

doi: 10.13241/j.cnki.pmb.2021.02.030

卡马西平与丙戊酸钠对儿童癫痫部分性发作脑电图的临床对照研究*

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摘要 目的:探究卡马西平与丙戊酸钠对儿童癫痫部分性发作患儿发作脑电图影响,并实施组间对照研究。**方法:**选择2017年1月至2020年1月于我院接受治疗的81例癫痫部分性发作患儿为研究对象,按照其接受治疗的差异将其分为卡马西平组(40例)和丙戊酸钠组(41例),对比两组患儿接受药物治疗后脑电图以及脑电地形图变化情况。**结果:**(1)卡马西平组患儿接受治疗后脑电图检测显示间歇期痫样活动减少 $\geq 50\%$ 者占比高达67.50%(27/40),而丙戊酸钠组占比仅为43.90%(18/41),两组比较差异明显($P<0.05$);(2)脑电背景活动变化比较显示,治疗后卡马西平组患儿 α 波无影响者占比65.00%,明显高于丙戊酸钠组36.59%,同时丙戊酸钠组患儿 δ 波数(20s内)药物治疗后变化较卡马西平组更为明显;(3)脑电功率比较显示,卡马西平组患儿治疗后仅 θ 频段相对功率出现明显变化($P<0.05$),但丙戊酸钠组患儿 α 频段相对功率、 θ 频段相对功率和 θ 频段绝对功率均出现明显变化($P<0.05$)。**结论:**丙戊酸钠应用于儿童癫痫部分性发作时患儿脑电背景活动会明显变慢,甚至有出现间歇期痫样放电的风险,而卡马西平相对更为稳定,对患儿脑电图的影响更小,安全性更高。

关键词:卡马西平;丙戊酸钠;癫痫部分性发作;脑电图

中图分类号:R742.1;R748 **文献标识码:**A **文章编号:**1673-6273(2021)02-338-04

A Clinical Comparative Study of Carbamazepine and Sodium Valproate on EEG in Children with Partial Seizure*

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ABSTRACT Objective: To explore the effects of carbamazepine and sodium valproate on children with partial seizures and to conduct electroencephalograms, and implement a controlled study between groups. **Methods:** 81 patients with partial seizures who were treated in our hospital from January 2017 to January 2020 were selected as the research object, and they were divided into carbamazepine group (40 cases) and C In the sodium valerate group (41 cases), compare the changes in EEG and EEG topography of the two groups of children after receiving drug treatment. **Results:** The EEG test of children in the carbamazepine group after treatment showed that intermittent epilepsy-like activity was reduced by $\geq 50\%$, accounting for up to 67.50% (27/40), while the sodium valproate group accounted for only 43.90% (18/41), the difference between the two groups was significant ($P<0.05$). After treatment, the proportion of children with no effect of alpha wave in the carbamazepine group accounted for 65.00%, which was significantly higher than 36.59% in the sodium valproate group. At the same time, the delta wave number (within 20 s) of children in the sodium valproate group changed more significantly than the carbamazepine group. Only the relative power of the θ frequency band changed significantly in the carbamazepine group ($P<0.05$), but the relative power of α frequency band, relative power of θ frequency band and absolute power of θ frequency band in the sodium valproate group showed significant changes ($P<0.05$). **Conclusion:** When valproate is used in children with partial seizures, the children's EEG background activity will be significantly slower, and there is even a risk of intermittent epilepsy-like discharges, while carbamazepine is relatively more stable. The impact of the graph is smaller and the security is higher.

Key words: Carbamazepine; Sodium valproate; Partial seizures; EEG

Chinese Library Classification (CLC): R742.1; R748 **Document code:** A

Article ID: 1673-6273(2021)02-338-04

前言

癫痫又被称为“羊角风”或“羊癫疯”,是一种以大脑神经元异常过度或同步化活动所引起突发性异常放电,进而导致

大脑功能出现短暂性障碍的慢性疾病,属于神经系统常见疾病之一^[1,2]。研究显示,约有60%的癫痫患者于儿童时期起病,国内癫痫的总体患病率约为7.0%,年发病率约为28.8/10万,1年内有发作的活动性癫痫患病率约为4.6%,当前我国约有

* 基金项目:内蒙古自治区卫生厅科研项目(201703097)

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(收稿日期:2020-05-06 接受日期:2020-05-31)

