

多瑞吉在带状疱疹疼痛治疗阿片类药物转换中的应用

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摘要 目的:探讨多瑞吉在带状疱疹疼痛治疗阿片类药物转换中的应用。方法:选择37例住院治疗的带状疱疹疼痛患者,年龄>45岁、VAS评分≥4分、所有病人常规抗病毒治疗、增加免疫力等常规治疗,予硬膜外腔置管间断注入消炎镇痛药物并持续泵吗啡,根据疼痛调整至止痛剂量,转换为多瑞吉贴剂后出院。疼痛控制后逐渐减药,每半个月减量半贴多瑞吉,对病人的疼痛评分、生活质量及并发症进行评估。结果:有1例病人应药物副作用出组,其余病人硬膜外泵吗啡后均在一周左右控制疼痛,等效转换为多瑞吉,定时定量减药,无疼痛反复,成瘾戒断等情况。结论:带状疱疹疼痛采用硬膜外间断注药持续泵吗啡迅速达到无痛后,转换为等效剂量的多瑞吉,定时定量减药,安全有效。

关键词 吗啡;芬太尼透皮贴剂;药物转换;带状疱疹

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The Effectiveness of Conversion from Epidural Opioids to Duragesic in Herpes Zoster Patients

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ABSTRACT Objective: To investigate the therapeutic effect of transdermal fentanyl (Duragesic) in patients with herpes zoster neuralgia, who have administrated with other opium analgesics. **Methods:** Thirty-seven patients suffering from HZ pain, average age above 45-year old, VAS greater than or equal 4. All patients were treated with continuous epidural morphine infusion and intermittent injection of antiphlogistic and analgesic drugs after epidural catheterization, adjusted the dosage according to pain, and then changed to transdermal fentanyl. After pain was controlled, Duragesic was slowing deducted by half patch per half-month. The analgesic effect, the quality of life, and the side effects were observed after Duragesic used. **Results:** One patient stopped the fentanyl treatment because of adverse events. The pain of all the other patients were controlled well in about one week after continuous epidural morphine infusion and intermittent epidural injection. When the epidural morphine switched to equal dosage Duragesic, no patient had pain recurred, addiction or withdrawal. **Conclusion:** HZ pain could quickly vanish by treated with continuous epidural morphine infusion and intermittent injection after epidural catheterization. Then analgesic was changed to equivalent dose transdermal fentanyl. Duragesic could provide excellent pain relief with relatively lower side effects.

Key words: Morphine; Transdermal fentanyl; Drug conversion; Herpes zoster

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前言

带状疱疹是人体免疫力低下时发生的一种沿神经走向、以皮肤破损为主要表现的常见病,其主要特征除皮损外,还有剧烈疼痛,治疗不及时,疼痛持续,还可发展为带状疱疹后神经痛。我们对带状疱疹疼痛明显的病人,予硬膜外间断注入消炎镇痛药物,持续泵吗啡达到无痛后,转换为等效剂量的多瑞吉(西安杨森制药有限公司从美国进口的芬太尼透皮贴剂,每贴25μg/h),每半月后逐渐减量,无疼痛反复,无成瘾戒断,安全有效。现报道如下。

1 材料与方法

1.1 一般资料

37例带状疱疹性疼痛患者,其中男17例,女20例,年龄48-86岁,平均为71.24±10.33岁。疱疹分布包括头面部1例,胸背部18例,腰腹部7例,颈肩及上肢10例,下肢1例。所有患者病程8天至10年,其中14例病程<1月,10例病程1-3月,13例病程>3月。患者入院时VAS评分4-9分。

1.2 治疗方法和用药剂量

患者入院后排除治疗禁忌,先行硬膜外腔置管,接止痛泵,持续泵入吗啡的同时,一周两次注入0.25%布比卡因3-6mL,内含地塞米松5mg,根据疼痛情况调整吗啡剂量至疼痛基本缓解后,根据阿片类药物等效价换算,硬膜外每天泵吗啡2mg=25μg/h多瑞吉1贴,转换为多瑞吉贴剂外用。患者达到完全或基本不痛程度后,逐渐减少多瑞吉剂量,具体方法:多瑞吉每15天减

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量一次,每次减半贴,减量至多瑞吉半贴后大部分病人可直接停药,少部分病人需换用奇曼丁 100mg bid,应用 1-2 周左右后停药。

1.3 观察指标及疗效评定

所有患者均硬膜外腔应用吗啡,调整吗啡剂量至疼痛控制满意,后转换为应用多瑞吉贴剂。

(1) 疗效评级:采用视觉模拟评分法(Vasual Analogue Scale,VAS)评价治疗后的疗效,VAS改善程度在 75%以上为疼痛消失,50%-75%为显效,25%-50%为有效,小于 25%为无效。

(2) 阿片类药物应用期间患者生活质量的评估:从病人情绪、睡眠、日常生活及病变部位疼痛等五方面评估患者的生活质量。

(3) 不良反应及并发症记录:记录应用吗啡、多瑞吉及减药过程中出现的不良反应,硬膜外腔穿刺置管并发症。

1.4 统计学分析

所有计量资料均以均数 $\pm$ 标准差($\bar{x} \pm s$)表示,采用 SPSS v16.0 统计软件进行配对 t 检验和方差分析,以 $P < 0.05$ 表示有显著性意义。

2 结果

所有患者中 1 例因出现气喘出组。36 例中,治疗后 VAS 评分,与治疗前相比差异有明显显著性意义($P < 0.01$)(表 1),其中治疗后 7 天疼痛消失 33 例,显效 3 例,治疗后 15 天,显效 36 例,总有效率均达 100%。表 2 记录了患者应用阿片类药物期间反映其生活质量的情绪、睡眠、日常活动及病变部位的瘙痒、触痛等五方面的数据,治疗后患者的生活质量明显得到改善($P < 0.01$)。

