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非阿片类镇痛复合静脉全麻在鼾症手术患者中的疗效 *

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摘要 目的：观察三重措施预防为基础，联合非阿片镇痛药复合静脉全麻在行鼾症手术患者术后恶心呕吐的应用效果。**方法：**选择择期行鼾症手术男性病人 80 例，随机分为两组：吸入麻醉组（inhalation group, IHLA 组）和静脉麻醉组（intravenous group, TIVA 组），每组 40 例，两组均采用三重措施预防恶心呕吐，IHLA 组采用以舒芬太尼为基础复合七氟烷吸入麻醉，TIVA 组以氯胺酮和右美托咪定镇痛基础上丙泊酚全凭静脉麻醉。评估两组病人恶心呕吐危险系数，采用李克特量表（Likert scale），记录并分析两组患者术后 6~8 h 在麻醉后监测治疗室（post anesthesia care unit, PACU）及病房 24 h 恶心呕吐发生情况及补救用药用量。**结果：**两组患者一般临床资料、恶心呕吐风险评分、手术时间、术后恢复期补救用药量人数无显著差异（$P>0.05$）；IHLA 组在 PACU 恶心呕吐发生率为 39.5%，TIVA 组发生率为 18.9%，两者相比有显著性差异（$P<0.05$）；IHLA 组病房 24 h 恶心呕吐严重程度高于 TIVA 组，两组术后需要补救应用抗呕吐药物用量无显著差异（$P>0.05$）。**结论：**以三重措施预防为基础，与吸入麻醉相比，非阿片类镇痛药复合静脉麻醉可以减少肥胖病人鼾症手术术后恶心呕吐发生率和严重程度，降低围术期风险，有利于患者早期恢复。

关键词：三重措施预防；静脉麻醉；吸入麻醉；鼾症手术；恶心呕吐

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The Efficacy of Non-opioid Analgesic Combined Intravenous General Anesthesia in Patients with Snoring Surgery*

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ABSTRACT Objective: To observe the effect of triple measures prevention based on combined non opioid analgesia combined with intravenous anesthesia for postoperative nausea. **Methods:** Eighty male patients scheduled for snoring surgery under general anesthesia were randomly divided into inhalation group (IHLA)and intravenous group (TIVA). The two groups were administered with triple prophylaxis to prevent nausea and vomiting. Group inhalation was treated with sufentanil based compound seven halothane inhalation anesthesia. Group intravenous received ketamine and dexmedetomidine analgesia based on total intravenous anesthesia. The risk factors of nausea and vomiting were assessed in two groups. Likert scale was used to record the incidence of nausea and vomiting in post anesthesia care unit (PACU) and the ward and the dosage of remedial drugs of the two groups. **Results:** There was no significant difference between the two groups in general clinical data, risk score of nausea and vomiting, operation time and number of patients with remedial dosage in recovery period ($P>0.05$). Compared with the IHLA group, the incidence of nausea and vomiting in TIVA group was 18.9%, and there was significant difference between the two groups ($P<0.05$). The severity of nausea and vomiting in group IHLA was still higher than that in group TIVA, and there was no significant difference in the dosage of antiemetic drugs needed in the two groups after operation($P>0.05$). **Conclusion:** On the basis of triple measures prevention, non opioid analgesics combined with intravenous anesthesia can reduce the incidence and severity of nausea and vomiting after the operation of snoring patients in obese patients, reduce perioperative risk, and facilitate early recovery of patients.

Key words: Triple measures prevention; Intravenous anesthesia; Inhalation anesthesia; Snoring surgery; Nausea and vomiting

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前言

鼾症术后气管导管拔除时间延迟导致麻醉时间延长 6~8 h，易增加术后恶心呕吐（postoperative nausea and vomiting, PONV）发生率，同时，研究显示耳鼻喉科头颈咽部手术、心脏手术、睡眠呼吸暂停综合征、肥胖等因素与 PONV 的发生具有一定的相关性[1-3]。PONV 的发生导致腹压增高，增加苏醒期气管导管脱出等意外事件的风险，加重手术区域肿胀，延迟术后

