral oxygen saturation

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老年肱骨干骨折患者器官功能退化严重,此类患者进行手术时麻醉方法的选择应谨慎<sup>[1,2]</sup>。寻找效果较好的麻醉药进行全身麻醉,以降低气管插管或拔管所带来的应激,控制老年患者围麻醉期的风险,是目前的研究重点<sup>[3~5]</sup>。研究表明术后认知功能障碍(post operative cognitive dysfunction,POCD)是老年患者手术全麻后最常见的中枢神经系统并发症,脑功能改变可能与脑部氧供应改变有关<sup>[6,7]</sup>。为此,本研究探讨了右美托咪定复合芬太尼对老年肱骨干骨折患者全麻后脑氧饱和度和术后早期认知功能的影响。

## 1 对象与方法

### 1.1 研究对象

回顾性分析2013年3月至2016年12月期间深圳市龙岗区第二人民医院麻醉科因肱骨干骨折手术的老年患者272例,根据麻醉方式不同分为研究组和对照组,每组136例。纳入标准:年龄65~70岁;影像学检查确诊肱骨干(均为骨干中段)骨折;均由间接暴力所致。排除标准:病理性骨折;有明显药物或手术治疗禁忌证;伴显著器质性疾病;并发症如神经损伤严重或身体状况欠佳。患者本人或家属已签署知情同意书,并获得本院医学伦理委员会批准(20130105)。

### 1.2 方法

对照组患者采用七氟醚-瑞芬太尼静吸复合麻醉<sup>[8]</sup>,给予1.2%~3.5%的七氟醚(江苏恩华药业股份有限公司,国药准字H20120021)持续吸入,而后瑞芬太尼(宜昌人福药业有限责任公司,国药准字H20030197)按照0.5 μg/(kg·min)的维持剂量持续静脉泵入。

研究组患者采用右美托咪定复合芬太尼全身麻醉。罗库溴铵(荷兰欧加农公司,国药准字H20130486)联合注射用咪达唑仑(江苏恩华药业股份有限公司,国药准字H10980025)进行麻醉诱导,药物起效后立即进行气管内插管和机械通气(氧气

2 L/min,潮气量8 ml/kg,呼吸频率12次/min,呼吸比1:2,呼吸末二氧化碳分压维持在35~45 mmHg,1 mmHg=0.133 kPa)。同时,右美托咪定(四川国瑞药业有限责任公司,国药准字H20110097)按照0.5 μg/kg剂量以4 μg/ml浓度约10 min内静脉泵入<sup>[9]</sup>。

### 1.3 监测指标

1.3.1 常规监测指标 术毕停药后呼唤患者睁眼时间、术后苏醒评分、拔管时间、复苏室停留时间、心率、呼吸频率、平均动脉压、疼痛程度评分。Steward苏醒评分包括清醒程度、呼吸道通畅情况、肢体活动度3个内容,每个项目评分范围0~2分,和为总粗分,评分越高表示患者苏醒情况越好。疼痛程度评分:采用数字评分法(numeric rating scale,NRS),即11点数字评分法(以无痛的0依次增强到最剧烈疼痛的10共计11个点来描述疼痛强度),0:无痛;1~3:轻度疼痛;4~6:中度疼痛;7~10:重度疼痛。

1.3.2 脑氧饱和度 使用FORE-SIGHT脑氧饱和度监护仪(CASMED公司,美国)进行连续监测,监测4个时间点数据,即入室(T1)、麻醉准备(T2)、手术30 min(T3)、手术结束(T4)<sup>[4]</sup>。

1.3.3 认知功能评分 使用原韦氏成人智力测验(Wechsler Adult Intelligence Scale, WAIS)基础上中国修订的韦氏成人智力量表(WAIS-RC)进行调查<sup>[8~10]</sup>。该量表包括11项测验,其中语言测验有6项(常识、领悟、算术、相似、数字广度、词汇),操作测验5项(数字符号、填图、木块图、图片排列、图形拼凑)。测验题为二级评分,答对为1分,答错为0分。分别将语言测验和操作测验分相加,得到量表的总粗分,得分越高表示智力水平相对越高。

### 1.4 统计学处理

应用SPSS 22.0统计软件对数据进行分析。计量资料用均数±标准差( $\bar{x} \pm s$ )表示,组间比较采用t检验和方差分析。计数资料用例数(百分率)表示,

组间比较用 $\chi^2$ 检验。 $P < 0.05$ 为差异有统计学意义。

## 2 结 果

### 2.1 2组患者基线资料比较

研究组无基础疾病者61例,对照组无基础疾病者58例,2组患者年龄、性别、体质质量指数、教育程度及基础疾病差异无统计学意义( $P > 0.05$ ;表1),资料具有可比性。

