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溴隐亭治疗非急性泌乳素型垂体腺瘤的临床效果*

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摘要 目的:研究溴隐亭治疗非急性泌乳素型垂体腺瘤的临床效果。**方法:**选择2016年1月~2019年12月内蒙古医科大学第三附属医院神经外科和妇产科收治的120例非急性泌乳素型垂体腺瘤患者,随机分为两组。对照组给予手术治疗,观察组在对照组基础上口服溴隐亭治疗,起始时每天的剂量为2.5 mg,给药3~5 d后,逐渐将每天的剂量增加至7.5 mg,分成2~3次服用,维持给药3个月。比较两组治疗前、治疗1个月和3个月,比较两组的血清泌乳素水平和症状评分,并观察两组的心理领域、社会领域、环境领域和生理领域评分。**结果:**观察组的有效率明显高于对照组($P<0.05$);治疗1个月和3个月,两组非急性泌乳素型垂体腺瘤患者的血清泌乳素水平均明显降低($P<0.05$),且观察组的血清泌乳素水平明显低于对照组($P<0.05$);治疗1个月和3个月,两组的泌乳素型垂体腺瘤症状评分均明显降低($P<0.05$),且观察组的泌乳素型垂体腺瘤症状评分明显低于对照组($P<0.05$);治疗后,两组的心理领域、社会领域、环境领域和生理领域评分明显升高($P<0.05$),且观察组的心理领域、社会领域、环境领域和生理领域评分明显高于对照组($P<0.05$)。**结论:**肿瘤切除术后联合服用溴隐亭能更好的改善非急性泌乳素型垂体腺瘤患者的症状,降低血清泌乳素水平,提高生活质量,值得推广。

关键词:溴隐亭;非急性;泌乳素型垂体腺瘤;生活质量;泌乳素

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Clinical Effect of Bromocriptine in the Treatment of Non-acute Prolactin Pituitary Adenoma*

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ABSTRACT Objective: To investigate the effect of bromocriptine in the treatment of non-acute prolactin pituitary adenoma.

Methods: A total of 120 patients with non-acute prolactin-type pituitary adenoma who were admitted to the Department of Neurosurgery and Obstetrics and Gynecology of the Third Affiliated Hospital of Inner Mongolia Medical University from January 2016 to December 2019 were randomly divided into two groups. The control group was given surgical treatment, and the observation group was treated with bromocriptine on the basis of the control group. The initial daily dose was 2.5 mg. After 3 to 5 days of administration, the daily dose was gradually increased to 7.5 mg and divided into 2 to 3 times, maintain the medicine for 3 months. Compare the two groups before treatment, 1 month and 3 months of treatment, compare the serum prolactin levels and symptom scores of the two groups, and observe the psychological, social, environmental and physiological scores of the two groups. **Results:** The effective rate of the observation group was significantly higher than control group ($P<0.05$). After 1 month and 3 months of treatment, the serum PRL levels of non-acute prolactin pituitary adenoma patients in the two groups were significantly reduced ($P<0.05$), and the serum PRL levels in the observation group were significantly lower than those in the control group ($P<0.05$). After 1 month and 3 months of treatment, the prolactin pituitary adenoma symptom scores in both groups were significantly reduced ($P<0.05$), and the prolactin pituitary adenoma symptom scores in the observation group were significantly lower than those in the control group ($P<0.05$). After treatment, the scores of the psychological, social, environmental, and physiological fields in the two groups increased significantly ($P<0.05$), and the scores of the psychological, social, environmental, and physiological fields in the observation group were significantly higher than those in the control group ($P<0.05$). **Conclusion:** The combined use of bromocriptine after tumor resection can better improve the symptoms of patients with non-acute

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prolactin-type pituitary adenomas, reduce serum PRL levels, and improve quality of life, which is worth promoting.

