氢吗啡酮替代吗啡改善术后镇痛的效能

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摘　要:【目的】调研氢吗啡酮应用于术后镇痛的效能。【方法】择期 ASA Ⅰ-Ⅱ级肝胆或胃肠开腹手术 120 例,手术后随机双盲等分为 4 组,每组 30 例,根据术后镇痛方法分为静脉氢吗啡酮组(VH)、静脉吗啡组(VM)、硬膜外氢吗啡酮组(EH)、硬膜外吗啡组(EM)。VH 组首剂量生理盐水 5 mL+氢吗啡酮 0.4 mg,维持为生理盐水 100 mL+氢吗啡酮 3.6 mg;VM 组首剂量生理盐水 5 mL+吗啡 2 mg, 维持为生理盐水 100 mL+吗啡 18 mg;EH 组首剂量 0.25%罗派卡因 5 mL+氢吗啡酮 0.4 mg,维持为 0.125%罗派卡因 100 mL+氢吗啡酮 1.6 mg;EM 组首剂量 0.25%罗派卡因 5 mL+吗啡 2 mg,维持为 0.125%罗派卡因 100 mL+吗啡 8 mg,所有镇痛泵速度 2 mL/h,镇痛 48 h。围术期监测呼吸、循环、镇静、镇痛效果及不良反应。【结果】所有患者均顺利完成手术安返病房,术后镇痛满意度达 98%,Ramsey 镇静评分均为 2~3 分,属于满意镇静。VH 组镇痛后 12 h、24 h、48 h 时与镇痛前 SPO_2 比较下降,$P < 0.05$;VM 组镇痛后 2 h SpO_2 较镇痛前下降,$P < 0.05$;VH 组镇痛后 48 h R-VAS 评分较镇痛后 6 h 下降,$P < 0.05$;VH 组镇痛后 24 h、48 h M-VAS 评分较镇痛后 2 h、6 h 下降,$P < 0.05$;VM 组镇痛后 6 h M-VAS 评分较镇痛后 2 h 下降,$P < 0.05$。EH 组镇痛后 2、6、12、24、48 h 较镇痛前 SBP 下降,$P < 0.05$;EH 组镇痛后 12、24、48 h 较镇痛前 HR 增快,$P < 0.05$;EH 组镇痛后 6、12、24、48 h 较镇痛前 SPO_2 下降,$P < 0.05$;EH 组镇痛后 48 h M-VAS 评分较镇痛后 2 h 下降,$P < 0.05$。EH 组镇痛后 24 h、48 h 时 DBP 较 VH 组下降,$P < 0.05$;VH 组镇痛后 12 ~ 48 h SpO_2 较镇痛前下降,$P < 0.05$。四组术后恶心、呕吐的发生率无明显差异($P < 0.05$),硬膜外用药组瘙痒发生率均高于静脉用药组,$P < 0.05$;EM 组和 VH 组嗜睡发生率均多于 EH 组,$P < 0.05$;EM 组和 VM 组头晕发生率分别多于 EH 组和 VH 组,$P < 0.05$。【结论】氢吗啡酮可以代替吗啡,无论静脉与硬膜外应用都能取得良好的术后镇痛效果,氢吗啡酮的副作用相对少于吗啡,值得临床推广应用。

关键词:氢吗啡酮;术后镇痛;硬膜外;静脉
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Efficacy of Morphine Rotation to Hydromorphone in Postoperative Analgesia

