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普瑞巴林、加巴喷丁联合神经阻滞治疗带状疱疹后神经痛的临床疗效比较*

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摘要 目的:比较普瑞巴林、加巴喷丁联合神经阻滞治疗带状疱疹后神经痛(PHN)的临床疗效。**方法:**选择2014年8月至2016年11月我院门诊收治的带状疱疹后神经痛患者80例,并将其随机分为两组,每组40例。A组患者接受普瑞巴林联合神经阻滞治疗,B组患者接受加巴喷丁联合神经阻滞治疗,比较两组患者治疗前后的视觉疼痛模拟(VAS)评分、失眠严重程度指数(ISI)评分、生活质量满意指数(LSIB)评分及治疗期间不良反应的发生情况。**结果:**A组患者治疗后4、7、14 d的VAS评分均显著低于B组(P<0.05),LSIB评分显著高于B组(P<0.05),A组患者治疗后4、7 d的ISI评分均显著低于B组(P<0.05);A组发生不良反应的总发生率显著低于B组(P<0.05)。**结论:**普瑞巴林联合神经阻滞治疗PHN缓解疼痛和失眠的效果显著优于巴喷丁联合神经阻滞治疗,其可显著提高患者的生活质量,并减少不良反应。

关键词:带状疱疹后神经痛;神经阻滞;普瑞巴林;疗效

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Comparison of the Curative Effect of Pregabalin, Gabapentin Combined with Never Blocking Respectively on the Postherpetic Neuralgia*

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ABSTRACT Objective: To compare the curative effect of pregabalin, gabapentin combined with never blocking on the postherpetic neuralgia (PHN). **Methods:** 80 cases of patients with postherpetic neuralgia were collected in our hospital from August 2014 to November 2016, they were randomly divided into two groups. Group A (n=40) was given pregabalin combined with never blocking treatment, and Group B was given gabapentin combined with never blocking. The visual analogue score (VAS), insomnia severity index (ISI) score and life satisfaction index B (LSIB) score before and after treatment and the incidence of adverse reactions during the treatment were compared between two groups. **Results:** On the 4th, 7th, 14th day after treatment, the VAS scores of patients in Group A were significantly lower than those patients in Group B(P<0.05), while the LSIB score were significantly higher(P<0.05). On the 4th, 7th day after treatment, the ISI score of Group A were lower than those of Group B(P<0.05). The incidence of adverse reactions in Group A was significantly lower than that of Group B(P<0.05). **Conclusions:** Pregabalin combined with never blocking had better clinical efficacy in the treatment of PNH than gabapentin combined with never blocking, it not only significantly relieved pain and insomnia, but also increased the quality of life and decreased the incidence of adverse reactions.

Key words: Postherpetic neuralgia; Nerve blocking; Pregabalin; Curative effect

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前言

带状疱疹后神经痛(Postherpetic neuralgia,PHN)是临床疼痛科常见的疾病之一,属于感染性神经病理性疼痛,患者常表现为局部阵发性或持续性灼痛、刺痛、刀割痛,严重影响患者的生活质量[1,2]。目前,PHN的发病机制并不清楚,只能采用对抗疗法缓解患者的疼痛症状,药物治疗是治疗该病最基本、最主要的方法,如抗病毒药物、三环类抗抑郁药物、抗癫痫、消炎镇痛药物等[3]。加巴喷丁作为新一代抗癫痫药用于中枢性镇痛作用临床疗效显著[4]。普瑞巴林属于抑制性神经递质γ-氨基丁酸的三位异丁基取代物,同样作为新型抗癫痫药物,具有良好的抗癫痫、镇痛及抗焦虑作用[5-7]。然而,临床研究表明PHN疼痛的顽固性以及发病的持续性使得临床通过单一药物治疗,很难达到理想的止痛效果[8]。