900 万左右癫痫患者, 其中约有 500~600 万属于活动性癫痫, 每年新增癫痫患者数约为 40 万左右, 目前癫痫已经成为神经科仅次于头痛的第二大常见病^[3,4]。当前癫痫的主要治疗措施包括药物治疗、手术治疗和神经调控治疗等, 其中药物治疗仍是国内外癫痫治疗主流措施, 通过良好的药物干预, 约 70% 的患者临床症状会得以控制, 约有 50%~60% 的患者经 2~5 年的治疗可以达到痊愈效果^[5-7]。卡马西平和丙戊酸钠都是临床上常用的癫痫治疗药物, 尤其是在治疗儿童部分性发作中效果尤佳^[8,9], 当前临床上关于上述药物对部分性发作癫痫患儿脑电图的影响研究较少, 本研究旨在分析两种药物对患儿脑电图的干预效果, 以期对比两种药物治疗效果, 为临床用药提供实践指导, 现详述如下。

1 资料与方法

1.1 一般资料

选择 2017 年 1 月至 2020 年 1 月于我院接受治疗的 81 例癫痫部分性发作患儿为研究对象, 按照其接受治疗的差异将其分为卡马西平组(40 例)和丙戊酸钠组(41 例)。

纳入标准:(1)入组患儿均符合 1981 年国际抗癫痫联盟制定的癫痫部分性发作诊断标准, 并经脑电图检测确诊为部分性发作^[10,11];(2)调研经医院伦理学会批准实施;(3)血常规、肝肾功能及头颅影像检测正常者;(4)病历资料齐全;(5)患儿家属签署知情同意书。

排除标准:(1)除部分性发作外其他癫痫类型者;(2)合并智力低下、神经系统进行性或变性病变者;(3)合并遗传代谢性疾病者;(4)合并严重肝肾功能或其他脏器功能障碍者;(5)合并恶性肿瘤者。

1.2 干预方法

卡马西平组患儿接受卡马西平(湖南汉森制药股份有限公司, 规格 0.2 g/片, 国药准字 H43021638)单药治疗, 应用剂量为首次 0.05~0.1 g, 服用 2 次后, 隔周增加 0.1 g 直至出现疗效, 维持剂量调整至最小有效量(一般为 0.4~0.8 g, 3~4 次/d);丙戊酸钠组患儿接受丙戊酸钠(赛诺菲制药有限公司, 规格 500 mg/片, 国药准字 H20010595)单药治疗, 初始剂量为 10~15 mg/kg, 随后递增至有效, 一般维持剂量为 20~30 mg/kg。

1.3 观察指标及评测标准

两组患儿在接受药物治疗前后均实施脑电图和脑电地形图检测, 脑电图选择仪器为意大利 EB Neuro 型脑电图分析仪, 脑电地形图选择 EK-8200 型脑电地形图仪, 检测时间均为 9~11 时, 参照国际 10/20 系统放置电极, 分别采集两组患儿用药前和用药后的脑电图、脑电背景活动、脑电功率情况, 并实施组内前后以及组间差异性比较^[11,12]。

1.4 统计学方法

将采集的数据录入至 SPSS 20.0 软件中实施统计学分析, 对于计量数据采取($\bar{x} \pm s$)的形式来表示, 组间的差异性比较应用 Student's t test 检验, 对于计量资料采取[n(%)]的形式表示, 组间的差异性比较采用卡方检验, 多组间比较差异性采取 F 检验, 取 $P < 0.05$ 为差异具有统计学意义。

2 结果

2.1 两组患儿一般临床资料比较

两组患儿一般临床资料诸如性别、平均年龄、平均病程、平均智商、发作类型等实施组间比较差异不具有统计学意义($P > 0.05$), 具有可比性, 如表 1。

表 1 两组患儿一般临床资料差异性比较

Table 1 Comparison of general clinical data differences between two groups of children

Index		Carbamazepine group(n=40)	Sodium valproate group(n=41)
Sex	Male	21	21
	Female	19	20
Age (years)		12.19± 3.22	12.31± 3.01
Weight(kg)		36.18± 3.22	36.01± 3.41
Course(month)		20.19± 3.22	19.98± 3.44
IQ(point)		103.18± 19.21	103.21± 19.31
Seizure type	Simple partial seizure	15	15
	Complex partial seizure	25	26

2.2 两组患儿接受药物治疗后脑电图间歇期痫样放电变化分析

卡马西平组患儿药物治疗后脑电图间歇期痫样放电减少 50% 及以上(含消失)占比 67.50%, 明显高于丙戊酸钠组的 43.90%, 组间比较差异明显($P < 0.05$), 如表 2 所示。

