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外周神经组织中Nav1.7的表达在奥沙利铂诱发神经病理性疼痛中的作用

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Effects of Nav1.7 Expression on Neuropathic Pain Induced by Oxaliplatin

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摘要

目的 探讨电压门控性钠离子通道（voltage-gated sodium channel，VGSC）$Na_V1.7$在奥沙利铂诱发神经病理性疼痛中的作用。方法 96只雄性Sprague-Dawley(SD)大鼠随机分为2组：奥沙利铂诱发神经病理性疼痛（oxaliplatin-induced neuropathic pain，OINP）组及介质葡萄糖注射组（Vehicle组）。前者一次性腹腔注射给予奥沙利铂6 mg/kg；后者一次性腹腔注射给予相应体积5%葡萄糖注射液。von Frey纤维丝测定大鼠50%缩足阈值（paw withdrawal threshold, PWT)作为神经病理性疼痛大鼠痛觉反应指标；分别于第3、7、10 d取大鼠L3~5背根神经节（dorsal root ganglions，DRG），通过免疫组织化学(immunohistochemistry, IHC)、RT-PCR、Western blot法测定DRG Nav1.7及其mRNA表达情况。结果 IHC结果显示$Na_V1.7$在OINP组与Vehicle组DRG神经元均有阳性表达，定位于胞质，呈棕黄色颗粒状染色；$Na_V1.7$在OINP组较Vehicle组染色深，差异有统计学意义（P<0.05）。RT-PCR结果显示Nav1.7 mRNA在OINP组与Vehicle组DRG均有表达，但在OINP组与Vehicle组表达差异无统计学意义。Western blot结果显示Nav1.7在OINP组与Vehicle组DRG均有表达，且在OINP组中相对表达量高于Vehicle组，两组间的表达差异有统计学意义（P<0.05）。结论 奥沙利铂通过上调外周神经$Na_V1.7$的表达，参与神经病理性疼痛的发生与维持。

关键词 ： 钠通道，$Na_V1.7$，奥沙利铂，神经病理性疼痛，背根神经节

Abstract :

Objective To investigate the effects of voltage-gated sodium channel(VGSC) Nav1.7 expression on oxaliplatin-induced neuropathic pain. Methods A total of 96 SD male mice were randomized into two groups: oxaliplatin-induced neuropathic pain(OINP) group received a single intraperitoneal oxaliplatin administration 6 mg/kg, and medium glucose injection (Vehicle) group received a single intraperitoneal injection of 5% glucose injection. 50% paw withdrawal threshold(PWT) was measured by von Frey filament when observing allodynia before administration and after administration from d1 to d10. The L3-5 dorsal root ganglions(DRG) were removed 3, 7 and 10 days after administration. Immunohistochemistry(IHC), RT-PCR and Western blot were applied to detect DRG Nav1.7and mRNA expression. Results HC analysis showed that Nav1.7 was positively expressed in DRG neurone in both groups, in brown granule, and mainly located in cytoplasm. Moreover, the difference between two groups was statistically significant(P<0.05). RT-PCR analysis showed that Nav1.7 mRNA was expressed in both groups, with no significant difference(P<0.05). Western blot analysis showed that Nav1.7 was expressed in both groups, and the level in OINP group was significantly higher than that in Vehicle group (P<0.05). Conclusion Oxaliplatin may induce the development of neuropathic pain by upregulating Nav1.7 expression in peripheral nerve.

Key words : Sodium channelNav1.7 Oxaliplatin Neuropathic pain Dorsal root ganglions (DRG)

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