doi: 10.13241/j.cnki.pmb.2018.20.018

中药止痛贴与吗啡联合应用于癌症疼痛的镇痛效果及安全性 *

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摘要 目的:探讨中药止痛贴与吗啡联合应用于癌症疼痛治疗中的镇痛效果及安全性。**方法:**选取 2016 年 5 月至 2017 年 5 月我院收治的 100 例中重度癌症疼痛患者为研究对象,根据随机数字表方法将入选的患者分为对照组和研究组,每组 50 例。对照组患者给予吗啡治疗,研究组患者在此基础上联合应用中药止痛贴治疗,连续给药 14 天。比较两组患者的临床疗效、数字评分法(digital scoring method,NRS)、爆发痛次数、吗啡使用量、中医证候评分。**结果:**研究组患者治疗总有效率为 96.0%,显著高于对照组患者(86.0%,*P<0.05*)。研究组盐酸吗啡缓释片使用剂量[(83.23 ± 23.14)mg/d]低于对照组[(110.13± 25.23)mg/d](*P<0.05*)。治疗前,两组患者各中医证候评分比较差异均无统计学意义(*P>0.05*);治疗后,两组患者各中医证候评分均较治疗前明显降低,且研究组显著低于对照组,差异有统计学意义(*P<0.05*)。研究组患者的 NRS 评分、爆发痛次数显著低于对照组(*P<0.05*),两组患者均未见严重的不良反应。**结论:**中药止痛贴与吗啡联合应用于癌症疼痛的可有效提高镇痛效果,改善患者的中医证候,减少吗啡使用量,且安全性高。

关键词:中药止痛贴;吗啡;癌症疼痛;镇痛效果;安全性

中图分类号:R730.5 **文献标识码:**A **文章编号:**1673-6273(2018)20-3883-04

Analgesic Effect and Safety of Traditional Chinese Medicine Analgesic Ointment Combined with Morphine in the Treatment of Cancer Pain*

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ABSTRACT Objective: To explore the analgesic effect and safety of traditional Chinese medicine analgesic ointment combined with morphine in the treatment of cancer pain. **Methods:** 100 patients with moderate severe cancer pain were selected as the subjects from May 2006 to May 2017. According to random number table method, all patients were divided into the control group and the study group. 50 patients in each group were treated with morphine treatment, the study group was additionally given TCM analgesic ointment treatment. All the patients were continuously treated for 14 days. The clinical effect, NRS, the number of eruptions, the amount of morphine used and the traditional Chinese medicine (TCM) syndrome score were compared between two groups. **Results:** The total effective rate of experimental group was obviously higher than that of the control group (96.0% vs 86.0%) (*P<0.05*). The amount of morphine of two groups were 83.23 ± 23.14 mg/d and 110.13± 25.23 mg/d, respectively (*P<0.05*). There was no significant differences in the TCM syndrome score between the two groups before treatment (*P>0.05*). After treatment, the TCM syndrome scores of both groups were significantly reduced, which was significantly lower in the study group than that of the control group(*P<0.05*). The numerical rating scale (NRS) and the number of eruptions of study group were significantly decreased, which were significantly lower in the study group (*P<0.05*). No serious adverse reactions was found in both groups. **Conclusions:** TCM analgesic ointment combined with morphine can effectively increase the analgesic effect in the treatment of patients with cancer pain, it can improve the TCM syndrome, reduce the use of morphine with high safety.

Key words: Traditional Chinese medicine(TCM) analgesic ointment; Morphine; Cancer pain; Analgesic effect; Safety

Chinese Library Classification(CLC): R730.5 Document code: A

Article ID: 1673-6273(2018)20-3883-04

前言

癌性疼痛简称癌痛,指抗癌治疗、癌症相关性病变、癌症所致的疼痛症状[1]。疼痛在癌症患者临床症状中很常见,且很难控制,有研究显示超过 80%的晚期肿瘤患者会伴随剧烈的疼痛[2]。炎症和神经性因素同时发生可能导致癌症疼痛,严重影响患者的身心健康以及生活质量,患者经常因身体疼痛而悲观、绝望、失去求生的意志[3,4],治疗中如何有效控制癌痛是临床工作中需