2.3 两组患儿接受药物治疗后脑电背景活动影响比较

卡马西平组患儿 α 波无影响占比 65.00%, 明显高于丙戊酸钠组的 36.59%, 差异明显($P < 0.05$), 卡马西平组患儿 δ 波数治疗前后差异不大($P > 0.05$), 但丙戊酸钠组患儿 δ 波数治疗前后差异更为明显($P < 0.05$), 如表 3。

2.4 两组患儿接受药物治疗前后脑电功率变化分析

卡马西平组患儿治疗前后 α 频段相对功率、 θ 频段绝对功率比较不具有差异性($P > 0.05$), 丙戊酸钠组患儿治疗前后 α 频段相对功率、 θ 频段相对功率和 θ 频段绝对功率出现了明显的改变, 前后差异明显($P < 0.05$), 如表 4。

3 讨论

癫痫是一种具有持续性产生癫痫样发作倾向的脑部疾病, 是因大脑神经元过度或同步放电所产生的一过性症状^[13,14]。癫

痫是当前神经科较为常见的疾患,具有神经生物、认知、心理和社会后果,流调学显示,当前癫痫的发病率约为 3.5 %~6.5 %,尤以儿童最为常见,有研究指出癫痫还与精神发育迟缓、注意力缺陷障碍和自闭症等较为严重的神经发育障碍有密切的关系^[15,16]。癫痫不仅会损伤脑细胞,对儿童的身心健康与正常发育

造成影响,同时还会明显降低患儿的生活质量,给其个人和家庭带来沉重的负担^[17]。癫痫按照发作类型可区分为部分性发作和全身性发作,其中部分性发作又可分为简单部分性发作和复杂部分性发作,不同的临床类型在治疗方式上存在一定的差异^[18,19]。

表 2 两组患儿接受药物治疗后脑电图间歇期痫样放电变化分析[例(%)]

Table 2 Analysis of changes in EEG seizures after intermittent treatment of two groups of children[n(%)]

Groups	n	0%~24% reduction	26%~49% reduction	Reduce by 50% or more (including disappearance)	Increase
Carbamazepine group	40	3(7.50)	10(25.00)	27(67.50)	0(0.00)
Sodium valproate group	41	8(19.51)*	12(29.27)	18(43.90)*	3(7.32)

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

表 3 两组患儿接受药物治疗后脑电背景活动影响比较

Table 3 Comparison of the effects of EEG background activity between two groups of children after receiving drug treatment

Index	Carbamazepine group(n=40)	Sodium valproate group(n=41)	
α rhythm	α wave has no effect	26(65.00) [#]	15(36.59)
	Decrease>1.0 Hz	5(12.50) [#]	14(34.15)
	Decrease0.5~1.0 Hz	5(12.50)	8(19.51)
	Increase $\geq$ 1.0 Hz	4(10.00)	4(9.76)
θ wavenumber (Within 20 s)	Before treatment	18.28 $\pm$ 5.44	18.31 $\pm$ 5.43
	After treatment	20.49 $\pm$ 6.54* [#]	25.51 $\pm$ 8.54*
δ wavenumber (Within 20 s)	Before treatment	4.42 $\pm$ 3.22	4.39 $\pm$ 5.11
	After treatment	5.11 $\pm$ 4.33 [#]	9.01 $\pm$ 8.22*

Note: compared with before treatment, * $P<0.05$, compared with the sodium valproate group, [#] $P<0.05$.

表 4 两组患儿接受药物治疗后脑电功率变化比较

Table 4 Comparison of changes in brain electrical power between two groups of children after receiving drug treatment

Groups	n	α band Relative power of frequency band (%)		θ band Relative power of frequency band (%)		θ band Absolute power(μ V2)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Carbamazepine group	40	34.87 $\pm$ 14.87	35.18 $\pm$ 14.45	36.11 $\pm$ 13.21	31.28 $\pm$ 13.21*	37.18 $\pm$ 10.31	38.01 $\pm$ 9.88
Sodium valproate group	41	34.31 $\pm$ 15.41	39.29 $\pm$ 16.31*	34.71 $\pm$ 10.21	32.18 $\pm$ 10.31*	37.17 $\pm$ 10.21	33.18 $\pm$ 20.12*

Note: compared with before treatment, * $P<0.05$.

