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左乙拉西坦治疗小儿癫痫的临床疗效及对血清 IgA、IgM、IgG 水平的影响 *

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摘要 目的：探讨左乙拉西坦用于治疗小儿癫痫的临床疗效及对血清 IgA、IgM、IgG 含量的影响。**方法：**选择 2014 年 1 月 -2017 年 1 月在我院就诊的癫痫患儿 102 例为研究对象，按治疗方式不同将其分为各 51 例患儿的观察组与对照组，观察组给予患儿左乙拉西坦片进行治疗，对照组给予患儿丙戊酸钠口服液进行治疗，两组患儿均治疗时间为 24 周。对比两组患儿的临床疗效、不良反应发生率、治疗前后血清 IgA、IgM、IgG 水平、认知功能评分和癫痫发作次数变化。**结果：**治疗后，观察组的总有效率 96.09%(49/51)高于对照组 84.31%(43/51)(P＜0.05)；两组患儿的 IgA、IgM 和 IgG 含量均比治疗前有所下降，且观察组 IgA 和 IgM 含量低于对照组(P＜0.05)，两组 IgG 含量无差异(P＜0.05)；观察组的不良反应发生率 11.76%(6/51)低于对照组 25.49%(13/51)(P＜0.05)；观察患儿的 FIQ、PIQ 和 VIQ 评分均比治疗前有所升高，对照组患儿的 FIQ、PIQ 和 VIQ 评分均比治疗前有所下降，观察组评分高于对照组(P＜0.05)；治疗后，两组各类型癫痫患儿的发作次数均比治疗前有所降低(P＜0.05)，且观察组各类型癫痫患儿的发作次数均明显少于对照组(P＜0.05)。**结论：**左乙拉西坦治疗小儿癫痫的疗效显著，可显著降低癫痫患儿的血清免疫球蛋白水平，改善认知功能，降低癫痫的发作次数，且安全性较高。

关键词：左乙拉西坦；小儿癫痫；血清免疫球蛋白；不良反应；认知功能

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Clinical Efficacy of Levetiracetam in the Treatment of Pediatric Epilepsy and Its Effects on the Serum IgA, IgM and IgG Levels*

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ABSTRACT Objective: To investigate the clinical efficacy of Levetiracetam in the treatment of pediatric epilepsy and its effects on the serum IgA, IgM and IgG levels. **Methods:** 102 cases of epileptic children were selected from January 2014 to January 2017 in our hospital. According to the treatment, they were divided into the observation group and control group with 51 children in each group. The observation group was treated with Levetiracetam tablets. The control group was treated with Valproate oral liquid. Both groups were treated for 24 weeks. The clinical efficacy, changes of serum IgA, IgG, IgG levels, cognitive function score before and after treatment, incidence of adverse reaction rate and seizures frequency were compared between the two groups. **Results:** The total effective rate of observation group was 96.09% (49/51), which was significantly higher than that of the control group[84.31%(43/51)](P<0.05). After treatment, the serum levels of IgA, IgM and IgG in both groups were lower than those before treatment(P＜0.05), At the same time, the serum levels of IgA and IgM in the observation group were lower than those in the control group (P<0.05), and there was no difference in serum level of IgG between the two groups(P<0.05). The incidence rate of adverse reaction in observation group[11.76%(6/51)] was lower than that in the control group [25.49%(13/51)](P<0.05). The FIQ, VIQ and PIQ score of observation group were increased than before treatment, which were decreased in the control group than those before treatment(P<0.05). After treatment, the times of seizures in both groups were lower than those before treatment (P<0.05), which was significantly lower in the observation group than that in the control group (P<0.05). **Conclusions:** Levetiracetam is remarkably effective in treating pediatric epilepsy, it can significantly reduce the serum immunoglobulin levels, improve the cognitive function, reduce the number of epileptic attack with high safety.