* 基金项目:辽宁省中医药临床学(专)科能力建设项目(2013-Lnzyxzk-01)

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(收稿日期:2018-02-08 接受日期:2018-02-28)

要攻克的难题之一。

单纯西药的治疗癌痛患者的不良反应增加，Graversen [5]等研究易普利姆玛治疗晚期恶性肿瘤，增加患者免疫相关性皮肤和胃肠道不良反应发生率。随着中西医结合的深入发展，中西药联用遍及各个临床学科，联用机率呈上升趋势，尤其对一些疑难重症的治疗，有时可取得意想不到的收获。如中药止痛贴在癌痛方面有明显优势，有较好的镇痛效果，显示了中药外用不损害身体的其他器官，具有不良反应小，无药物依耐性的特点[6-8]。国外文献研究显示[9,10]中药治疗癌症的优势。

中药止痛贴是经我院长期摸索及反复实验所得，具有通络、行气止痛、活血化瘀之功效[11,12]。本研究选取 2016 年 5 月至 2017 年 5 的住院中重度癌痛患者为研究对象，探讨中药止痛贴联合吗啡对中重度癌痛患者的镇痛效果及安全性，以期为外用中药止痛贴的临床应用提供参考依据。

1 资料与方法

1.1 一般资料

选取本院肿瘤科 2016 年 5 月至 2017 年 5 月收治的中重度癌痛患者 100 例，所有患者均自愿参与本次研究。将所有患者(包括肝癌、肺癌、胃癌、食管癌、结直肠癌、子宫颈癌等)随机分为两组，各 50 例。对照组中，男 27 例，女 23 例；年龄 32-75 岁，平均(52.17± 3.59)岁，病程 1-6 年，平均(3.17± 0.72)年；研究组中，男 26 例，女 24 例；年龄 28-74 岁，平均(50.86± 2.12)岁，病程 1-7 年，平均(2.99± 0.41)年。两组一般资料比较差异均无统计学意义($P>0.05$)，具有可比性。

纳入标准：符合诊断标准[13,14]，所有患者均已确诊，伴有疼痛患者，中重度疼痛 4≤ NRS≤ 8。排除标准：合并重大器官疾病者；过敏体质；皮肤破溃、瘙痒者；妊娠及哺乳期妇女、感染性疾病、接受过系统性治疗者除外；判断不适宜本实验的对象除外。

1.2 诊断标准

参照中医证候诊断标准[15]。气滞血瘀证的临床表现及辩证要点：胸胁胀满疼痛，性情急躁，兼见痞块刺痛拒按，唇紫暗或瘀斑，脉涩；每项分值 0-8 分，0 分：无症状；2 分：症状轻微；4 分：症状尚可；6 分：症状严重。痊愈：证候积分减少超过 95%)；显效：证候积分减少 70-95%；有效：证候积分减少 30-70%；无效：证候积分减少小于 30%[16]。

1.3 治疗方法

中药止痛贴(组方：黄芪 30g、茯苓 20g、金银花 20g、蒲公英 20g、香附 10g、白芍 10g、柴胡 10g、白花蛇舌草 40g、半枝莲 40g、僵蚕 20g、瓜蒌 20g、胆南星 30g、黄芩 20g、蜈蚣 20g)，14 味中药研成细粉，用淀粉糊调制混匀，然后将调制好的中药膏均匀滩涂在防粘纸上面，注意不能太薄，太薄容易干，敷于疼痛部位，每贴 7 cm× 10 cm；由我院制剂中心制备。对照组给予口服盐酸吗啡缓释片 (西南药业股份有限公司，国药准字：H10930001)，疗程 14 天。研究组在口服盐酸吗啡缓释片的基础上加用中药止痛贴，中药止痛贴的用药方法每日一次，12h/ 次，疗程 14 天。NRS 0-3 分，按需给予有效剂量；NRS≥ 4 分，适当增加口服剂量，若出现 4 个周期疗效仍不佳地患者，视为无效。治疗期间，除使用规定的止痛药，其余止痛药物不可使用。若出现瘙痒、发红、疼痛时应停止外敷药并对症处理。

