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# Ketamine: A Review of Clinical Pharmacokinetics and Pharmacodynamics in Anesthesia and Pain Therapy.

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## Abstract

Ketamine is a phencyclidine derivative, which functions primarily as an antagonist of the N-methyl-D-aspartate receptor. It has no affinity for gamma-aminobutyric acid receptors in the central nervous system. Ketamine shows a chiral structure consisting of two optical isomers. It undergoes oxidative metabolism, mainly to norketamine by cytochrome P450 (CYP) 3A and CYP2B6 enzymes. The use of S-ketamine is increasing worldwide, since the S(+)-enantiomer has been postulated to be a four times more potent anesthetic and analgesic than the R(-)-enantiomer and approximately two times more effective than the racemic mixture of ketamine. Because of extensive first-pass metabolism, oral bioavailability is poor and ketamine is vulnerable to pharmacokinetic drug interactions. Sublingual and nasal formulations of ketamine are being developed, and especially nasal administration produces rapid maximum plasma ketamine concentrations with relatively high bioavailability. Ketamine produces hemodynamically stable anesthesia via central sympathetic stimulation without affecting respiratory function. Animal studies have shown that ketamine has neuroprotective properties, and there is no evidence of elevated intracranial pressure after ketamine dosing in humans. Low-dose perioperative ketamine may reduce opioid consumption and chronic postsurgical pain after specific surgical procedures. However, long-term analgesic effects of ketamine in chronic pain patients have not been demonstrated. Besides analgesic properties, ketamine has rapid-acting antidepressant effects, which may be useful in treating therapy-resistant depressive patients. Well-known psychotomimetic and cognitive adverse effects restrict the clinical usefulness of ketamine, even though fewer psychomimetic adverse effects have been reported with S-ketamine in comparison with the racemate. Safety issues in long-term use are yet to be resolved.

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