Key words: Levetiracetam; Pediatric epilepsy; Serum immunoglobulin; Adverse reactions; Cognitive function

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前言

小儿癫痫是一种临床上常见的儿科神经系统疾病，具有暂时性、突然性、反复性等发病特点，主要发病年龄在 2-9 岁，且男性患儿的发病率高于女性患儿，抽搐和意识混乱是该类疾病的主要临床表现[1,2]。影响癫痫的发病因素较多，包括脑肿瘤、颅内感染、脑血管疾病、先天性中枢神经系统疾病、先天性心脏畸形、发热、精神刺激、脑损害等因素。由于学龄期儿童正处于身体机能和神经系统发育的活跃时期，若长时间、频繁癫痫发作可引发其出现神经系统发育障碍等不良后果，严重影响患儿及其家属的生活质量[3,4]。

目前，临床上治疗小儿癫痫主要通过口服药物控制的方式。据相关文献报道，传统的抗癫痫药物对小儿癫痫的控制效果较好，可显著降低癫痫的发作次数，但药物引起的肝损伤、胃肠道不适等不良反应较多，应用具有一定的局限性[5]。小儿由于自身特殊性，故临床上应选择高效、低毒副作用的抗癫痫药物对其进行治疗。新型抗癫痫药物左乙拉西坦作为一种吡咯烷酮衍生物，具有起效迅速、安全性高、生物利用度好、广谱等优点，正广泛被应用于临床小儿癫痫的治疗过程中[6,7]。传统抗癫痫药物主要通过提高癫痫患儿脑组织中γ- 氨基丁酸的浓度，从而选择性改善神经元的拮抗特性，使得突发脑功能紊乱得到抑制，达到降低机体发生癫痫次数的目的[8-10]。左乙拉西坦治疗小儿癫痫的作用机制较为复杂，单药用于治疗小儿癫痫的疗效显著，该药物可有效抑制患儿痫性放电，且安全性较高[11-13]。本研究主要探讨了左乙拉西坦治疗小儿癫痫的疗效及对血清 IgA、IgM、IgG 水平的影响，旨在为临床治疗癫痫提供新的思路，具体内容如下：

1 材料与方法

1.1 一般临床资料

选择 2014 年 1 月 -2017 年 1 月在我院就诊的癫痫患儿 102 例为研究对象，按治疗方式不同将其分为各 51 例患儿的观察组与对照组，观察组中男性患儿 30 例、女性患儿 21 例，年龄在 6 个月 -12 岁，计算平均年龄为 7.14± 1.55 岁，病程在 1 个月 -5 年，计算平均病程为 2.90± 0.85 年；癫痫类型：简单部分性 16 例，复杂部分性 14 例，局部继发全面性 9 例，强直性 6 例，肌阵 4 例，全面性强直阵挛 2 例。对照组中男性患儿 28 例、女性患儿 23 例，年龄在 7 个月 -12 岁，计算平均年龄为 7.20± 1.38 岁，病程在 1 个月 -5 年，计算平均病程为 2.85± 0.91 年；癫痫类型：简单部分性 17 例，复杂部分性 13 例，局部继发全面性 10 例，强直性 5 例，肌阵 5 例，全面性强直阵挛 1 例。统计学对比上述基础资料，两组患儿间无差异(P＞0.05)。

1.2 纳入及排除标准

纳入标准：① 经临床诊断、脑电图、头颅 CT、MRI 检查确诊为癫痫者；② 年龄≤ 15 岁，临床资料完整者；③ 入组前未服用过任何抗癫痫药物者；④ 患者家属对本次研究知情且已签署知情同意书。

排除标准：① 患有肝肾功能不全者；② 依从性较差、不能配合本次研究者；③ 患有严重精神疾病者；④ 研究前期服用过激素类药物者；⑤ 对本次研究使用药品过敏者。

1.3 治疗方法

给予观察组患儿左乙拉西坦片进行治疗，口服左乙拉西坦片(商品名：开浦兰；生产企业：UCB Pharma S.A.(比利时)，批准文号：注册证号 H20160254)起始治疗剂量为每天 20 mg/kg，分两次服用，并根据临床效果及耐受性，逐渐增加使用剂量，使维持剂量为每天 30-40 mg/kg。

给予对照组患儿丙戊酸钠口服液进行治疗，口服丙戊酸钠口服液(商品名：德巴金；生产企业：赛诺菲(杭州)制药有限公司；批准文号：国药准字 H20041435；起始治疗剂量为每天 20-30 mg/kg，分两次服用，并根据临床效果及耐受性，逐渐增加使用剂量，使其血药浓度维持在 50-100 μg/mg。

两组患儿均治疗时间为 24 周。

1.4 观察指标

1.4.1 临床疗效 判断标准：治疗后患儿的癫痫发作次数减少 90%以上者即为完全控制；治疗后患儿的癫痫发作次数减少在 75%-90%之间者即为显效；治疗后患儿的癫痫发作次数减少在 50%-75%之间者即为有效；治疗后患儿的癫痫发作次数减少在 50%以下者即为无效；

