

卡马西平联合托吡酯治疗部分性癫痫的临床观察

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摘要 目的:观察卡马西平联合托吡酯治疗部分性癫痫的疗效和安全性。方法:130例部分性癫痫患者随机均分为对照组和观察组。对照组患者给予卡马西平片100 mg,口服,3次/d;观察组患者在对照组治疗基础上给予托吡酯片初始剂量25 mg,口服,1次/d,之后每周增加25 mg,最大剂量≤200 mg,口服,1次/d。两组患者均治疗6个月后评价疗效,观察两组患者治疗前后癫痫发作频率,脑电图痫样放电波改善情况及不良反应发生情况。结果:观察组患者总有效率显著高于对照组,差异有统计学意义($P < 0.05$)。治疗后,两组患者癫痫发作频率均显著低于同组治疗前,治疗6个月后<3个月后<1个月后,且观察组低于对照组同期,差异均有统计学意义($P < 0.05$)。观察组患者脑电图痫样放电波改善情况显著优于对照组,差异有统计学意义($P < 0.05$)。两组患者不良反应发生率比较,差异无统计学意义($P > 0.05$)。结论:卡马西平联合托吡酯治疗部分性癫痫较单用卡马西平疗效更显著,安全性相当。

关键词 卡马西平;托吡酯;部分性癫痫;发作频率

Clinical Observation of Carbamazepine Combined with Topiramate in the Treatment of Partial Epilepsy

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ABSTRACT OBJECTIVE: To observe the efficacy and safety of carbamazepine combined with topiramate in the treatment of partial epilepsy. METHODS: 130 patients with partial epilepsy were randomly divided into observation group and control group. Control group was orally treated with carbamazepine 100 mg, 3 times a day. Based on the treatment of control group, observation group was orally treated with topiramate initial dose of 25 mg, once a day, and then increased 25 mg every week, the maximum dose was no more than 200 mg, once a day. After 6 months, the efficacy was evaluated, frequency of epileptic seizures, EEG epileptiform discharges wave and incidence of adverse reactions were observed. RESULTS: The total effective rate in observation group was significantly higher than control group ($P < 0.05$). After treatment, the frequencies of epileptic seizures in 2 groups were significantly lower than before, 6 months < 3 months < 1 month, and observation group was lower than control group ($P < 0.05$). The EEG epileptiform discharges wave were in observation significantly better than control group ($P < 0.05$). There were no significant differences incidence of adverse reactions between 2 groups ($P > 0.05$). CONCLUSIONS: Carbamazepine combined with topiramate has better efficacy than carbamazepine alone in the treatment of partial epilepsy, with similar safety.

KEYWORDS Carbamazepine; Topiramate; Partial epilepsy; Seizure frequency

癫痫是一种十分常见的神经内科疾病,发病率较高,对人类身体健康危害较大。部分性癫痫是癫痫局灶性发作的症状,卡马西平治疗部分性癫痫发作已有数十年的历史,且被国内外学者推荐为首选治疗药物,效果较好^[1]。但近年来有国外报道指出,单纯应用卡马西平治疗部分性癫痫疗效仍然有限^[2]。托吡酯为新型抗癫痫药物。在本研究中,笔者观察了卡马西平联合托吡酯治疗部分性癫痫的疗效和安全性,以为临床治疗提供参考。

1 资料与方法

1.1 资料来源

选择2013年6月—2014年6月四川医科大学附属第一医院

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院治疗的部分性癫痫患者130例。纳入标准:(1)符合世界卫生组织(WHO)关于部分性癫痫的诊断标准^[3-4];(2)经脑电图等诊断确诊为部分性癫痫;(3)年龄>20岁;(4)治疗后成功观察6个月。排除标准:(1)既往服用卡马西平或托吡酯后无明显疗效或有严重不良反应者;(2)颅内占位或脑血管病等其他疾病导致发作者;(3)频繁发作无法进行单药治疗者;(4)妊娠期或哺乳期妇女。按随机数字表法将所有患者均分为观察组和对照组。观察组男性45例、女性20例,年龄(31.4±2.2)岁,病程(31.7±2.9)个月;对照组男性47例、女性18例,年龄(31.6±2.5)岁,病程(31.5±2.5)个月。两组患者性别、年龄等基本资料比较,差异均无统计学意义($P > 0.05$),具有可比性。本研究方案经该院医学伦理委员会批准,所有患者家属均签署了知情同意书。