1.4 根据疼痛的程度分级法[17]

完全缓解，没有疼痛；部分缓解，疼痛减轻，睡眠基本不受干扰；轻度缓解，疼痛减轻但仍能感觉到较明显疼痛，睡眠受到干扰；无效，疼痛无减轻。

1.5 观察指标

根据数字分级法(NRS)：0：无痛；1-3：轻度疼痛；4-6：中度疼痛；7-10：重度疼痛。每日对患者进行评分，记录 NRS、疼痛缩短时间、爆发痛次数、睡眠时间、吗啡使用量。

1.6 统计学方法

采用 SPSS 19.0 进行统计学分析，计量资料以($\bar{x}\pm s$)表示，组间比较使用 t 检验计数资料以百分比表示，组间比较采用卡方检验，以 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组患者的临床疗效比较

经过 14 天的治疗，研究组临床疗效总有效率显著高于对照组，差异具有统计学意义($P<0.05$)，见表 1。

表 1 两组患者的临床疗效比较【例(%)】

Table 1 Comparison of the clinical efficacy between two groups of patients[n(%)]

Groups	Complete remission	Partial remission	Mild remission	Invalidation	Total effective rate
Control group(n=50)	17(34.00)	21(42.00)	5(10.00)	7(14.0)	43(86.00)
Study group(n=50)	22(44.00)	24(48.00)	2(4.00)	2(4.00)	48(96.00)
P			0.044		

2.2 两组患者疼痛相关指标的比较

连续用药 14 天后，研究组的疼痛减轻时间、睡眠时间及 NRS 评分均明显高于对照组，而爆发痛次数、吗啡使用量均显著低于对照组，差异有统计学意义($P<0.05$)，见表 2。

2.3 两组患者治疗前后的中医证候评分比较

治疗前，两组患者的中医证候评分比较差异无统计学意义($P>0.05$)；连续 14 天治疗后，两组患者的中医证候评分均较治疗前明显降低，且研究组均显著低于对照组，差异有统计学意义($P<0.05$)，见表 3。

2.4 两组不良反应发生情况的比较

吗啡属于强阿片类药物，阿片类药物的常见不良反应的包括恶心、呕吐，便秘等，考虑与合并口服止痛药有关。无严重不良事件。14 天疗程结束后，对 100 例患者复查生命体征、检查血常规、尿常规、肝功能、肾功能、心电图等未发现与药物相关的改变，未见与中药止痛贴有关不良反应，也未见中药止痛贴对皮肤产生皮肤刺激的情况。

表 2 两组患者疼痛程度及疼痛相关指标的比较($\bar{x}\pm s$, mg/d, h/d)

Table 2 Comparison of the pain-related indicator between two groups of patients($\bar{x}\pm s$, mg/d, h/d)

Groups	NRS drop scores	Pain reduction time	Burst pain times	Sleep add time	Morphine usage
Control group(n=50)	1.91± 1.52	6.51± 4.62	1.67± 1.21	0.81± 1.61	110.13± 25.23
Study group(n=50)	2.91± 1.22*	7.21± 5.32	0.55± 0.78*	1.25± 1.78	83.23 ± 23.14*
P	0.038	0.121	0.041	0.203	0.000

表 3 两组治疗前后中医证候评分的变化($\bar{x}\pm s$, scores)

Table 3 Comparison of the changes of TCM syndrome scores between two groups before and after treatment($\bar{x}\pm s$, scores)

Groups	Time	Fullness chest pain	Quick temper	Lump piece tingling	Cold dark purple or ecchymosis
Control group(n=50)	Before treatment	3.99± 2.14	4.41± 1.90	4.45± 1.99	6.01± 2.21
	After treatment	2.62± 1.15	2.39± 1.41	2.35± 1.60	3.91± 2.03
P		<0.05	<0.05	<0.05	<0.05
Study group(n=50)	Before treatment	4.27± 1.62	3.39± 1.84	4.39± 2.06	5.60± 2.11
	After treatment	2.21± 1.19*	2.11± 1.50*	2.02± 1.59*	2.17± 0.79*
P		<0.05	<0.05	<0.05	<0.05

Note: compared with control group, *$P<0.05$.

