Ketamine: friend or foe?

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Ketamine, a dissociative anaesthetic drug, acts on the central nervous system (CNS) primarily through antagonism of the n-methyl-d-aspartate (NMDA) receptor.[1] Methods of administration include intravenous, intramuscular, snorting, and smoking.[2] Intranasal use which has a very rapid onset of action is common amongst recreational users.[3]

Ketamine may be used as an anti-depressant and for recovery from drug abuse.[1] Doses used in abuse are significantly higher than for therapy.[3] For recreational use the usual intranasal dose is 50 mg with abusers regularly using multiple doses to prolong intoxication.[2 3]

Ketamine's potential as a recreational drug may have hindered its usefulness in addiction rehabilitation. Studies suggest that ketamine has to be taken chronically in high doses to develop complications. The risks of using ketamine as treatment in appropriately selected patients is small, but repeated administration might be associated with the danger of dependency and complications in vulnerable individuals.[1 3 4]

Proposed mechanisms by which ketamine may exert its therapeutic effects in addiction include augmentation of neuroplasticity, interruption of related functional neural networks and blocking reconsolidation of drug-related memories.[1]

There is an on-going international debate regarding the ideal legislation for this drug.[1] Ketamine currently is classified as a schedule III controlled substance.[2]

Long-term ketamine misuse can produce toxicity in the urological and hepatobiliary tracts and cause neurocognitive impairment. Common urological manifestations include cystitis, detrusor dysfunction, ureteral obstruction, hydronephrosis and renal impairment. Emerging evidence suggests that ketamine abuse is associated with hepatic parenchymal injury, cholangiopathy, cholestasis and biliary dilatation.[2 5] Negative psychological effects include blunted affect, dissociation, paranoia and cognitive decline.[2] Habitual use of ketamine affects prefrontal dopaminergic transmission which is involved in working memory and executive function.[4]

A strong association between ketamine abuse and upper gastrointestinal tract (GIT) symptoms has been reported.[5] Most patients who abuse ketamine develop upper GI symptoms years prior to uropathy-related symptoms which is prevalent in up to 100% of people using more than 5 g daily.[6] A high index of suspicion for abuse should be retained when assessing patients with chronic upper GI symptoms to allow early detection and enable appropriate intervention.[5]

The cachexia observed in this patient could have been related to upper GIT disease and the associated malnutrition, biliary dysfunction and acute kidney injury.[2]

The exact pathophysiological mechanism by which ketamine produces upper GI, urological and hepatobiliary toxicity remains unknown[5] Its NMDA antagonist effect may affect gastric motility. Microvascular damage by ketamine and its metabolites are believed to be a causative factor for ketamine uropathy. Circulating ketamine in the bloodstream may trigger autoimmune responses leading to inflammation in the urinary and upper GI tracts. Prolonged contact can also induce direct cytotoxic effects. Ketamine can reduce the contractile response of visceral smooth muscle by its effects on the CNS. [5 7] S-ketamine has been shown to be hepatotoxic in vitro.[3]

There is increasing evidence that ketamine causes psychological and physical dependence, especially at doses of over 4 g daily for years.[7] Ketamine has great therapeutic, but also great abuse, potential.

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