### 2.2 2组患者常规监测指标比较

研究组患者的睁眼时间、苏醒评分、拔管时间、复苏室停留时间、心率、呼吸频率、平均动脉压以及疼痛程度评分均明显优于对照组患者,差异具有统计学意义( $P < 0.05$ ;表2)。

### 2.3 2组患者麻醉前后脑氧饱和度比较

对照组不同时点脑氧饱和度差异无统计学意义( $F = 2.04, P = 0.11$ ),研究组不同时点脑氧饱和度差异有统计学意义( $F = 41.57, P = 0.00$ )。相比对照组患者,研究组患者T2、T3和T4时间点脑氧饱和度低,差异具有统计学意义( $P < 0.05$ ;表3)。

### 2.4 2组患者麻醉前后WAIS-RC得分比较

对照组患者麻醉前后WAIS-RC各项目得分差异无统计学意义( $P > 0.05$ );研究组患者麻醉前后WAIS-RC各项目得分差异有统计学意义( $P < 0.05$ )。研究组患者麻醉后1 d和3 d的常识、领悟、算术、相似、数字广度、填图、木块图、图片排列、图形拼凑得分低于对照组患者,差异有统计学意义( $P < 0.05$ ;表4)。

表1 2组患者基线资料比较

Table 1 Comparison of baseline data between two groups ( $n = 136$ )

Item	Control group	Study group	$t/\chi^2$	P value
Age (years, $\bar{x} \pm s$ )	66.7 ± 2.5	67.2 ± 3.1	-1.46	0.14
Gender (male/female, n)	65/71	61/75	0.23	0.62
BMI (kg/m <sup>2</sup> , $\bar{x} \pm s$ )	22.03 ± 2.61	21.60 ± 2.74	1.32	0.18
Educational level [n (%)]			1.18	0.75
Junior high school and below	39(28.7)	32(23.5)		
High school or secondary school	61(44.9)	63(46.3)		
College and above	36(26.4)	41(30.2)		
Basic disease [n (%)]			0.45	0.92
Diabetes mellitus	12(8.8)	10(7.4)		
Hypertension	32(23.5)	34(25.0)		
Respiratory disease	34(25.0)	31(22.8)		

BMI: body mass index

表2 2组患者常规监测指标比较

Table 2 Comparison of routine monitoring indices between two groups ( $n = 136, \bar{x} \pm s$ )

Item	Control group	Study group	t	P value
Blink time (h)	15.8 ± 1.1	13.7 ± 1.6	12.613	0.000
Awakening (score)	0.9 ± 0.1	1.8 ± 0.2	46.932	0.000
Extubation time (h)	14.1 ± 1.8	12.4 ± 1.3	-8.938	0.000
Length of resuscitation chamber stay (h)	15.8 ± 2.1	11.6 ± 1.4	-19.412	0.000
Heart rate (times/min)	87.7 ± 10.2	84.1 ± 7.6	-3.305	0.002
Respiratory frequency (times/min)	20.1 ± 2.0	18.7 ± 2.4	-5.226	0.000
Mean arterial pressure (mmHg)	100.8 ± 10.7	95.4 ± 12.4	-3.842	0.001
Pain (score)	8.1 ± 1.3	6.4 ± 1.7	-9.267	0.000

1 mmHg = 0.133 kPa

表3 2组患者麻醉前后脑氧饱和度的比较

Table 3 Comparison of cerebral oxygen saturation before and after anesthesia between two groups ( $n = 136, \%, \bar{x} \pm s$ )

Group	T1	T2	T3	T4
Control	73.10 ± 10.52	72.56 ± 9.80	70.23 ± 11.25	72.47 ± 9.88
Study	73.02 ± 10.04	64.82 ± 9.87	62.03 ± 11.05	69.20 ± 9.47
t	0.06	6.49	6.06	2.78
P	0.95	0.00	0.00	0.01

T1: admission into the operating room; T2: anesthesia preparation; T3: 30 min into operation; T4: end of the operation

表4 2组患者麻醉前后WAIS-RC得分比较

Table 4 Comparison of WAIS-RC test scores before and after anesthesia between two groups ( $n=136$ , score,  $\bar{x} \pm s$ )