Key words: Bromocriptine; Non-emergency; Prolactin-type pituitary adenoma; Quality of life; Prolactin

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前言

泌乳素型垂体腺瘤是最为常见的一种垂体肿瘤,大部分属于良性肿瘤,大约占有垂体肿瘤的40%~60%,主要多发于20~30岁的妇女^[1,2]。按照肿瘤的大小,可将泌乳素型垂体腺瘤分成大腺瘤(>10 mm)以及微腺瘤(<10 mm),患者的症状表现与肿瘤大小、病程及进展速度相关,临床表现主要为高泌乳素血症,出现溢乳、闭经以及不孕等症状,高泌乳素血症严重时有可能造成患者的骨密度降低,导致的骨折发生^[3,4]。当泌乳素型垂体腺瘤患者的瘤体增大到一定程度时,就会引起头痛、视野缺损以及视力减退等占位性压迫症状,还有可能引起脑水肿,其治愈率比较低,最终会导致机体出现垂体机能减退^[5,6]。目前治疗泌乳素型垂体腺瘤的方法主要有药物治疗、放射治疗和手术治疗。溴隐亭作为半合成的一种生物碱溴化物,可以持久且有效的刺激机体内的多巴胺受体,能通过血脑屏障作用于患者机体中垂体泌乳素细胞内的多巴胺受体,使泌乳素的释放和合成受到明显的抑制,进而降低泌乳素含量^[7,9]。以往临床大多研究单独手术治疗泌乳素型垂体腺瘤,或者单独溴隐亭药物治疗该病。本研究创新性地分析了肿瘤切除术后联合服用溴隐亭对非急性性泌乳素型垂体腺瘤的效果,且分析了联合服用溴隐亭对患者症状、血清泌乳素水平和生活质量的改善效果。

1 资料与方法

1.1 一般资料

选择2016年1月~2019年12月内蒙古医科大学第三附属医院神经外科和妇产科收治的120例非急性性泌乳素型垂体腺瘤患者,纳入标准:(1)均经过内分泌检查以及影像学检查确诊为泌乳素型垂体腺瘤,且均为非急性性;(2)患者血清泌乳素水平 ≥ 200 ng/mL(正常水平的范围为6~2.9 ng/mL);(3)头颅磁共振检查发现患者的鞍区垂体出现占位性病变,而最大肿瘤直径小于10 cm;(4)均知情同意。排除标准:(1)有应激反应、药物、终末期肾病以及甲状腺功能低下等导致的血清PRL水平升高的刺激因素的患者;(2)急性性患者;(3)有原发性的重要脏器功能障碍;(4)曾经接受过与本研究治疗无关的放射治疗、手术治疗的时间小于3个月的患者;(5)合并患有其它种类激素异常的分泌增多,如促甲状腺激素、促肾上腺激素、生长激素。用抽签法随机分为两组。观察组60例,年龄23~65岁,平均(45.19 $\pm$ 7.22)岁;月经周期2~8 d,平均(3.72 $\pm$ 1.06) d;肿瘤直

径<1 cm的患者15例,1~3 cm的患者39例,>3 cm的患者9例;临床症状:闭经20例,头痛22例,月经紊乱54例;年龄23~65岁,平均(46.17 $\pm$ 6.53)岁;月经周期2~8 d,平均(3.85 $\pm$ 1.14) d;肿瘤直径<1 cm的患者15例,1~3 cm的患者38例,>3 cm的患者7例;临床症状:闭经19例,头痛21例,月经紊乱55例。两组的基线资料具有可比性($P>0.05$)。

1.2 治疗方法

对照组给予手术治疗,观察组在对照组基础上口服溴隐亭(生产厂家:Novartis Farma S.p.A(意大利),批号:H20160030,规格:2.5 mg/粒)治疗,起始时每天的剂量为2.5 mg,给药3~5 d后,逐渐将每天的剂量增加至7.5 mg,分成2~3次服用,维持给药3个月。

1.3 观察指标

疗效标准:(1)显效:非急性性泌乳素型垂体腺瘤患者治疗后在影像学上肿瘤基本消失,血清泌乳素水平<20 ng/mL,不适的症状基本消失;(2)有效:非急性性泌乳素型垂体腺瘤患者治疗后在影像学上肿瘤有所减少,血清泌乳素水平有向正常水平恢复的趋势,不适的症状基本得到改善;(3)无效:非急性性泌乳素型垂体腺瘤患者治疗后影像学检查结果和血清PRL水平没有变化。