1.2 治疗方法

对照组患者给予卡马西平片(北京诺华制药有限公司,规格:100 mg/片)100 mg,口服,3次/d;观察组患者在对照组

治疗基础上给予托吡酯片(西安杨森制药有限公司,规格:25 mg/片)初始剂量25 mg,口服,1次/d,之后每周增加25 mg,最大剂量≤200 mg,口服,1次/d。两组患者均治疗6个月评价疗效。

1.3 观察指标

观察两组患者治疗前后癫痫发作频率,脑电图痫样放电波改善情况及不良反应发生情况。

1.4 疗效判定标准^[5-9]

控制:癫痫发作完全消失;显效:癫痫发作频率较治疗前减少≥75%;有效:癫痫发作频率较治疗前减少≥50%;无效:癫痫发作频率较治疗前减少<50%。总有效率=(控制例数+显效例数+有效例数)/总例数×100%。

1.5 统计学方法

采用SPSS 13.0统计软件对数据进行分析。计量资料以 $\bar{x} \pm s$ 表示,采用 t 检验;计数资料以率或例表示,采用 χ^2 检验。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者临床疗效比较

观察组患者总有效率显著高于对照组,差异有统计学意义($P < 0.05$),详见表1。

表1 两组患者临床疗效比较[例(%)]

Tab 1 Comparison of clinical efficacies between 2 groups [case (%)]

组别	n	控制	显效	有效	无效	总有效率, %
观察组	65	43(66.15)	10(15.38)	9(13.85)	3(4.62)	95.38
对照组	65	26(40.00)	16(24.62)	12(18.46)	11(16.92)	83.08

2.2 两组患者治疗前后癫痫发作频率比较

治疗前,两组患者癫痫发作频率比较,差异无统计学意义($P > 0.05$);治疗后,两组患者癫痫发作频率均显著低于同组治疗前,治疗6个月后<3个月后<1个月后,且观察组低于对照组同期,差异均有统计学意义($P < 0.05$),详见表2。

表2 两组患者治疗前后癫痫发作频率比较($\bar{x} \pm s$,次)

Tab 2 Comparison of the frequencies of epileptic seizures between 2 groups before and after treatment ($\bar{x} \pm s$, times)

组别	n	治疗前	治疗1个月后	治疗3个月后	治疗6个月后
观察组	65	12.24±5.68	5.24±2.17**	2.57±2.01***	2.24±1.73***
对照组	65	12.25±6.17	6.55±3.24*	3.69±2.74*	3.08±2.21**

注:与治疗前比较,* $P < 0.05$;与对照组比较,** $P < 0.05$;与治疗1个月后,3个月后比较,*** $P < 0.05$;与治疗1个月后比较,* $P < 0.05$

Note: vs. before treatment, * $P < 0.05$; vs. control group, ** $P < 0.05$; vs. after 1 and 3 months, *** $P < 0.05$; vs. after 1 month, * $P < 0.05$

2.3 两组患者脑电图痫样放电波改善情况比较

治疗后,观察组患者脑电图痫样放电波改善情况显著优于对照组,差异有统计学意义($P < 0.05$),详见表3。

表3 两组患者脑电图痫样放电波改善情况比较(例)

Tab 3 Comparison of improvement of EEG epileptiform discharges wave between 2 groups (case)

组别	n	消失	放电减少	无变化	轻微增加
观察组	65	39	21	3	3
对照组	65	28	26	6	5

2.4 不良反应

两组患者不良反应发生率比较,差异无统计学意义($P > 0.05$),详见表4。

3 讨论

表4 两组患者不良反应发生率比较[例(%)]

Tab 4 Comparison of incidence of adverse reactions [case (%)]