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Abstract:【Objective】To investigate the efficacy of hydromorphone in postoperative analgesia.【Methods】Selected 120 patients undergoing hepatobiliary or gastrointestinal surgery of ASA I~II levels ,were randomly and double-blindly divided into four groups (n = 30 each): VH group patients were treated by a bolus dose of normol saline 5 mL and hydromorphone 0.4 mg, continuously intravenous infusion with normal saline 100 mL and hydromorphone 3.6 mg; VM group were treated by a bolus dose normol saline 5 mL and morphine 2 mg, continuously intravenous infusion with normal saline 100 mL and morphine 18 mg; EH group were treated by a bolus dose of 0.25% ropivacaine 5 mL and hydromorphone 0.4 mg, continuously epidural pumping with 0.125% ropivacaine 100 mL and hydromorphone 1.6 mg; EM group were treated by a bolus does 0.25% ropivacaine 5 mL and morphine 2 mg, continuously epidural pumping with 0.125% ropivacaine 100 mL and morphine 8mg. All the analgesia pump speed 2 mL/h during 48 h. Then the respiration, circulation, sedation, pain scores and side effects were perioperatively monitored in all groups.【Result】Postoperative analgesia satisfaction reached 98%. Ramsey's Sedation Scales are 2-3 scores belong to satisfied with sedation. SpO_2 was significantly

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lower at 12, 24, 48 h after analgesia than that before analgesia in VH group ($P < 0.05$); SpO_2 was significantly lower at 2 h after analgesia than that before analgesia in VM group ($P < 0.05$); R-VAS was significantly lower at 48 h than that at 6h after analgesia in VH group ($P < 0.05$); M-VAS was significantly lower at 24 h, 48 h than that at 2 h, 6 h after analgesia in VH group ($P < 0.05$); M-VAS was significantly lower at 6h than that at 2h after analgesia in VM group ($P < 0.05$); Compared with SBP before analgesia, there was significantly decrement at 2, 6, 12, 24, 48 h after analgesia in EH group ($P < 0.05$); HR was significantly higher at 12, 24, 48 h after analgesia than that before analgesia in EH group ($P < 0.05$); SpO_2 was significantly lower at 6, 12, 24, 48 h after analgesia than that before analgesia in EH group ($P < 0.05$); M-VAS was significantly lower at 48 h than that at 2 h after analgesia in EH group ($P < 0.05$); Compared with DBP of VH group, there was significantly decrement at 24 h,48 h after analgesia in EH group ($P < 0.05$). There was no signify difference in the rate of nausea and vomiting among four group ($P > 0.05$). The incidence of pruritus in epidural group was higher than that in patients with intravenous administration ($P < 0.05$). The rate of drowsiness in EM group and VH group was higher than that of EH group ($P < 0.05$). The rate of dizzy in EM group and VM group was respectively higher than that of EH group and VH group ($P < 0.05$).【Conclusion】This study found hydromorphone to be at least as effective as morphine when delivered by continuous intravenous or epidural infusion in postoperative analgesia, and side effects may be less.

Key words: hydromorphone; postoperative analgesia; epidural; venous

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吗啡作为阿片类药物的代表一直被广泛应用于癌性疼痛和术后镇痛，但副作用仍令人担忧。减少吗啡的剂量,降低副作用,寻找替代药物是当前术后镇痛临床研究的热点[1]。盐酸氢吗啡酮(hydromorphone)是半合成阿片类药物,作为一种强效阿片类镇痛药物,在临床上已有 80 余年的历史。它通过激动中枢神经系统 μ-阿片类受体起作用,由于在化学结构上的变化,其在理化性质、临床镇痛应用等方面均优于传统吗啡。现在越来越多的文献报道其用于术后镇痛较吗啡更有优势[2]，临床随机对照试验也表明不良反应较吗啡有更多的改善[3],但对于盐酸氢吗啡酮的临床研究仍缺少各科不同手术完整的镇痛资料，仅在个别手术(如产科、骨科、心胸外科)的临床观察中有所研究[4-6]。为了了解更多关于盐酸氢吗啡酮在麻醉和镇痛作用上的优势，需要更多的临床随机对照试验，以达到更加安全有效且不良反应少的镇痛效果。因此,我们设计了随机对照临床研究,观察氢吗啡酮术后镇痛的整体情况，为其临床应用提供理论依据。