硬膜外泵吗啡不良反应见表 3,转换多瑞吉芬太尼透皮贴剂不良反应见表 4。有 1 例病人,半贴多瑞吉停药后出现心悸、出汗等不适症状,经口服奇曼丁 100mg bid 后症状缓解,继续用药 1 周后无不适,停药。

表 1 患者硬膜外吗啡治疗前后 VAS 比较(分 $\bar{x} \pm s$)

Table 1 VAS changes after epidural morphine infusion

Before treatment	1 day after treatment	3 days after treatment	7 days after treatment	15 days after treatment
5.81 $\pm$ 1.33	2.54 $\pm$ 1.24 [▲]	1.53 $\pm$ 1.11 [▲]	0.85 $\pm$ 0.78 [▲]	0.40 $\pm$ 0.52 [▲]

Note: [▲] $P < 0.01$ 1st day, 3rd day, 7th day and 15th day after treatment compared with before treatment.

表 2 患者生活质量的评估

Table 2 Evaluation the quality of life

Group	Depression	Poor sleep	Limited mobility	Itchy skin	Local tenderness
Before treatment	36	35	34	20	35
10 day after treatment	0*	0*	2*	4*	1*

Note: * $P < 0.01$ compared with before treatment.

表 3 吗啡不良反应的评估

Table 3 Evaluation the side effects of morphine

After treatment(day)	Nausea(%)	Vomiting(%)	Vomiting(%)	Asthma(%)	Uroschesis(%)	Constipation(%)
1	5.4	5.4	2.7	0	8.1	0
3	2.7	2.7	2.7	0	2.7	2.7
7	2.7	2.7	0	5.4	2.7	2.7
15	0	0	2.7	0	5.4	5.4

表 4 多瑞吉不良反应

Table 4 The side effects of Duragesic

Symptom	Case	Treatment
Lethargy	1	Reduce the dosage
Defluxion	2	Re-stick
Erythema	3	Change the location

3 讨论

Fabian 等指出带状疱疹的神经损害为炎性脱髓鞘改变,此过程是可逆的^[1]。带状疱疹后遗神经痛(postherpetic neuralgia, PHN)是水痘-带状疱疹病毒感染皮损治愈后的慢性疼痛综合征,是急性带状疱疹(herples zoster, HZ)最常见的也是最难治疗的并发症^[2]。美国神经协会(the American Academy of neurology)将带状疱疹皮损消退后,局部疼痛持续超过3个月以上者定义为 PHN^[3]。带状疱疹治疗越早发生带状疱疹后神经痛的几率越少。尤其在老年人或免疫缺陷患者,如不能有效的处理急性带状疱疹的疼痛容易发展为后遗神经痛。因疼痛剧烈,治疗上以联合治疗为主,包括:药物治疗、神经阻滞、心理干预等。药物治疗中,阿片类药物是重要的药物,可能需大剂量药物才能控制疼痛^[4]。临床工作中,肖礼祖^[5]等已论证了多瑞吉治疗带状疱疹及疱疹后神经痛的可行性,多名研究者^[6-9]指出早期硬膜外腔应用消炎镇痛药物对减轻疼痛、预防带状疱疹后遗神经痛的发生有良好的作用。

本文中应用硬膜外间断注入消炎镇痛药物,持续泵入吗啡滴定后转换为多瑞吉贴片止痛治疗带状疱疹相关疼痛,有如下特点:第一,硬膜外腔注入局麻药提供了镇痛和交感阻滞的作用,阻碍感觉传导过程^[10],药液中的糖皮质激素可起到抗炎、消除水肿、改善皮损区血液循环的作用,减轻局部软组织及神经根的水肿,促使受损神经末梢和皮肤功能的恢复^[11]。第二,硬膜外药量是口服剂量的1/30^[12],剂量小,药效高,副作用少,可迅速滴定至止痛剂量,快速止痛,避免后遗神经痛的发生。第三,吗啡持续均匀给药,直接作用于脊髓的阿片受体,阻断疼痛信息传导,同时激活内啡肽的释放,产生很强的镇痛作用^[13,14]。第四,多瑞吉是芬太尼的缓释透皮贴剂,属于强阿片类药物,通过缓慢持续地给药方式使血液和脑脊液中阿片类药物的含量得到维持,从而减少了药物的波峰和波谷效应^[15]。贴剂应用方便,不良反应少,耐受性好,易于患者接受^[16]。第五,依据本文的等效换算比例,吗啡与多瑞吉之间^[17],硬膜外腔与经皮用药途径之间,可达到等效换算,安全有效。第六,不能突然停药或大剂量减药,结合多瑞吉三天更换,制定减药周期为半个月,每次减药半贴多瑞吉,减药末期可用奇曼丁过渡,减药过程平稳安全,无疼痛反复,无成瘾戒断情况发生。

综上所述,对于疼痛剧烈,口服药物不能耐受副作用的带状疱疹相关性患者,可选择硬膜外间断注入消炎镇痛药物,同时持续泵入吗啡,短时间内达到止痛效果,为带状疱疹早期有效治疗争取了时间,减少后遗神经痛的发生,对后遗神经痛的病人,可迅速缓解疼痛,改善因疼痛导致的抑郁、焦虑等心理问题,改善睡眠,大大提高了患者的生活质量。疼痛控制平稳后,转换为等效剂量的多瑞吉,药物转换及减量标准安全平稳,可作为疼痛剧烈、口服止痛药物效果不佳的带状疱疹相关疼痛病人治疗选择。

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