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恢复[4,5]。由于 PONV 发生多重因素的影响，目前提倡多种药物预防治疗，有报道尽管应用地塞米松，恩丹西酮和东莨菪碱为基础的三重 PONV 预防治疗，约 31.7% PONV 高危病人仍需要抗呕吐补救治疗（antiemetic rescue medication，AERM）[6]。也有研究发现，右美托咪啶和氯胺酮可以有效地减少或替代芬太尼在术中的应用 [7]，应用芬太尼维持全凭静脉麻醉可以降低 PONV 风险[8]，而静脉应用阿片类镇痛增加 PONV 风险[9]，降低阿片类镇痛药物用量。因此，本研究以三重措施预防为基础，对比阿片类复合吸入麻醉下全麻与非阿片类镇痛复合静脉全麻下 PONV 发生情况，研究报道如下。

1 资料与方法

1.1 一般资料

本研究经西安交通大学第二附属医院医学伦理会批准，选择 2017 年 8 月 -2017 年 12 月择期行鼾症手术，颚咽成型 + 舌根切除术男性病人 80 例，所有患者均签署麻醉知情同意书，美国麻醉医师协会（American Society of Anesthesiologists, ASA）评分[10]I-II 级。排除标准：术前服用阿片类药物控制的慢性疼痛；对术中应用麻醉药过敏；合并高血压、糖尿病、消化性溃疡。其中 5 例病人不符合研究方案，其中 IHAL 组 2 例病人对一种或几种研究用药过敏，TIVI 组有 2 例病人术中复合吸入七氟烷，1 例病人合并慢性恶心呕吐。采用随机的原则，将其分为吸入麻醉组（IHLA 组）和静脉麻醉组（TIVA 组），两组分别 38 例，37 例。两组患者的年龄、体重指数（body mass index, BMI）、手术、麻醉及麻醉后监测治疗室（PACU）停留时间、术中输液量比较差异无统计学意义（P>0.05）（表 1）。

表 1 两组患者一般资料的比较（$\bar{x}\pm s$）

Table 1 The general data comparison in two groups（$\bar{x}\pm s$）

General data	IHAL group (n=38)	TIVA group (n=37)
Age (Year)	36.6± 8.4	34.5± 9.7
BMI(kg·m^{-2})	32.72± 5.67	31.11± 6.21
Operative time(min)	121.4± 14.2	119.6± 13.7
Anesthesia time(min)	157.4± 18.7	149.6± 15.2
Retention time in PACU(min)	251.6± 47.6	267.5± 51.9
Intraoperative infusion volume(mL)	1020.8± 97.1	972.5± 82.6

1.2 麻醉方法

所有病人术前未服用任何药物。入室后开放静脉通路，监测无创血压、脉搏氧饱和度（saturation pulse oxygen, SpO_2），心电图。给予病人预充氧 SpO_2>93%且不能再升高开始行麻醉诱导。IHLA 组麻醉诱导应用咪达唑仑 0.5 mg·kg^{-1} 和舒芬太尼 0.3~0.6 μg 镇静镇痛，七氟烷吸入维持麻醉最低肺泡浓度达到 0.7~1.3，麻醉医生根据手术需要间断静注舒芬太尼或瑞芬太尼。TIVA 组诱导前泵注右美托咪啶 0.5 μg·kg^{-1}·h^{-1} 10 min，麻醉维持持续泵注右美托咪定 0.1~0.3 μg·kg^{-1}·h^{-1}，丙泊酚 4~8 mg·kg^{-1}·h^{-1} 保持脑电双频指数（bispectral, BIS）在 40~60 之间，手术开始前静注氯胺酮 0.3 mg·kg^{2}。两组均采用丁卡因充分表麻下纤支镜引导下经鼻插管，插管时静注丙泊酚 2-2.5 mg·kg^{-1}，罗库溴铵 0.5~1.0 mg·kg^{-1}，插管后 10 min 静注酮咯酸氨丁三醇 30 mg，间断静注罗库溴铵 10~20 mg 为外科手术提供良好的肌松条件。所有病人采用 60%氧浓度行机械通气，根据测定呼末 CO_2 浓度调整呼吸参数。所有病人行三重预防恶心呕吐治疗：麻醉诱导前 15 min 肌注东莨菪碱 0.3 mg，诱导后 10 min 静注 4 mg 地塞米松，手术结束前约 20 min 给予静注 4 mg 托烷司琼。所有病人阿片类药物以实际体重给药，余麻醉用药皆按体重计算用药，均由三位工作 5 年以上麻醉医生完成。