治疗前、治疗1个月和3个月,比较两组的血清泌乳素水平;并且观察两组非急性性泌乳素型垂体腺瘤患者的症状变化,主要包括泌乳、脱发、视物模糊、继发性月经改变、头痛精神疲乏、性欲降低以及饮食减少等,0分:表示无症状,2分:表示症状轻微,4分:表示症状中度,6分:表示症状比较严重。

用WHO生存质量测定量表(WHOQOL-BREF)判断非急性性泌乳素型垂体腺瘤患者的生活质量。分成心理领域、社会领域、环境领域和生理领域,总共包含26个条目,每个条目的评分为0~5分,分值越低,非急性性泌乳素型垂体腺瘤患者的生活质量越差。

1.4 统计学分析

采用SPSS 21.0,两组间计量资料对比用t检验,计数资料用 χ^2 检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 疗效对比

观察组治疗后的有效率为96.67%,明显高于对照组的73.33%($P<0.05$),见表1。

表1 疗效比较[例(%)]

Table 1 Comparison of the clinical effect [n(%)]

Groups	n	Effective	Valid	Invalid	The total effect rate
Control group	60	29(48.33)	15(25.00)	16(26.67)	44(73.33)
Observation group	60	31(51.67)	27(45.00)	2(3.33)	58(96.67)*

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

- 2.2 两组治疗前、治疗 1 个月和 3 个月的血清泌乳素水平对比 者的血清泌乳素水平均明显降低($P<0.05$),且观察组的血清泌乳素水平明显低于对照组($P<0.05$),见表 2。

表 2 两组治疗前、治疗 1 个月和 3 个月的血清泌乳素水平对比($\bar{x}\pm s$)Table 2 Comparison of serum PRL levels before treatment, 1 month and 3 months in the two groups ($\bar{x}\pm s$, $\mu\text{mol/L}$)

Groups	n	Before treatment	After treatment 1 month	After treatment 3 months
Control group	60	117.34 $\pm$ 11.29	59.14 $\pm$ 10.25 [#]	49.15 $\pm$ 6.72 [#]
Observation group	60	118.52 $\pm$ 13.56	38.14 $\pm$ 10.26 ^{*#}	32.21 $\pm$ 4.57 ^{*#}

Note: Compared with the control group, ^{*} $P<0.05$; compared with before treatment, [#] $P<0.05$.

- 2.3 两组治疗前、治疗 1 个月和 3 个月的泌乳素型垂体腺瘤症状评分对比 均明显降低($P<0.05$),且观察组的泌乳素型垂体腺瘤症状评分明显低于对照组($P<0.05$),见表 3。

治疗 1 个月和 3 个月,两组的泌乳素型垂体腺瘤症状评分

表 3 两组治疗前、治疗 1 个月和 3 个月的泌乳素型垂体腺瘤症状评分对比($\bar{x}\pm s$)Table 3 Comparison of prolactin pituitary adenoma symptom scores before treatment, 1 month and 3 months in two groups ($\bar{x}\pm s$)

Groups	n	Before treatment	After treatment 1 month	After treatment 3 months
Control group	60	19.17 $\pm$ 2.24	16.34 $\pm$ 1.78 [#]	14.38 $\pm$ 1.42 [#]
Observation group	60	20.39 $\pm$ 1.75	12.27 $\pm$ 1.59 ^{*#}	11.67 $\pm$ 1.03 ^{*#}

Note: Compared with the control group, ^{*} $P<0.05$; compared with before treatment, [#] $P<0.05$.

- 2.4 两组治疗前后的生活质量对比 评分明显升高($P<0.05$),且观察组的心理领域、社会领域、环境领域和生理领域评分明显高于对照组($P<0.05$),见表 4。

治疗后,两组的心理领域、社会领域、环境领域和生理领域

表 4 两组治疗前后的生活质量对比($\bar{x}\pm s$)Table 4 Comparison of quality of life between the two groups before and after treatment ($\bar{x}\pm s$)