1 材料与方法

1.1 材 料

选择我院 2013 年 4 月至 2015 年 3 月开腹手术患者 120 例,主要为肝胆及胃肠手术种类,ASA Ⅰ-Ⅱ 级,术前未有相关的镇痛治疗。手术后以计算机产生随机数字的方法随机等分为 4 组，每组 30 例、静脉氢吗啡酮组(VH)、静脉吗啡组(VM)、硬膜外氢吗啡酮组(EH)、硬膜外吗啡组(EM);配药由研究助理实施,对术者和患者双盲。本研究已获医院伦理委员会批准(批准号 201308),在治疗前向患者或家属告知可能出现的疗效及副作用并签署知情同意书。

1.2 方 法

1.2.1 常规用药 所有的患者常规使用术前用药,苯巴比妥钠 0.1 g,东莨菪碱 0.3 mg 肌注。入室后开放外周和中心静脉通路，围术期监测 BP、HR、ECG、SpO_2 和 $P_{ET}CO_2$。硬膜外组患者采用手术部位相应间隙穿刺置钢丝硬膜外导管。麻醉诱导丙泊酚 2 mg/kg，芬太尼 4 μg/kg，顺阿曲库铵 0.25 mg/kg，麻醉维持为静脉输注瑞芬太尼 0.1 ~ 0.15 μg/(kg·min)，丙泊酚 2 mg/(kg·h),1.5% ~ 2%七氟醚吸入，维持 Narcotrend 脑电指数 30 ~ 45,间断追加顺阿曲库铵 0.1 mg/kg 麻醉维持。气管插管后行机械通气，设定 VT 8 ~ 10 mL/kg,RR 12 min^{-1},吸呼比 1:2,氧流量 1.5 ~ 2 L/min。手术结束前 30 min 静注凯纷（氟比洛芬酯注射液)50 mg,长效止吐药(帕洛诺司琼)0.25 mg,地塞米松 5 mg。手术结束时停所有麻醉药物,评估安全后拔除气管导管,拔管指征:呼之睁眼,自主呼吸恢复,RR 12 ~ 20 min^{-1},VT > 8 mL/kg,呼吸空气 $SpO_2 \geqslant 94\%$。拔除气管导管后 5 min 给予术后镇痛首剂量药物,随后连接镇痛泵维持 48 h,镇痛泵给药速度 2 mL/h,患者留观 PACU 30 ~ 60 min。

1.2.2 各组术后镇痛配方 VH 组首剂量生理盐水 5 mL+氢吗啡酮 0.4 mg，维持为生理盐水 100 mL+氢吗啡酮 3.6 mg,持续泵 2 mL/h,镇痛 48 h。

VM组首剂量生理盐水 5 mL+吗啡 2 mg,维持为生理盐水 100 mL+吗啡 18 mg,持续泵 2 mL/h,镇痛 48 h。EH 组首剂量 0.25%罗派卡因 5 mL+氢吗啡酮 0.4 mg, 维持为 0.125%罗派卡因 100 mL+氢吗啡酮 1.6 mg,持续泵 2 mL/h,镇痛 48 h。EM 组首剂量 0.25%罗派卡因 5 mL+吗啡 2 mg, 维持为 0.125%罗派卡因 100 mL+吗啡 8 mg, 持续泵 2 mL/h,镇痛 48 h。镇痛不全补救方法为病房静注凯纷 50 mg,每日 2 次。

1.2.3　研究药品来源　盐酸吗啡注射液 10 mg/mL,东北制药集团沈阳第一制药有限公司,批号:120909-2。盐酸氢吗啡酮注射液（锐宁)2 mL(2 mg),宜昌人福医药有限公司,批号:1141001。盐酸罗哌卡因注射液 10 mL（100 mg),Astrazene Co. Sweden,批号:650075-77。

1.2.4　监测记录项目　记录首剂量镇痛前和镇痛后 2、6、12、24、48 h 不同时间静息及翻身运动 VAS 疼痛评分,Ramsey 镇静评分, 呼吸、循环情况,随访术后恶心、呕吐、瘙痒等不良反应,调查镇痛患者满意度(满意、一般、较差)。