1.3 PONV 预防及治疗

手术结束后送至 PACU 继续监测患者一般生命体征，按照前述 1.2 中方法轻度镇静，以耐受气管插管为标准，观察 6~8 h 直至协助耳鼻喉科医生拔除气管导管。在 PACU 病人发生 PONV 给予氟哌利多 0.6 mg 或异丙嗪 6 mg 静注。病人离开 PACU 返回病房发生 PONV 静注 4 mg 托烷司琼或 6~10 mg 异丙嗪。术后应用（visual analog scales, VAS）评分进行疼痛评估，采用多模式镇痛措施，术后 24 h 内给予酮咯酸氨丁三醇 30 mg·6 h^{-1}，发生难以忍受的疼痛给予患者口服羟考酮 20 mg。病人发生恶心呕吐，补救措施的选择由麻醉医生判断。

1.4 观察指标

收集患者 PONV 风险因素，手术、麻醉及 PACU 停留时间，分别于 PACU 及病房 24 h，应用 VAS 评分 [11] 评估患者 PONV 程度（无，轻度，中度，重度），记录发生例数及抗呕吐药物用量，术后疼痛程度 VAS 评分及阿片类药物用量。

1.5 统计学分析

采用 SPSS22.0 统计软件进行分析，计量资料以 $\bar{x}\pm s$ 表示，计量资料的组间比较检查方差齐性后采用非配对独立样本 t 检验进行统计分析，组间率的比较采用 x^2 或 Fisher 精确检验，非正态分布资料采用 Wilcoxon 计量和等级资料秩和检验，以 P<0.05 为差异具有统计学意义。

2 结果

2.1 PONV 风险评估比较

参考 PONV 风险评估方法 [12]，1~4 分分别针对年龄 <50 岁，非吸烟，PONV 史或晕动病，术后应用阿片类药物。所有病人 PONV 风险评估中没有 0 分，只有 1 个病人是 1 分。所有病人被要求术前禁烟。两组间 PONV 风险系数无显著差异（P>0.05）（表 2）。

表 2 两组患者 PONV 风险评估比较[例(%)]

Table 2 Comparison of PONV risk assessment between the two groups [n(%)]

PONV risk assessment	IHAL group (n=38)	TIVA group (n=37)
1	1(2.6)	0(0)
2	25(65.8)	24(64.9)
3	9(23.7)	9(24.3)
4	3(7.9)	4(10.8)

Note: Test results: (z=0.523, *P*=0.619).

2.2 PONV 及需要补救人数的比较

IHAL 组在 PACU 恶心呕吐发生率为 39.5%,TIVA 组发生率为 18.9%,两组相比有显著差异(*P*＜0.05)。两组于 PACU 及病房需要补救及 PONV 发生病例数没有显著差异(*P*>0.05)(表3)。

表 3 两组患者术后发生恶心呕吐及需要补救人数比较[例(%)]

Table 3 Comparison of postoperative nausea and vomiting and the number of patients in need of remedy between the two groups [n (%)]

	IHAL group (n=38)	TIVA group (n=37)
AERMPACU	13(34.2)	7(18.9)
AERM ward	8(21.1)	3(8.1)
PONV PACU	15(39.5)	6(16.2)*
PONV ward	11(28.9)	5(13.5)

Note: compared with ihal group, **P*<0.05.

2.3 两组恶心呕吐程度及发生率的比较

IHLA 组于病房 24 h 恶心呕吐严重程度高于 TIVA 组 IHAL 组,发生干呕发生率高,所有发生干呕的病人均发生严重恶心,两组间 PONV 严重程度有差异(*P*＜0.05)(表 4)。

表 4 两组患者恶心呕吐严重程度及发生率的比较[例(%)]

Table 4 Comparison of the severity and incidence of nausea and vomiting between the two groups [n (%)]

Severity of PONV	IHAL group (n=38)	TIVA group (n=37)
No	21 (55.3)	29 (78.4)
Mild	8 (21.1)	5 (13.5)
Moderate	3 (7.9)	2 (5.4)
Severe	6 (15.8)	1 (2.7)
Retch	6 (15.8)	0 (0)*
Vomit	5 (13.2)	0(0)#

Note: compared with ihal group, **P*<0.05; compared with ihal group, #*P*<0.05.