组别	n	头晕	乏力	嗜睡	粒细胞减少	皮疹	轻度肝功能异常	总发生率, %
观察组	65	5(7.69)	1(1.54)	5(7.69)	1(1.54)	3(4.62)	2(3.08)	26.15
对照组	65	4(6.15)	3(4.62)	2(3.08)	0(0)	1(1.54)	1(1.54)	16.92

癫痫为大脑神经元发生突发性的异常放电,致使大脑功能发生短暂时性障碍的一类慢性疾病,严重影响患者生活质量,因此采取积极有效的治疗措施具有重大意义^[7]。

卡马西平是亚氨基苊类抗癫痫药物,能降低患者神经元膜内的钠离子通透性,进而抑制神经元过度兴奋,提高神经元膜稳定性,达到抗癫痫的目的。

托吡酯是一种结构独特的新型抗癫痫药物,可增加患者小脑颗粒细胞的 γ -氨基丁酸A型受体所介导的氯离子内流,发挥调节作用,同时可对电压依赖性钠离子通道进行调节,降低神经元持续性放电,阻断机体内海人藻酸所介导的局部电流,降低神经元兴奋性,从而发挥药理作用。Aydin-Abidin S等^[8]报道,托吡酯与其他类抗癫痫药物联合后耐受性较好,可增加疗效。卡马西平联合托吡酯可从不同作用方向发挥协同增效作用,对部分性癫痫患者疗效更佳^[9]。

本研究结果显示,观察组患者总有效率显著高于对照组,差异有统计学意义;治疗后,两组患者癫痫发作频率均显著低于同组治疗前,治疗6个月后<3个月后<1个月后,且观察组低于对照组同期,差异均有统计学意义。观察组患者脑电图痫样放电波改善情况显著优于对照组,差异有统计学意义。这表明卡马西平联合托吡酯可增加疗效,有效地降低癫痫发作频率。安全性方面,两组患者不良反应发生率比较,差异无统计学意义。这表明卡马西平联合托吡酯安全性较好,与相关报道结果一致^[10-11]。

综上所述,卡马西平联合托吡酯治疗部分性癫痫较单用卡马西平疗效更显著,安全性相当。由于本研究纳入观察的样本量较小,此结论还有待大样本、多中心研究进一步证实。

参考文献

- [1] 李乐超,狄晴,张燕芳,等.卡马西平治疗新诊断部分性发作癫痫患者的预后[J].中华神经科杂志,2013,46(8):524.
- [2] Kanemura H, Sano F, Tando T, et al. Effects of topiramate on headache in children with epilepsy[J]. *No To Hattatsu*, 2015, 47(1):18.
- [3] 中华医学会神经病学分会脑电图与癫痫学组.抗癫痫药物应用专家共识:节选[J].中华医学信息导报,2011,26(4):20.
- [4] Pasini A, Pitzianti M, Baratta A, et al. Timing and clinical characteristics of topiramate-induced psychosis in a patient with epilepsy and tuberous sclerosis[J]. *Clin Neuropharmacol*, 2014, 37(1):38.
- [5] 喻文,罗红敏.卡马西平中毒患者并发癫痫的危险因素及预后:一项为期2年的横断面研究[J].中华危重病急救医学,2015,2(4):284.
- [6] Florek-Luszczki M, Wlaz A, Luszczki JJ, et al. Interactions of levetiracetam with carbamazepine, phenytoin, topiramate and vigabatrin in the mouse 6 Hz psychomotor seizure model: a type II isobolographic analysis[J]. *Eur J*