1.2.5　统计分析　采用 SPSS 16.0 软件进行统计分析。计量资料以均数±标准差($\bar{x} \pm s$)表示,组间比较采用单因素方差分析, 计数资料比较采用 χ^2 检验,以 $P < 0.05$ 为有统计学意义。

2　结　果

2.1　患者一般情况

所有患者均顺利完成手术安返病房, 术后镇痛满意度达 98%,Ramsey 镇静评分均为 2 ~ 3 分,属于满意镇静, 表现安静合作, 或嗜睡能听从指令。4 组一般资料见表 1,资料数据比较无统计学意义($P > 0.05$,表 1)。

2.2　静脉氢吗啡酮与静脉吗啡的镇痛效能比较

VH 组与 VM 组监测数据比较见表 2。VH 组镇痛后 12、24、48 h 时与镇痛前 SPO_2 比较下降,$P < 0.05$;VM 组镇痛后 2 h SpO_2 较镇痛前下降,$P < 0.05$;VH 组镇痛后 48 h R-VAS 评分较镇痛后 6 h 下降,$P < 0.05$;VH 组镇痛后 24、48 h M-VAS 评分较镇痛后 2 h 下降,$P < 0.05$;VH 组镇痛后 24、48 h M-VAS 评分较镇痛后 6 h 下降,$P < 0.05$;VM 组镇痛后 6 h M-VAS 评分较镇痛后 2 h 下降,$P < 0.05$。

2.3　硬膜外氢吗啡酮与硬膜外吗啡镇痛效能比较

EH 组与 EM 组监测数据比较见表 3。EH 组镇痛后 2、6、12、24、48 h 较镇痛前 SBP 下降,$P < 0.05$;EH 组镇痛后 12、24、48 h 较镇痛前 HR 增快,$P < 0.05$;EH 组镇痛后 6、12、24、48 h 较镇痛前 SpO_2 下降,$P < 0.05$;EH 组镇痛后 48 h M-VAS 评分较镇痛后 2 h 下降,$P < 0.05$。

2.4　静脉氢吗啡酮与硬膜外氢吗啡酮镇痛效能比较

VH 组与 EH 组监测数据比较见表 4。 EH 组镇痛后 2 ~ 48 h 时 SBP 均下降,$P < 0.05$;EH 组镇痛后 24 h、48 h 时 DBP 较 VH 组下降,$P < 0.05$;VH 组镇痛后 12 ~ 48 h SpO_2 较镇痛前下降,$P < 0.05$。

2.5　四组镇痛的不良反应的比较

各组不良反应比较见表 5。EM 组瘙痒发生率高于 VM 组,$P < 0.05$;EH 组瘙痒发生率也高于 VH 组,$P < 0.05$;EM 组嗜睡发生率多于 EH 组,$P < 0.05$;VH 组嗜睡发生率也多于 EH 组,$P < 0.05$;EM 组头晕发生率多于 EH 组,$P < 0.05$;VM 组头晕发生率也多于 VH 组,$P < 0.05$。

表 1　四组一般资料比较

Table 1　Descriptive data of 4 groups　　($\bar{x} \pm s$)

Group(n = 30)	VM	VH	EM	EH
Gender(M/F)	13/17	15/15	10/20	11/19
Age/years	54.8 ± 10.7	55.9 ± 7.6	60.3 ± 10.8	56.4 ± 11.2
Body mass/kg	56.3 ± 8.4	53.6 ± 8.8	55.0 ± 9.1	54.7 ± 7.6
Height/cm	163.2 ± 9.2	161.3 ± 10.1	164.8 ± 5.6	165.3 ± 8.7
Operation time/min	162 ± 28	158 ± 31	153 ± 38	163 ± 29
Anesthesia time/min	175 ± 29	168 ± 41	166 ± 46	172 ± 46
Remedial dose of Flurbiprofen/mg	6.7 ± 5.3	8.3 ± 6.1	5.0 ± 4.5	8.3 ± 6.1