3 讨论

ANTÓN 等[18]对 64 个肿瘤内科的调查显示 67%的癌痛患者由于止痛不佳、不良反应剧烈等而对癌痛治疗不十分满意。中医认为肿瘤由于人体体虚、正气不足、外邪侵入最终致使热毒内结、经络痹阻、气滞血瘀[19,20]。中药治疗癌症疼痛是中医最主要的方法之一，且已有研究表明苦寒中药抗肿瘤疗效确切，其毒副作用较小，且效果明显[21,22]。本方中 14 味中药黄芪味甘，性微温，主治血痹肢麻，半身不遂；茯苓味甘、淡，性平；金银花具甘寒清泄，轻芳疏透的特点，善清热解毒[23]，主治痈疮疖肿；蒲公英味苦、甘，性寒，具有消痈散结的功效；香附辛散苦降，味甘能和，平而不偏，功善疏肝理气止痛；白芍味酸、甘、苦，性微寒，具柔肝止痛的功效；柴胡苦辛微寒，芳香疏泄，主治胁肋疼痛，月经不调，痛经；白花蛇舌草苦寒清泄，甘寒渗利，善清热解毒、消散痈肿，治疮痈、咽痛、肠痈；半枝莲辛能行散，苦寒清泄，既散瘀凉血而止血，又清热利水而通淋消肿，善治疮肿与癌肿；僵蚕咸软辛散，平而偏凉，具有息风止痉，祛风止痛，化痰散结的功效；瓜蒌甘寒润滑，具清肺润燥化痰，消肿散结功效；胆南星苦燥辛散，药力较强，尤善祛经络风痰，既燥湿化痰，又祛风止痉，治风痰诸证，外用散结消肿而止痛；黄芩苦寒清泄而燥，能凉血止血；蜈蚣辛温有毒，有息风止痉、通络止痛、功毒散结的功效。各种药物仪器应用，发挥通络散结、行气止痛、活血化瘀的效果。中药止痛贴将传统的中药粉末与辅料调成糊状，与适宜的材料制成的供粘贴在皮肤上的可产生全身性或局部作用的一种薄片状制剂。可用于完整皮肤表面，也可用于有疾患或不完整的皮肤表面，药力直达病所，对不能口服用药的患者尤其适用，具有无毒、无刺激性、不引起过敏、性质稳定的特点[24]，避免了西药单独用量过大，用药时间过久，产生较大不良反应的缺点。

本实验研究结果显示两组患者经过 14 天的治疗，研究组临床疗效的总有效率明显比对照组高，提示中药止痛贴可有效缓解疼痛，增强吗啡的止痛效果，同时也说明 14 味中药合用的功效；研究组的疼痛减轻时间、睡眠时间及 NRS 评分均明显高于对照组，而爆发痛次数、吗啡使用量均显著低于对照组，说明中药止痛贴对疼痛以及发作次数有较大影响，这与文献研究也具有一致性[25]；两组患者治疗后各中医证候评分均显著降低，进一步提示中药止痛贴具有活血止痛的效果，符合 Soleimani 等的研究[26,27]。中西药联用使用可提高疗效，降低化学药物用量、毒副等不良反应，促进康复。此外，随着中医的发展，其联用不仅有贴剂，而且有汤剂、注射剂、丸剂、散剂、胶囊剂等与西药联用，如芍药甘草汤与西药解痉药联用，可提高疗效；丹参注射液加泼尼松，治结节性多动脉炎，有协同作用，治疗风湿性多肌痛有良好效果[28-30]。

总之，中药止痛贴与吗啡联合应用于癌症疼痛的可有效提高镇痛效果，改善患者的中医证候，减少吗啡使用量，且安全性高。

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