1.4.2 血清 IgA、IgM 和 IgG 的含量检测 所有患儿于治疗前后晨起空腹取 2 mL 非抗凝静脉血，采用免疫比浊法经日立 7600-020 全自动生化分析仪检测其血清免疫球蛋白 IgA、IgM 和 IgG 的含量。

1.4.3 不良反应的发生情况 统计两组患儿的不良反应发生情况，包括头晕、腹泻、胃肠道痉挛和嗜睡等。

1.4.4 认知功能评分 经韦氏儿童智力量表(中国修订版)于治疗前后评价两组患儿的操作智商(PIQ)、计算语言智商(VIQ)和总智商(FIQ)，得分越高者表明其智力水平越高。

1.4.5 癫痫发作次数对比 对比两组治疗前后各类型癫痫患儿的发作次数。

1.5 统计学分析

数据资料分析应用 SPSS20.0 统计学软件，计量资料以($\bar{x}$± s)表示，组间比较采用 t 检验；计数资料以(%)表示，组间比较采用卡方分析，以 P＜0.05 为差异具有统计学差异。

2 结果

2.1 两组治疗效果对比

观察组的总有效率 96.09%(49/51) 高于对照组 84.31%(43/51)(P＜0.05)，见表 1。

表 1 两组治疗效果对比[n(%)]

Table 1 Comparison of treatment effects between the two groups [n(%)]

Group	n	Complete control	Excellent	Effective	Invalid	Total
Observation group	51	11(21.57)	29(56.86)	9(17.65)	2(3.92)	49(96.09)*
Control group	51	6(11.76)	18(35.29)	19(37.25)	8(15.69)	43(84.31)

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

2.2 两组患儿治疗前后免疫球蛋白含量对比

治疗前，两组患儿的血清免疫球蛋白 IgA、IgM 和 IgG 含量无差异(P＞0.05)；治疗后，两组患儿的 IgA、IgM 和 IgG 含量均比治疗前有所下降，且观察组 IgA 和 IgM 含量低于对照组(P＜0.05)，见表 2。

表 2 两组免疫球蛋白含量对比($\bar{x}\pm s$)，g/L)

Table 2 Comparison of immunoglobulin content in the two groups($\bar{x}\pm s$), g/L)

Group	n	IgA		IgM		IgG	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	51	1.05± 0.42	0.52± 0.17*#	0.98± 0.62	0.68± 0.21*#	7.89± 1.25	6.17± 0.97*
Control group	51	1.04± 0.37	0.68± 0.31*	0.97± 0.64	0.78± 0.25*	7.87± 1.31	6.28± 1.02*

Note: compared with before treatment, *P<0.05; compared with control group, #P<0.05.

2.3 两组不良反应的发生情况对比

观察组的不良反应发生率 11.76%(6/51) 低于对照组 25.49%(13/51)(P＜0.05)，见表 3。

表 3 两组不良反应的发生情况对比[n(%)]

Table 3 Comparison of adverse reactions between the two groups [n(%)]

Group	n	Dizzy	Diarrhea	Gastrointestinal spasm	Appetite decreases	Somnolence	Total
Observation group	51	2(3.92)	1(1.96)	2(3.92)	0(0.00)	1(1.96)	6(11.76)*
Control group	51	4(7.84)	2(3.92)	2(3.92)	2(3.92)	3(5.88)	13(25.49)

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

2.4 两组患儿治疗前后的认知功能对比

治疗前，两组患儿的认知功能各指标评分无差异 (P＞0.05)；治疗后，观察患儿的 FIQ、PIQ 和 VIQ 评分均比治疗前有所升高，对照组患儿的 FIQ、PIQ 和 VIQ 评分均比治疗前有所下降，观察组评分高于对照组(P＜0.05)，见表 4。

表 4 两组患儿治疗前后的认知功能对比($\bar{x}\pm s$)，分)

Table 4 Comparison of cognitive function before and after treatment of two groups of children($\bar{x}\pm s$), points)

Group	n	FIQ		PIQ		VIQ	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	51	97.05± 2.25	99.85± 3.07*#	98.52± 3.25	103.91± 2.69*#	94.21± 2.85	97.85± 3.17*#
Control group	51	97.01± 2.69	95.12± 3.04*	98.04± 2.98	96..28± 2.51*	94.05± 3.07	92.82± 3.15*

Note: compared with before treatment, *P<0.05; compared with control group, #P<0.05.