All measurements, $P > 0.05$ among 4 groups

表 2 VH 组与 VM 组监测数据比较

Table 2 Comparison of data between VH group and VM group ($\bar{x} \pm s$)

Item	Group(n = 30)	Before analgesia	2 h later	6 h later	12 h later	24 h later	48 h later
SBP/mmHg	VH	119.7 ± 9.8	113.3 ± 11.5	116.4 ± 9.2	116.5 ± 9.1	115.8 ± 8.2	116.8 ± 9.2
	VM	116.4 ± 13.5	112.0 ± 9.3	112.3 ± 8.7	112.8 ± 11.8	116.7 ± 7.5	117.0 ± 9.2
DBP/mmHg	VH	75.5 ± 11.7	72.0 ± 7.2	70.4 ± 3.9	74.6 ± 6.5	74.9 ± 7.0	75.8 ± 6.9
	VM	73.8 ± 2.1	72.2 ± 5.8	73.6 ± 3.4	71.4 ± 6.2	72.3 ± 6.3	72.4 ± 4.9
HR/min^{-1}	VH	79.3 ± 10.6	77.7 ± 7.2	78.7 ± 7.3	80.7 ± 7.1	80.8 ± 7.0	79.3 ± 6.4
	VM	79.2 ± 8.0	80.1 ± 8.4	80.0 ± 8.9	80.6 ± 8.3	82.2 ± 7.8	81.3 ± 7.3
SPO_2/%	VH	99.2 ± 1.0	98.0 ± 1.2	98.3 ± 0.7	97.7 ± 1.1[1)]	97.8 ± 0.6[1)]	97.8 ± 0.6[1)]
	VM	98.4 ± 0.9	97.0 ± 1.0[2)]	97.9 ± 0.7	97.7 ± 1.0	97.3 ± 1.3	97.6 ± 0.7
RR/min^{-1}	VH	16.8 ± 1.6	17.2 ± 2.2	17.7 ± 2.2	17.8 ± 1.6	17.1 ± 1.4	17.6 ± 1.4
	VM	17.3 ± 1.3	17.3 ± 1.5	18.3 ± 1.3	17.4 ± 1.5	17.7 ± 1.2	17.6 ± 1.8
R-VAS	VH	0.0 ± 0.0	1.0 ± 0.5	1.2 ± 0.8	0.9 ± 0.7	0.8 ± 0.6	0.5 ± 0.5[3)]
	VM	0.0 ± 0.0	0.9 ± 0.6	1.3 ± 0.7	1.3 ± 0.7	1.2 ± 0.7	0.9 ± 0.9
M-VAS	VH	0.0 ± 0.0	1.9 ± 0.6	2.0 ± 0.5	1.8 ± 0.6	1.4 ± 0.5[4)5)]	1.1 ± 0.7[4)5)]
	VM	0.0 ± 0.0	1.6 ± 0.5	2.0 ± 0.5[6)]	1.9 ± 0.6	1.7 ± 0.5	1.3 ± 0.7

1) compared with SpO_2 before analgesia in VH group, $P < 0.05$; 2) compared with SpO_2 before analgesia in VM group, $P < 0.05$; 3) compared with R-VAS at 6 h after analgesia in VH group, $P < 0.05$; 4) compared with M-VAS at 2 h after analgesia in VH group ,$P < 0.05$; 5) compared with M-VAS at 6h after analgesia in VH group, $P < 0.05$;6) compared with M-VAS at 2 h after analgesia in VM group, $P < 0.05$.