Groups	n		Environmental field	Psychological field	Social field	Physiological field	Total score of quality of life
Control group	60	Before treatment	11.17 $\pm$ 1.43	10.32 $\pm$ 1.17	10.64 $\pm$ 1.32	10.33 $\pm$ 1.62	41.73 $\pm$ 4.45
		After treatment	14.19 $\pm$ 1.36 [#]	13.54 $\pm$ 2.13 [#]	13.27 $\pm$ 1.51 [#]	13.89 $\pm$ 1.31 [#]	47.53 $\pm$ 6.72 [#]
Observation group	60	Before treatment	11.25 $\pm$ 1.43	10.14 $\pm$ 1.52	10.57 $\pm$ 1.48	10.27 $\pm$ 1.45	42.82 $\pm$ 5.19
		After treatment	18.79 $\pm$ 2.64 ^{*#}	17.39 $\pm$ 3.75 ^{*#}	17.63 $\pm$ 2.42 ^{*#}	16.57 $\pm$ 1.34 ^{*#}	56.59 $\pm$ 8.34 ^{*#}

Note: Compared with the control group, ^{*} $P<0.05$; compared with before treatment, [#] $P<0.05$.

3 讨论

随着现代内分泌学、神经外科学、神经影像学 and 神经病理学的快速发展,使得垂体腺瘤能得以早期诊断^[10]。垂体瘤包括无功能型垂体瘤以及具有激素分泌功能的垂体瘤两种,其中,泌乳素型垂体腺瘤是妇产科较为常见的一种神经内分泌肿瘤,也是引起高泌乳素血症的一个常见病因^[11-14]。患者则主要表现为停经、泌乳以及不孕等^[15,16]。近些年来,泌乳素型垂体腺瘤在人群中的发病率极高,不仅不利于女性的身体健康,也会影响到心理健康,造成沉重的经济负担,不利于患者及其家属的生活质量^[17]。泌乳素型垂体腺瘤引发临床症状的基础主要包括高泌乳素血症、肿瘤卒中导致激素水平发生异常、肿瘤持续增长压迫周围组织结构等 3 个方面,因而,该病治疗目标也比较明确,即缩小肿瘤体积以及降低血清泌乳素含量,而且尽可能保留患者的垂体功能,必要时采取激素替代疗法^[18-29]。

近年来,随着以溴隐亭作为代表的多巴胺激动剂在临床上

被应用于治疗泌乳素型垂体腺瘤,患者的肿瘤控制率、泌乳素水平正常化率以及生活质量等多个方面均获得了明显的改善^[20-24]。溴隐亭是一种能快速降低机体血液内泌乳素含量异常升高的药物,被越来越多的医师和患者所接受^[25-27]。溴隐亭的药动力学研究发现,溴隐亭在服药后两小时就能起效,大约 3 小时达血药浓度高峰,作用可以持续 8~12 h^[28,29]。本研究发现,治疗 1 个月和 3 个月,两组非急性性泌乳素型垂体腺瘤患者的血清泌乳素水平均明显降低,且观察组的血清泌乳素水平明显低于对照组;表明肿瘤切除术后联合服用溴隐亭能使非急性性泌乳素型垂体腺瘤患者的血清泌乳素水平明显降低。分析其原因为,溴隐亭的药理学研究发现,溴隐亭与机体内的多巴胺受体进行结合,而进一步产生类多巴胺效应,使泌乳素的释放和合成受到抑制,降低血清泌乳素水平,从而使患者的垂体腺瘤快速缩小。Colao 等^[30]发现即使中止溴隐亭治疗后 2~5 年,仍然有 6.6%~37.5% 的患者血清泌乳素水平保持正常。治疗 1 个月和 3 个月,两组的泌乳素型垂体腺瘤症状评分均明显降低,

且观察组的泌乳素型垂体腺瘤症状评分明显低于对照组;表明服用溴隐亭能更好的改善非急性性泌乳素型垂体腺瘤患者的症状。与王林等^[10]的研究结果相一致。治疗后,观察组的心理领域、社会领域、环境领域和生理领域评分明显高于对照组。表明肿瘤切除术后联合服用溴隐亭能通过减轻患者的症状,提高非急性性泌乳素型垂体腺瘤的疗效,从而改善生活质量。

综上所述,肿瘤切除术后联合服用溴隐亭能更好的改善非急性性泌乳素型垂体腺瘤患者的症状,降低血清泌乳素水平,从而有助于提高患者生活质量,值得临床推广。

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