2.5 两组不同类型癫痫患儿治疗前后的发作次数对比

治疗后，两组各类型癫痫患儿的发作次数均比治疗前有所降低(P＜0.05)，且观察组各类型癫痫患儿的发作次数明显少于对照组(P＜0.05)，见表 5。

表 5 两组不同类型癫痫患儿治疗前后发作次数的对比($\bar{x}\pm s$)，次)

Table 5 Comparison of the number of seizures in different types of epileptic children before and after treatment($\bar{x}\pm s$), times)

Type	Observation group(n=51)		Control group(n=51)	
	Before treatment	After treatment	Before treatment	After treatment
Simple partial epilepsy	32.44± 11.52	8.69± 2.51*#	32.89± 12.56	18.26± 5.69*
Complex partial epilepsy	27.32± 14.27	3.61± 1.25*#	27.69± 12.39	15.26± 4.25*
Local secondary epilepsy	52.12± 22.46	21.34± 12.01*#	51.95± 20.23	32.65± 16.85*
Severe epilepsy	11.02± 5.20	2.04± 0.89*#	10.85± 6.03	6.35± 2.01*
Myoclonic epilepsy	65.33± 12.85	25.07± 10.36*#	64.97± 13.08	38.75± 14.62*
Total coercive clonus	47.31± 10.30	15.03± 5.69*#	47.02± 11.16	28.69± 10.20*

Note: compared with before treatment, *P<0.05; compared with control group, #P<0.05.

3 讨论

目前，临床上 80%左右的癫痫患儿主要采取药物控制治疗，药物的选择基于以下几个因素：癫痫的种类、患儿的年龄、其他临床问题以及潜在的药物副作用[14-16]。卡马西平、丙戊酸钠等作为临床上常用的广谱类抗癫痫药，该类药物通过选择性提

高神经元拮抗特性，从而对突发脑功能紊乱起到抑制作用，进而减少癫痫的发作次数[17-19]。但临床资料显示传统抗癫痫药物易引起肝损伤、骨代谢功能异常、血液系统损伤等不良反应，应用具有一定的局限性[20-22]。癫痫治疗是一个长期的过程，确保治疗的有效性和安全性是评价抗癫痫药物优劣的重要指标。左乙拉西坦作为一种新型治疗小儿癫痫的药物，其抗癫痫作用机制较为独特，且药代动力学特征理想，具有生物利用度高、口服吸收快、疗效显著等优点[23-25]。

本研究结果显示，观察组患儿的总有效率 96.09%(49/51)高于对照组 84.31%(43/51)(P＜0.05)；观察组的不良反应发生率 11.76%(6/51)低于对照组 25.49%(13/51)(P＜0.05)；观察患儿的 FIQ、PIQ 和 VIQ 评分均比治疗前有所升高，对照组患儿的 FIQ、PIQ 和 VIQ 评分均比治疗前有所下降，观察组评分高于对照组(P＜0.05)；治疗后，两组各类型癫痫患儿的发作次数均比治疗前有所降低(P＜0.05)，且观察组各类型癫痫患儿的发作次数明显少于对照组(P＜0.05)。以上结果表明应用左乙拉西坦治疗小儿癫痫的疗效显著、且安全性较高，该结果与文献报道一致[26,27]。

相关研究表明小儿癫痫发作时，应激状态及脑部潜在的功能、结构异常均可引起患儿免疫系统的异常[28]，血清免疫球蛋白是一组由 B 细胞产生经浆细胞合成和分泌的具有抗体活性的蛋白质，其可根据结构不同分为 IgD、IgE、IgA、IgM 和 IgG 五类。其中，IgA、IgM 和 IgG 在免疫系统调节中较为重要，常以此作为衡量免疫功能的重要指标[29]。本研究结果显示治疗后，两组患儿的 IgA、IgM 和 IgG 含量均比治疗前有所下降，且观察组 IgA 和 IgM 含量低于对照组(P＜0.05)。相关研究通过对癫痫患儿的 IgA、IgM 和 IgG 水平进行检测，发现其值较正常儿童高，采用左乙拉西坦治疗后，IgA、IgM 和 IgG 等水平较之前均有所降低[30,31]，本研究结果与之相似，表明左乙拉西坦治疗小儿癫痫，可有效改善其免疫功能。

综上所述，左乙拉西坦治疗小儿癫痫的疗效显著，该药物可显著降低癫痫患儿的血清免疫球蛋白水平，改善认知功能，降低癫痫的发作次数，且安全性较高。

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