近几年,随着医疗水平的不断提高,微创介入治疗因其微创性且治疗安全有效的优势逐渐广泛应用于神经病理性疼痛

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的治疗,如神经阻滞治疗可通过阻断感觉神经信号的传入以及交感神经信号的传出迅速缓解疼痛，目前已经成为临床治疗PHN的主要手段[9,10]。近几年,药物联合神经阻滞治疗用于对抗PHN已有部分文章报道,但是比较普瑞巴林、加巴喷丁分别联合神经阻滞治疗PHN的临床疗效的报道并不多。因此,本研究以在我院进行治疗的PHN患者为研究对象，探讨和比较了普瑞巴林、加巴喷丁联合神经阻滞治疗PHN的临床疗效,现将研究结果报道如下：

1 资料和方法

1.1 临床资料

选择2014年8月至2016年11月在我院门诊收治的PHN患者80例,纳入标准:有带状疱疹史且皮损已经愈合;患者疱疹治愈后仍有持续性的、顽固的、剧烈疼痛;患者疼痛持续1个月以上且不足3个月;VAS评分在7分以上；排除患有其他恶性肿瘤患者。所有患者均对本研究知情同意,且经过医院伦理委员会批准。所有患者按照随机数字法分为两组,每组40例,两组患者一般资料包括性别、年龄、病程及疼痛部位等基本资料比较差异均无统计学意义(P<0.05),具有可比性,见表1。

表1 两组患者的一般资料比较

Table 1 The comparison of general conditions between two groups

Group	Number	Gender (F/M)	Age (year)	Course of disease (month)	Pain site		
					Chest back	Lumbar back	Gluteal thigh
Group A	40	21/19	63.34± 7.26	5.23± 3.26	19	14	7
Group B	40	22/18	62.76± 8.04	5.65± 3.45	21	16	3

1.2 治疗方法

所有患者均接受神经阻滞治疗:根据患者疱疹疼痛部位找到受损神经、皮肤痛点并进行标记,确定阻滞部位,根据疼痛部位及患者疼痛具体情况于标记点注入神经阻滞用药5-10 mL,每次注入完毕后,观察15 min,如患者生命体征平稳方可出院,每周进行1次。神经阻滞用药配方：将10 mL耐乐品 (规格:100 mg/10 mL,阿斯利康制药有限公司生产,进口药品注册证号:H20140763),1 mL醋酸曲安奈德注射液(规格:40 mg/1 mL,浙江仙琚制药股份有限公司生产,国药准字H20033525)以及生理盐水配制100 mL。A组患者在神经组织基础上服用普瑞巴林(规格:75 mg/片,辉瑞制药有限公司生产,进口药品注册证号:H20100623；国药准字J20100102)：第一天患者服用75 mg,2次/天,第二天150 mg,2次/天,待患者疼痛缓解后且情况较稳定,逐步减少用量。B组患者在神经阻滞基础上服用加巴喷丁胶囊(规格:0.1g/片,江苏恩华药业股份有限公司生产,国药准字H20040527),第一天100 mg,第二天200 mg,第三天300 mg,此后维持剂量服用4周。所有患者均治疗4周。

1.3 观察指标和疗效评价标准

采用视觉模拟疼痛VAS评分[11]比较两组患者治疗前后的疼痛缓解情况,评价标准:无痛记为0分,有轻微疼痛且能够忍受记为0-3分,患者感觉疼痛并影响睡眠,且可以忍受记为4-6分;患者有强烈的疼痛感,并且难以忍受,影响睡眠和食欲记为7-10分。采用失眠严重程度指数(ISI)量表[12]评价两组患者治疗前后的睡眠情况，总分28分,22-28分表示重度失眠,15-21分表示中重度失眠,8-14分表示阈下失眠症,0-7分表示没有显著临床失眠症。采用生活满意度指数B(LSIB)量表[13]评价两组患者治疗前后的生活质量。所有量表调查均有专业医师协助患者完成。记录并分析两组患者治疗期间不良反应的发生程度。