2.4 术后补救药物用量及不良反应的比较

两组术后抗呕吐治疗用药及剂量无显著差异,无病例发生术后躁动,在 PACU 1 例病人发生低血压,另 1 例病人发生需要治疗心动过缓,两组疼痛 VAS 评分无显著性差异,观察期间病人无不良事件发生(表 5)。

表 5 两组术后补救药物用量及疼痛 VAS 评分的比较($\bar{x}\pm s$)

Table 5 Comparison of the dosage of remedial drugs and VAS score of pain between the two groups($\bar{x}\pm s$)

remedial drugs and VAS score	IHAL group(n=38)	TIVA group(n=37)
Droperidol(mg)	0.33± 0.004	0.25± 0.008
Tropisetron(mg)	2.21± 0.18	2.34± 0.37
Promethazine(mg)	3.62± 0.41	3.06± 0.46
VAS score	2.8± 0.3	2.4± 0.5

3 讨论

PONV 的防治是术后快速康复的重要组成部分[13-15],病人在医院的主观体验和不良反应的观察处理直接影响到病人的

住院体验，有报道 PONV 在高危险因素手术的发生率高达 80%,应用单种或多种抗呕吐药物将发生率下降到 10%~50%[16,17]，长期以来 PONV 一直是麻醉医生关注的重点。恶心和呕吐的发生是由高级皮层中枢受到刺激后激活呕吐中枢,尤其是前庭中枢和脑干中枢再通过化学感受器触发中心发生的一系列不良感受[18-20]。外周与 PONV 相关的有 5-HT3 受体、毒蕈碱受体、多巴胺受体和组胺受体等，糖皮质激素地塞米松的抗 PONV 作用与托烷司琼等效,可能作用于化学感受器触发区、α- 肾上腺素能受体和抗炎等作用有关[21,22]。尽管如此,目前还未发现单一敏感因素或具体评估 PONV 风险因素或并全方位预防 PONV 的发生的相关研究。

有研究发现,肥胖病人中枢阿片类受体降低,外周 β- 内啡肽水平增高,肠外周阿片类受体的激活与 PONV 有关[23-25],非阿片类镇痛药物氯胺酮是 N- 甲基 -D- 天门冬氨酸（N-methyl-D-aspartate,NMDA）受体拮抗剂,作为静脉麻醉药有强镇痛作用[26],在本研究中与右美托咪定合用可以降低其引起的交感神经过度兴奋,协同镇痛。以此为基础,观察托烷司琼、东莨菪碱和地塞米松作为 PONV 的三重预防基础,术后补救用药采用氟哌利多和异丙嗪,通过多途径预防并补救 PONV 的发生,对比阿片类复合吸入麻醉下全麻与非阿片类镇痛复合静脉全麻下 PONV 发生情况,研究发现:在 PACU 中吸入麻醉组 PONV 发生率为 39.5%，与静脉麻醉组 18.9%有显著差异,术后补救治疗用药量和人数无显著差异,考虑在早期术后恢复时间内,给予了积极的干预处理治疗;术后 24 h 在病房发生的 PONV 严重程度,吸入麻醉组仍高于静脉麻醉组,术后补救治疗用药量和人数仍无显著差异，考虑吸入麻醉方式在 PONV 发生中起主要作用。

本研究观察两组鼾症手术病人，术前 PONV 危险因素具有可比性,尽管在三重 PONV 预防基础上,吸入麻醉组 34.2% 在 PACU 和 21.1%病房的病人仍然需要术后补救治疗,避免应用吸入麻醉药和静脉应用阿片类药物降低 PONV 危险系数 RR(44.7%),有报道全凭丙泊酚静脉麻醉降低 PONV 危险系数为 RR(19%)[27],本研究结果除了与避免应用静脉阿片类药物有关,更可能是静脉麻醉组应用了右美托咪定和氯胺酮,这两种药物是否超过了阿片类药物的减少所带来的抗呕吐作用,右美托咪定和氯胺酮可能具有抗呕吐作用,也有类似的报道[28-30]。本研究未设计去降低补救措施的控制,这可能会引起研究人员给予 PONV 更多的关注和处理，但静脉麻醉组 PONV 发生率的降低并没有导致两组之间术后补救例数的差异。

本研究有一定的局限性,所有随机入组的病人,完成研究的患者均接受了允许的干预,这降低了 1 类错误的发生,对所有受试者的盲法可以增加数据的有效性,但手术及恢复过程中由于干预措施和药物的应用不可避免导致对研究者的非盲。综上所述,以三重预防为基础,与阿片类吸入麻醉组相比,非阿片类药物复合静脉麻醉在肥胖病人进行鼾症手术，可以降低 PONV 发生率和严重程度,降低围术期风险,有利于早期恢复。

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