表 3 EH 组与 EM 组监测数据比较

Table 3 Comparison of data between EH group and EM group ($\bar{x} \pm s$)

Item	Group(n = 30)	Before analgesia	2 h later	6 h later	12 h later	24 h later	48 h later
SBP/mmHg	EH	118.8 ± 10.2	110.5 ± 10.8[1)]	110.8 ± 10.5[1)]	111.5 ± 14.0[1)]	109.1 ± 15.2[1)]	109.7 ± 14.0[1)]
	EM	121.7 ± 10.9	117.7 ± 11.1	119.7 ± 7.4	113.9 ± 10.4	112.4 ± 13.1	108.6 ± 12.2
DBP/mmHg	EH	68.7 ± 9.9	65.2 ± 8.3	66.0 ± 6.6	67.3 ± 10.0	64.7 ± 12.6	66.5 ± 10.6
	EM	65.4 ± 11.3	66.3 ± 6.0	63.4 ± 8.9	65.4 ± 8.9	64.0 ± 10.8	63.6 ± 8.0
HR/min^{-1}	EH	75.5 ± 11.5	76.6 ± 7.1	81.0 ± 4.3	82.1 ± 6.5[2)]	83.1 ± 7.[92)]	82.2 ± 7.3[2)]
	EM	78.9 ± 7.7	80.4 ± 6.1	79.9 ± 9.8	82.1 ± 7.4	81.4 ± 10.1	81.9 ± 6.8
SPO_2/%	EH	99.0 ± 1.5	98.1 ± 1.4	97.7 ± 0.7[3)]	97.7 ± 1.7[3)]	97.1 ± 1.2[3)]	97.9 ± 0.7[3)]
	EM	98.7 ± 1.9	97.9 ± 1.6	98.1 ± 0.9	99.1 ± 0.9	98.6 ± 1.0	98.1 ± 1.1
RR/min^{-1}	EH	16.3 ± 1.6	17.4 ± 1.5	17.1 ± 2.1	17.5 ± 1.7	17.2 ± 1.3	17.1 ± 1.2
	EM	17.0 ± 2.3	17.6 ± 1.7	18.1 ± 1.4	18.2 ± 1.1	17.6 ± 1.0	17.7 ± 1.6
R-VAS	EH	0.0 ± 0.0	1.0 ± 0.0	1.1 ± 0.7	1.1 ± 0.9	1.1 ± 0.7	1.1 ± 0.4
	EM	0.0 ± 0.0	1.0 ± 0.0	1.1 ± 0.7	1.1 ± 0.9	1.1 ± 0.7	1.1 ± 0.4
M-VAS	EH	0.0 ± 0.0	2.0 ± 0.7	1.7 ± 0.7	1.8 ± 0.6	1.60 ± 0.5	1.4 ± 0.5[4)]
	EM	0.0 ± 0.0	2.0 ± 0.6	2.3 ± 0.5	2.0 ± 1.2	2.0 ± 0.8	1.7 ± 0.5

1) compared with SBP before analgesia in EH group, $P < 0.05$; 2) compared with HR before analgesia in EH group, $P < 0.05$;3) compared with SpO_2 before analgesia in EH group, $P < 0.05$; 4)compared with M-VAS at 2 h after analgesia, $P < 0.05$.

3 讨 论

阿片类药是最具有潜能的治疗疼痛的中枢性镇痛剂,自从脊髓阿片受体发现以来,脊髓阿片类药广泛用于临床实践中，人们一直希望有良好的镇痛效果，较少的副作用 ，而不像静脉应用时出现较多副作用。实验研究表明,脊髓周围应用阿片类水溶性药物,具有较高的选择性,如吗啡。近来的文献也推荐选择硬膜外应用氢吗啡酮，其也有中间药代动力学特点,同时推荐氢吗啡酮代替吗啡应用于术后镇痛，特别有改善患者心情的益处[7]。

表 4　VH 组与 EH 组监测数据比较

Table 4　Comparison of data between VH group and EH group　($\bar{x} \pm s$)