1.4 统计学分析

采用SPSS 17.0统计软件对数据进行分析，计量资料以均数± 标准差($\bar{x}$± s)表示,两组间差异通过两独立样本t检验进行分析;计数资料以例数(%)表示,组间差异通过x^2检验,以P<0.05表示差异具有统计学意义。

2 结果

2.1 两组治疗前后VAS评分及睡眠质量评分的比较

由表2可见,A组患者治疗后4 d、7 d以及14 d的VAS评分显著低于B组患者 (P<0.05),A组患者治疗后4 d及7 d的ISI评分显著低于B组(P<0.05)。

表2 两组患者治疗前后VAS及ISI评分的比较($\bar{x}$± s)

Table 2 Comparison of the VAS and ISI score of patients between two groups before and after treatment ($\bar{x}$± s)

	Group	Number	Pre-treatment	Post-treatment					
				2 d	4 d	7 d	14 d	21 d	28 d
VAS score	Group A	40	7.52± 0.59	4.29± 0.73	2.62± 0.63*	1.71± 0.55*	1.16± 0.49*	1.04± 0.54	0.73± 0.34
	Group B	40	7.49± 0.63	4.57± 0.60	3.68± 0.57	2.86± 0.46	1.66± 0.42	1.29± 0.31	0.91± 0.23
ISI score	Group A	40	15.24± 5.82	13.74± 5.33	11.26± 4.93*	9.26± 4.76*	8.37± 5.06	7.29± 4.76	6.87± 3.82
	Group B	40	14.76± 5.93	14.07± 6.11	12.67± 5.37	10.25± 5.37	8.86± 4.76	8.07± 5.26	6.76± 4.13

Note: compared with Group B, *P<0.05.

2.2 两组治疗前后生活质量评分的比较

由表3可见,A组患者治疗后4 d、7 d以及14 d的生活满

意度指数显著高于 B 组(P<0.05)。

表 3 两组患者治疗前后 LSIB 评分的比较($\bar{x}\pm s$)

Table 3 The comparison of LSIB score of patients before and after treatment between two groups($\bar{x}\pm s$)

Group	Number	Pre-treatment	Post-treatment					
			2 d	4 d	7 d	14 d	21 d	28 d
Group A	40	12.37± 1.82	13.38± 1.85	14.76± 1.76*	16.68± 1.93*	17.56± 1.59*	18.15± 1.66	19.21± 1.63
Group B	40	12.41± 1.76	13.07± 1.75	13.92± 1.57	15.26± 1.63	16.87± 1.62	17.56± 1.52	18.57± 1.51

Note: compared with Group B, *P<0.05.

2.3 两组不良反应发生情况的比较

由表 4 可见,A 组发生不良反应的总发生率显著低于 B 组(P<0.05)。

表 4 两组患者不良反应发生情况的比较[例(%)]

Table 4 Comparison of the incidence of adverse reactions between two groups [n (%)]

Group	Number	Dizzy	Gait abnormality	Peripheral edema	Sleepiness	Total incidence rate
Group A	40	6 (15.0)	1 (2.5)	2 (5.0)	3 (7.5)	12 (30.0)*
Group B	40	11 (27.5)	4 (10.0)	0 (0.0)	8 (20.0)	23 (57.5)

Note: compared with Group B, *P<0.05.

3 讨论

带状疱疹(Hepes zoster,HZ)是临床常见的皮肤病,是潜伏于感觉神经节中的水痘 - 带状疱疹病毒被激活之后引起的皮肤感染,主要沿感觉神经的部分出现,伴有严重疼痛感[14]。临床研究表明患者疼痛感不会因疱疹的治愈而消失,常常持续数月甚至数年,带状疱疹治愈消退后,感觉神经的神经性疼痛持续 1 个月以上则被认为是带状疱疹病毒感染的并发症之一 -- 带状疱疹后神经痛(post-herpetic neuralgia,PHN)[15]。PHN 属于典型的也是最顽固的神经病理性疼痛,目前发病机制并不清楚,患者主要表现为疼痛、瘙痒、焦虑抑郁等。据统计,50%的带状疱疹后神经痛患者疼痛发作时感到阵发性刀割样、自发性闪电样或撕裂样疼痛,严重影响患者的生活质量[16-18],也有患者表现为持续性灼烧样、针刺样疼痛或感觉到蚁行感、瘙痒抽动感,影响患者睡眠[19]。迄今为止,并没有行之有效的治疗手段可以有效缓解 PHN。