小剂量氯胺酮联合舒芬太尼对食管癌根治术后镇痛效果的影响

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摘要 目的:探讨小剂量氯胺酮联合舒芬太尼对食管癌根治术后镇痛效果的影响。方法:153例实施食管癌根治术的患者均分为A、B、C组。各组患者麻醉诱导后,手术结束前30 min应用镇痛药物。A组患者给予舒芬太尼2 μg/kg;B组患者给予舒芬太尼2.5 μg/kg;C组患者给予舒芬太尼2 μg/kg+氯胺酮85 μg/(kg·h)。观察各组患者麻醉前及麻醉后4、8、16、24、48 h时视觉模拟评分法(VAS)评分及Ramsay评分,镇痛泵按压次数及不良反应发生情况。结果:各组患者麻醉后4、8、16 h时Ramsay评分均显著高于同组麻醉前,差异均有统计学意义($P<0.05$),但各组间比较及各组患者麻醉后24、48 h时Ramsay评分与同组麻醉前比较,差异均无统计学意义($P>0.05$);各组患者麻醉后各时间点(C组48 h除外)VAS评分均显著高于同组麻醉前,但C组<B组<A组,差异均有统计学意义($P<0.05$)。C组患者镇痛泵平均按压次数<B组<A组,A、C组患者不良反应发生率<B组,差异均有统计学意义($P<0.05$)。结论:小剂量氯胺酮联合舒芬太尼用于食管癌根治术患者在不降低镇痛效果的情况下,可减少舒芬太尼的用量,且安全性较好。

关键词 氯胺酮;舒芬太尼;食管癌根治术;麻醉

Analgesia Effect of Low-dose Ketamine Combined with Sufentanil after Radical Surgery of Esophageal Cancer

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ABSTRACT OBJECTIVE: To investigate the analgesia effect of low-dose ketamine combined with sufentanil after radical surgery of esophageal cancer. METHODS: Totally 153 patients of pre-implementation esophageal cancer surgery were randomly divided into group A, B and C. After induction of anesthesia in patients in each group, patients in group A administered sufentanil 2 μg/kg; group B were treated with sufentanil 2.5 μg/kg; group C were treated with sufentanil 2 μg/kg + ketamine 85 μg/(kg·h). Visual analog (VAS) score and Ramsay score before and after anesthesia 4, 8, 16, 24 and 48 h, analgesia pump pressing times and incidence of adverse reactions in each group were observed. RESULTS: Ramsay score in 4, 8 and 16 h in each group were significantly higher than before anesthesia, the differences were statistically significant ($P<0.05$), however, compared with before, there was no significant difference in the Ramsay score in 48 h among each group ($P<0.05$); VAS scores in each group (except for group C in 48 h) at each time point were significantly higher than before, group C<group B<group A, the differences were statistically significant ($P<0.05$). Analgesia pump pressing times in group C<group B<group A, incidence of adverse reactions in group C and group A<group B, the differences were statistically significant ($P<0.05$). CONCLUSIONS: Without reducing analgesic effect, sufentanil combined with low-dose ketamine can reduce the dose of sufentanil for patients with anesthesia in radical surgery of esophageal cancer, with good safety.

KEYWORDS Ketamine; Sufentanil; Radical surgery of esophageal cancer; Anesthesia

- Pharmacol*, 2014, 15(723):410.
- [7] 黄从刚, 卞红强, 罗正利, 等. 左乙拉西坦和托吡酯治疗癫痫疗效和安全性的系统评价[J]. 中华神经医学杂志, 2014, 13(5):499.
- [8] Aydin-Abidin S, Yildirim M, Abidin İ, *et al.* Chronic application of topiramate and carbamazepine differentially affects the EEG and penicillin-induced epileptiform activity in rats[J]. *Neurol Res*, 2012, 34(3):246.
- [9] 庄华能. 左乙拉西坦联合卡马西平与托吡酯治疗难治性癫痫临床疗效观察[J]. 现代诊断与治疗, 2015, 2(6):1 326.
- [10] Johannessen Landmark C, Baftiu A, Tysse I, *et al.* Pharmacokinetic variability of four newer antiepileptic drugs, lamotrigine, levetiracetam, oxcarbazepine, and topiramate: a comparison of the impact of age and comedication [J]. *Ther Drug Monit*, 2012, 34(4):440.
- [11] Boldyreva SR, Ermakov Alu. Comparative efficacy of carbamazepine, valproic acid and topiramate in symptomatic and cryptogenic occipital lobe epilepsy in children[J]. *Zh Nevrol Psikhiatr Im S S Korsakova*, 2010, 110(1):39.

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