Item	Group(n = 30)	Before analgesia	2 h later	6 h later	12 h later	24 h later	48 h later
SBP/mmHg	VH	119.7 ± 9.8	113.3 ± 11.5	116.4 ± 9.2	116.5 ± 9.1	115.8 ± 8.2	116.8 ± 9.2
	EH	118.8 ± 10.2	110.5 ± 10.8[1)]	110.8 ± 10.5[1)]	111.5 ± 14.0[1)]	109.1 ± 15.2[1)]	109.7 ± 14.0[1)]
DBP/mmHg	VH	75.5 ± 11.7	72.0 ± 7.2	70.4 ± 3.9	74.6 ± 6.5	74.9 ± 7.0	75.8 ± 6.9
	EH	68.7 ± 9.9	65.2 ± 8.3	66.0 ± 6.6	67.3 ± 10.0	64.7 ± 12.6[2)]	66.5 ± 10.6[2)]
HR/min^{-1}	VH	79.3 ± 10.6	77.0 ± 7.2	78.7 ± 7.3	80.7 ± 7.1	80.8 ± 7.7	79.3 ± 6.4
	EH	75.5 ± 11.5	76.6 ± 7.1	81.0 ± 4.3	82.1 ± 6.5	83.1 ± 7.9	82.2 ± 7.3
SPO_2/%	VH	99.2 ± 1.0	98.0 ± 1.2	98.3 ± 0.7	97.5 ± 1.1[3)]	97.8 ± 0.6[3)]	97.8 ± 0.5[3)]
	EH	99.0 ± 1.5	98.1 ± 1.4	97.7 ± 0.7	97.7 ± 1.7	97.1 ± 1.2	97.9 ± 0.7
RR/min^{-1}	VH	16.3 ± 1.6	17.2 ± 2.2	17.7 ± 2.2	17.8 ± 1.6	17.1 ± 1.4	17.6 ± 1.4
	EH	16.3 ± 1.6	17.4 ± 1.5	18.1 ± 2.1	17.5 ± 1.7	17.7 ± 1.2	17.1 ± 1.2
R-VAS	VH	0.0 ± 0.0	1.0 ± 0.5	1.2 ± 0.8	0.9 ± 0.7	0.8 ± 0.6	0.5 ± 0.5
	EH	0.0 ± 0.0	1.0 ± 0.0	1.1 ± 0.7	1.1 ± 0.9	1.1 ± 0.7	1.1 ± 0.4
M-VAS	VH	0.0 ± 0.0	1.9 ± 0.6	2.0 ± 0.5	1.8 ± 0.6	1.4 ± 0.5	1.1 ± 0.7
	EH	0.0 ± 0.0	2.0 ± 0.7	1.7 ± 0.7	1.8 ± 0.6	1.6 ± 0.5	1.4 ± 0.5

1)compared with SBP before analgesia in EH group, $P < 0.05$; 2)compared with DBP after analgesia in VH group, $P < 0.05$; 3)compared with SpO_2 before analgesia in VH group, $P < 0.05$.

表 5　四组不良反应比较

Table 5　Comparison of the side effect data [%(n), N=30]

Groups	Nausea	Vomiting	Pruritus	Drowsiness	Dizziness
EM	26.6(8)	23.3(7)	36.6(11)[1)]	13.3(4)	10.0(3)[2)]
EH	20.0(6)	20.0(6)	10.0(3)[3)4)]	3.3(1)[3)4)]	0
VM	20.0(6)	30.0(9)	20.0(6)[5)]	16.7(5)	10.0(3)[5)]
VH	20.0(6)	20.0(6)	3.3(1)	13.3(4)	0

1) compared with VM group, $P < 0.05$; 2) compared with EH group, $P < 0.05$; 3) compared with VH group, $P < 0.05$; 4) compared with EM group, $P < 0.05$; 5) compared with VH group, $P < 0.05$.