临床治疗 PHN 以缓解疼痛、改善睡眠及提高生活质量为主,目前以传统药物治疗为主,包括抗癫痫药、局麻药、三环类抗抑郁药等[3]。加巴喷丁是临床用于治疗 PHN 的一线药物,属于新型抗癫痫药物,可迅速通过血脑屏障,与脑组织具有高度亲和性,发挥良好的中枢性神经镇痛作用[20,21]。然而,临床研究表明加巴喷丁用于治疗 PHN 疼痛缓解率能达到 50%的患者仅有 27.6%-33.3%,多数患者仍需要忍受强烈的疼痛感[22]。此外,临床研究表明患者易对加巴喷丁产生耐药性,且随着用药时间的延长而显著,患者易出现头晕、乏力等不良反应[23,24]。普瑞巴林属于新型 γ- 氨基丁酸受体激动剂,可通过作用神经突触前的 α2-δ 亚单位,一方面抑制神经元兴奋性,一方面通过调节神经末梢钙离子内流,减少神经递质的释放,从而协同减少疼痛信号的传导[25,26]。另外,普瑞巴林具有治疗抑郁和调节睡眠的作用,能增加健康志愿者慢波睡眠,减少夜间觉醒[27]。近几年,随着医疗水平的不断提高,通过介入治疗用于缓解神经痛已逐渐广泛应用于临床,目前常用的介入治疗神经阻滞是指利用穿刺针以最小的切口直接在引发神经痛的相关神经组织内或附近注射药物或给予物理刺激作用神经末梢,从而阻断神经功能的传导,有效缓解疼痛[28,29]。临床研究表明对于带状疱疹后神经痛患者及早施行神经阻滞临床疗效显著,可有效减轻患者疼痛[30]。目前,多数研究以药物治疗或介入治疗为主探讨其缓解 PHN 疼痛的临床疗效,其联合应用目前是临床用于治疗 PHN 的一个新方向。

本研究以本院收治的 PHN 患者为研究对象,探讨普瑞巴林、加巴喷丁分别辅助神经阻滞治疗 PHN 的临床疗效。结果显示普瑞巴林辅助神经阻滞治疗的患者治疗后 4、7 以及 14 d 的 VAS 评分显著低于加巴喷丁辅助神经阻滞治疗的患者,患者治疗后 4 d 及 7 d 的 ISI 评分显著低于加巴喷丁辅助神经阻滞治疗的患者,提示普瑞巴林和加巴喷丁分别联合神经阻滞均可显著缓解 PHN 患者的疼痛感,有效改善患者睡眠质量,但是在治疗后普瑞巴林联合神经阻滞发挥镇痛作用较为迅速,可尽早减轻患者的临床症状。普瑞巴林辅助神经阻滞治疗的患者治疗后 4 d、7 d 以及 14 d 的 LSIB 评分显著高于加巴喷丁辅助神经阻滞治疗的患者,进一步说明 A 组患者接受普瑞巴林联合神经阻滞可尽早减轻患者疼痛、失眠等临床症状,有利于提高患者的生活质量。此外,普瑞巴林联合神经阻滞用于治疗 PHN 诱发患者发生不良反应的发生率显著低于加巴喷丁联合神经阻滞,提示其安全性更高。

综上所述,普瑞巴林、加巴喷丁联合神经阻滞治疗 PHN 均可有效减轻患者疼痛、失眠等临床症状,但是普瑞巴林联合神经阻滞作用更加显著,可显著提高患者的生活质量,且安全性更高。

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