癫痫是因大脑神经元异常放电所引起的疾患,因而脑电图可以作为癫痫诊断和治疗重要参考依据,当前临床上也多将脑电图检测作为癫痫的首选筛查和治疗效果评估工具,为癫痫发作类型确定、定位等提供了有力支撑^[20,21]。目前药物治疗仍是癫痫的最主要治疗方法,但部分癫痫药物应用后会产生明显的不良反应,甚至有加重病情的可能,而通过检测用药后癫痫患者脑电图变化可以评估药物治疗效果,为癫痫患者用药提供更为安全有效的指导^[22,23]。卡马西平和丙戊酸钠都是临床上癫痫治疗常用药物,其中卡马西平主要通过限制突触前后神经元动作电位的发放来阻断兴奋性神经递质的释放,从而降低神经元兴奋性,达到抗惊厥效果,丙戊酸钠主要通过升高抑制性神经递质 γ -氨基丁酸的浓度来降低神经元兴奋性进而抑制惊厥发作,两种药物在治疗癫痫部分性发作中药理机制有一定的差异性^[24,25]。

本研究通过设立不同分组的方式,就卡马西平和丙戊酸钠

对儿童癫痫部分性发作脑电图的影响进行了分析,结果显示,在脑电图间歇期痫样放电方面,卡马西平组患儿经治疗后减少 50 %及以上(含消失)占比高达 67.50 %,而选择丙戊酸钠进行治疗的患儿减少 50 %及以上(含消失)占比仅为 43.90 %,两组患儿组间比较差异较为明显。与赵睿^[26]的研究不同,该学者探讨丙戊酸钠治疗部分性癫痫发作的临床疗效及对患者脑电图的影响,发现丙戊酸钠治疗组和卡马西平治疗组治疗有效率无差异,治疗 6 个月后丙戊酸钠德巴金治疗组患者发作期间痫样放电改善效果明显优于卡马西平得理多治疗组,说明丙戊酸钠在改善患者痫样放电方面效果更优。有研究指出,卡马西平能够快速而持续的减少广泛性棘波和临床失神性癫痫的发作,通过动物实验也可以发现卡马西平能够明显而持续的减少诱发颞叶癫痫的痫样放电出现^[27,28]。本文作者分析认为,卡马西平主要通过调节 Ca^{2+} 通道来发挥治疗癫痫发作效果,在体内具有多

个作用位点和多重作用机制,长期使用卡马西平治疗后药物能够与突触囊泡蛋白 SV2A 相结合,使神经递质释放减少,从而抑制异常放电的出现,达到治疗癫痫目的^[29],文中卡马西平组患儿一方面治疗后脑电图间歇期痫样放电减少较丙戊酸钠组更为明显,同时脑电图间歇期痫样放电增加明显低于丙戊酸钠组,这提示卡马西平治疗效果较好,同时安全性更高。文中还就两组患儿治疗后脑电背景活动情况进行了比较,结果显示卡马西平对患儿的 α 波、 δ 波的影响明显弱于丙戊酸钠组。有研究显示,随着个体年龄的增长, α 波会逐渐成熟增加,而 θ 波与 δ 波会逐渐减少,这是儿童正常脑电图发展规律^[30],文中通过比较发现,丙戊酸钠组患儿在用药后 α 波、 θ 波与 δ 波均出现了明显的变化,前后差异明显,与田苗^[31]等学者的研究类似,该学者研究奥卡西平和丙戊酸钠对成人部分性癫痫患者脑电图的影响,发现治疗前,奥卡西平治疗组和丙戊酸钠治疗组患者脑电图指标检查结果比较差异无统计学意义,治疗后两组患者 α 波减少超过 0.5 Hz, θ 波增多, δ 波增多发生率比较差异有统计学意义,与本研究不同的是研究对象不同,该学者选择的是成人。本研究提示丙戊酸钠对患儿的正常脑电波产生了明显的影响,临床上分析这是不利于儿童大脑发育的。进一步的研究结果提示,经药物治疗后丙戊酸钠组患儿的 α 频段相对功率、 θ 频段相对功率与 θ 频段绝对功率都出现了明显的变化,前后差异较大,提示丙戊酸钠明显改变了儿童的脑电波,甚至可以推测药物治疗可能影响了患儿的正常发育,安全性值得商榷。反观卡马西平,患儿治疗前后仅 θ 频段相对功率出现了一定变化,相对丙戊酸钠治疗安全性更高。本研究虽得到了丙戊酸钠与卡马西平治疗儿童癫痫部分性发作时患儿的优缺点,但是也存在一定的不足,没有分析二者联合治疗对患儿的脑电图的影响,同时样本量少,结果也存在一定的偏倚,因此,需要联合当地其他的医院,扩大样本量进行深入探究其优缺点,为儿童癫痫部分性发作时患儿的治疗提供治疗方法。

综上所述,丙戊酸钠应用于儿童癫痫部分性发作时患儿脑电背景活动会明显变慢,甚至有出现间歇期痫样放电的风险,而卡马西平相对更为稳定,对患儿脑电图的影响更小,安全性更高,值得进行临床推广应用。

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