因此，我们选择氢吗啡酮术后镇痛常用的两种方法,并与经典阿片类药物吗啡对照,探讨其临床应用效能。

氢吗啡酮的脂溶性是吗啡的 525 倍，药效是吗啡的 5 ~ 8 倍[8],我们应用规格的氢吗啡酮为 2 mg (2 mL/支),吗啡为 10 mg (1 mL/支),每支药物的效价相当。氢吗啡酮用于术后镇痛通过相应疼痛区域硬膜外注射达相等镇痛效果，用药剂量比静脉减少 50%。根据以上理论,我们制定了本研究的术后镇痛配方。

各组患者的一般资料齐同，临床观察比较是有实践意义,静脉应用氢吗啡酮组(VH)术后 12、24、48 h SpO_2 稍有下降,静脉吗啡组(VM)术后 2 h SpO_2 稍有下降,硬膜外氢吗啡酮组(EH)术后 6 ~ 48 h SpO_2 也有下降，以上其原因考虑镇痛前患者面罩吸氧,所以 SpO_2 维持较高水平,返回病房后改鼻导管吸氧,吸氧浓度明显下降,故 SpO_2 有所下降,但数值均在正常范围内波动,临床上不影响患者的安全性。呼吸系统对 CO_2 敏感性降低时,可能发生呼吸抑制，但镇痛剂量氢吗啡酮是非常罕见[9]。

相比硬膜外吗啡,硬膜外氢吗啡酮组(EH)镇痛后 SBP 均有下降,但数据仍在正常安全范围内,表明硬膜外氢吗啡酮扩血管效应强于硬膜外吗啡。硬膜外氢吗啡酮组术后 12 ~ 24 h HR 增快,可能与上述扩血管效应及其代偿机制相关。

氢吗啡酮硬膜外应用相比静脉应用，术后镇痛 2 ~ 48 h SBP 均有明显下降,术后镇痛 24、48 h 时 DBP 也有明显下降,可能原因是硬膜外应用低浓度局麻药抑制交感神经的影响，但数值仍在安全的正常范围内。四组术后镇痛效果良好,无明显差异,完全满足临床 VAS≤3 分的要求。

针对术后镇痛相关副作用的观察，恶心呕吐发生率两种药物基本相同，在等效镇痛剂量下两种药物的副作用应该是相似的，因为两者具有相似的化学结构、药效学和药代动力学[10]。硬膜外氢吗啡酮恶心呕吐的发生率为 9%[11],比我们的结果低,可能与手术种类以及人种不同相关。硬膜外吗啡镇痛的发生率为 17% ~ 35%[12]，氢吗啡酮静脉

注射与硬膜外应用发生率相同[13],结果与我们的一致。恶心呕吐是由延髓催吐中枢感受器触发。

硬膜外阿片类用药瘙痒发生率均高于静脉用药[14],与我们观察结果一致。瘙痒可能与中央区的 μ 受体分布有关,也可能与硬膜外用药更容易激发中枢瘙痒受体有关,瘙痒可以使用纳洛酮拮抗[15]。资料显示与吗啡相比,使用氢吗啡酮皮肤较少瘙痒[14],本研究也证明瘙痒发生率氢吗啡酮比吗啡低。围手术期硬膜外使用吗啡瘙痒率为 11% ~ 77%[16],但使用氢吗啡酮仅为 5%[11],比本研究结果 10%低。另外,研究还发现硬膜外氢吗啡酮术后镇痛时,重度皮肤瘙痒也较吗啡少(11%和 44%)[15],与我们的观察相似。

本研究显示吗啡无论静脉用药还是硬膜外用药头晕发生率均高于氢吗啡酮,可能与体位性低血压相关。硬膜外氢吗啡酮应用嗜睡发生率最低,仅 3.3%,与文献一致[17]。嗜睡和认知功能障碍是所有阿片类药物的副作用,多发生在静脉或皮下注射氢吗啡酮和频繁使用吗啡治疗的患者。

总之,氢吗啡酮可以代替吗啡,无论静脉与硬膜外应用都能取得良好的术后镇痛效果,氢吗啡酮的副作用相对少于吗啡,值得临床广泛应用。

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