Item	Control group			Study group		
	1 d before anesthesia	1 d after anesthesia	3 d after anesthesia	1 d before anesthesia	1 d after anesthesia	3 d after anesthesia
Common sense	21.72 ± 6.49	20.60 ± 5.03	21.21 ± 6.32	21.64 ± 6.33	16.30 ± 4.09 **	18.33 ± 3.28 **
Understanding	19.42 ± 5.11	19.09 ± 4.67	19.37 ± 5.07	19.32 ± 5.04	13.10 ± 3.22 **	15.49 ± 3.05 **
Arithmetics	11.49 ± 3.49	10.03 ± 3.00	11.40 ± 3.26	11.30 ± 3.07	7.24 ± 4.28 **	9.11 ± 2.11 **
Similarity	20.39 ± 7.52	19.11 ± 6.78	20.35 ± 7.44	20.21 ± 7.06	15.32 ± 3.75 **	17.65 ± 4.76 **
Digit span	6.08 ± 2.07	5.89 ± 1.83	6.04 ± 2.53	6.10 ± 2.43	3.17 ± 0.73 **	5.23 ± 2.40 **
Vocabulary	61.47 ± 25.06	60.30 ± 22.11	61.33 ± 24.21	61.25 ± 24.09	65.82 ± 9.76	71.46 ± 9.29
Digit symbol	62.17 ± 14.05	60.08 ± 12.56	62.02 ± 13.62	62.20 ± 13.77	63.25 ± 7.62	70.78 ± 9.88
Filling in the chart	9.17 ± 2.40	9.04 ± 2.04	9.09 ± 2.25	9.22 ± 2.43	6.18 ± 2.15 **	8.22 ± 3.14 **
Block diagram	33.60 ± 11.42	33.11 ± 9.28	33.55 ± 11.39	33.60 ± 11.42	20.46 ± 5.42 **	23.51 ± 6.40 **
Picture arrangement	20.46 ± 6.13	19.24 ± 5.27	20.20 ± 6.02	19.97 ± 6.10	10.45 ± 2.16 **	13.46 ± 2.17 **
Graphic patchwork	21.43 ± 5.08	19.35 ± 4.21	21.39 ± 4.97	21.40 ± 5.21	13.45 ± 4.70 **	15.85 ± 6.46 **

WAIS-RC: Wechsler Adult Intelligence Scale-Revised China. Compared with 1 d before anesthesia, \* $P<0.05$ ; compared with control group, \*\* $P<0.05$ 

### 3 讨论

老年患者POCD的治疗以防控为主,研究人员主张严格管理麻醉过程,选取最佳麻醉药物以降低不良并发症。右美托咪定是一种高度选择性 $\alpha_2$ 受体激动剂,主要作用于脑干发挥镇静和催眠作用,并有一定的神经保护功能<sup>[11]</sup>。因此,我们尝试对右美托咪定和芬太尼两种麻醉药进行复合使用,取得了一定效果,但仍存在一定弊端。

研究发现,右美托咪定复合芬太尼用于老年骨科患者,麻醉前后患者疼痛程度差异显著,研究组患者的疼痛程度明显低于对照组,副作用同其他麻醉药一致,由此说明右美托咪定复合芬太尼适合用于老年骨科患者麻醉。产生作用的原因可能是因为芬太尼为一种超短效的阿片类药物,具有靶控输注可控性好、药物代谢速度快、可减轻患者拔管痛苦的优势而被普遍应用于老年患者的麻醉过程<sup>[12]</sup>。但学者通过研究证实阿片类药物可广泛性地损害脑边缘系统,降低用药对象的认知功能和行为自理能力<sup>[13]</sup>。同时老年患者的焦虑情绪应及时干预,麻醉过程中也应严格执行插管深度和注意拔管手法。

本研究表明,2组患者麻醉前后不同时点认知功能变化明显,但局限于患者麻醉前、后的3 d内。同时,研究组患者的认知变化主要在常识、领悟、算术、相似、数字广度、填图、木块图、图片排列、图形拼凑方面,该结果与张曙报等<sup>[6]</sup>的研究结果总体一致。全麻患者术后认知功能降低一方面可能与芬太尼对脑部的损害有关。芬太尼为强效、高选择性中枢激动药,其对抗交感神经活动的效果较强,因此用药后对患者认知功能的影响将明显强于对照组。另

一方面可能与患者麻醉过程中脑氧饱和度线性降低有关<sup>[14,15]</sup>。老年患者由于心血管系统衰弱,其脑氧供需能力本身有一定下降,另外手术等外界的应激可导致脑氧供需失去平衡。为此,我们通过右美托咪定以减轻患者应激状态下交感神经的兴奋,缓解神经细胞的凋亡速度,发挥脑保护效应,但本研究表明研究组患者麻醉诱导和插管(T2)、手术30 min(T3)、手术结束(T4)3个时点患者脑氧饱和度均低于对照组患者,并在手术30 min时最低。因此,麻醉医生在使用右美托咪定复合芬太尼对患者麻醉时,手术过程中应密切观察并稳定患者的脑氧饱和度,以保障手术麻醉安全。另外,右美托咪定复合芬太尼降低患者认知功能和脑氧饱和度的时限较短,具备一定的用药安全性,可用于老年肱骨干骨折患者。

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(编辑: 王彩霞)