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综述

维拉唑酮：多靶标和新机制抗抑郁药研发的新方向

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摘要 维拉唑酮是兼有5-羟色胺1A(5-HT_{1A})受体部分激动作用和5-HT重摄取抑制作用的双重活性药物。该药物的设计是基于特异性加速5-HT_{1A}自身受体脱敏的原理, 以达到加快起效和增强疗效的目的。临床前研究结果表明, 维拉唑酮是重组细胞系和正常组织的5-HT_{1A}受体的高效的部分激动剂, 能占有并功能性阻断5-HT转运蛋白的活性位点, 抑制5-HT重摄取; 在多个动物模型中具有抗抑郁和抗焦虑活性。维拉唑酮已经被美国食品药品监督管理局批准用于重度抑郁症的治疗。目前尚无将维拉唑酮与其他抗抑郁药进行直接比较的报道, 但现有临床研究已表明该药物抗抑郁的治疗效果与其他抗抑郁药相当。与5-HT重摄取抑制剂一样, 维拉唑酮也存在胃肠道不良反应, 但性功能障碍和体质量增加的不良反应发生率极低, 并且起效可能更快速。维拉唑酮全新的抗抑郁机制, 为重度抑郁症的治疗提供了新的选择。

关键词 重度抑郁症 维拉唑酮 抗抑郁药
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Vilazodone：a new generation of antidepressants with multiple targets and new mechanisms

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Abstract

Vilazodone is a specific combined serotonin reuptake inhibitor (SSRI) and 5-HT_{1A} receptor partial agonist, *ie*, a serotonin partial agonist and reuptake inhibitor(SPARI), the molecule of which was designed based on the finding that negative feedback circuitry and mediated via 5-HT_{1A} receptors, limits the acute SSRI-induced enhancements in serotonergic neurotransmission. The *in vitro* and *in vivo* functional assays demonstrated the two components of the action mechanism of vilazodone: SSRI activity compared with the SSRI fluoxetine and agonist activity at the 5-HT_{1A} receptor. Vilazodone was proved to be selective for serotonin *versus* norepinephrine and dopamine reuptake. Vilazodone demonstrated dose-related efficacy in several anxiety animal models and depression animal models, and the latest approved antidepressant available in the United States. It has randomized, controlled empirical data which have guaranteed its approval for treating major depressive disorder(MDD). Although no head-to-head studies against other antidepressants are published, the efficacy data for vilazodone appear comparable to other known antidepressants, with associated gastrointestinal side effects similar to those of SSRI and serotonin norepinephrine reuptake inhibitor antidepressants, but potentially with a lower incidence of sexual side effects and body mass gain. As a new option for the treatment of MDD,