Pain-Dose Ketamine in Adults: IV Push vs Slow Infusion

Introduction

1. Low dose or sub-dissociative dose ketamine is often used to treat acute pain in the emergency department
2. Sub-dissociative ketamine is usually not associated with risk of respiratory or hemodynamic effects, making it an attractive option for pain control
3. The most common side effects associated with sub-dissociative ketamine are dysphoria, nausea, and dizziness, and are found to be greatly reduced when given as a short infusion rather than an IV push

Pharmacology	
	Sub-Dissociative Ketamine
Mechanism of Action	The NMDA receptors are involved in the amplification of pain signals and the development of central sensitization. Ketamine works to block NMDA receptors in the brain and spinal cord.
Dose	0.1-0.3 mg/kg
Administration	IV push over 3-5 minutes or slow infusion over 10-15 minutes
PK/PD	Onset: 1-2 minutes Half-life: alpha 2-4 minutes, beta 2-4 hours
Adverse Effects	Depersonalization, conceptual and mental disorganization, hallucinations, and cognitive or emotional blunting, nystagmus, dizziness, vomiting, diplopia, mydriasis *Dose-dependent and most resolve within 30 minutes
Contraindications and Precautions	**Precautions:** severe or uncontrolled cardiovascular disease, severe liver disease, increased intracranial pressure, elevated intraocular pressure, pregnancy, underlying psychiatric diseases associated with psychosis While ketamine should not affect cardiac output, mean arterial pressure, or respiratory drive at sub-dissociative doses, caution is still advised with its use due to its sympathetic stimulation than can lead to increased myocardial oxygen demand and theoretical elevated intracranial pressure
Compatibility	D5W or NS

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Overview of Evidence			
Author, year	Design/ sample size	Intervention & Comparison	Outcome
Clattenburg E, et al; 2018	Randomized, double-blind, double-dummy, placebo-controlled trial (n = 59)	Ketamine 0.3 mg/kg via IV push over 1 minute along with a 100 mL minibag of NS over 15 minutes (n = 29) Vs Ketamine 0.3 mg/kg via slow infusion in 100 mL bag over 15 minutes along with a 10 mL syringe of NS over 1 minute (n = 30)	**SERSDA** is a nine-component scale (fatigue, headaches, dizziness, feelings of unreality, generalized discomfort, changes in hearing, changes in mood, hallucinations, and changes in vision) that measures the severity of each component from "0" (weak) to "4" (very bothersome) -There was no difference in any side effect (SERSDA>0) between groups (86% vs 70%) -More patients experienced more moderate or greater side effects (SERSDA $\geq$ 2) in the IVP group compared to the slow infusion group -More patients experienced feelings of unreality in the IVP group compared to the slow infusion group (52% vs 10%; p = 0.01) -More patients experienced hallucinations in the IVP group compared to the slow infusion group (28% vs 7%; p=0.03) -Pain scores were similar between groups
Motov s, et al; 2017	Prospective, randomized, double-dummy trial comparing	Ketamine 0.3 mg/kg IV push (n = 24) Vs Ketamine 0.3 mg/kg short infusion over 15 minutes (n = 24)	-More patients experienced feelings of unreality in the IV push than the slow infusion group (91.7% vs 54.2%; p =0.008) -The SERSDA score for unreality was significantly higher for the IVP group compared to the slow infusion group (3 vs 0; p=0.001) -The RASS score was significantly lower in the IVP group compared to the slow infusion group (-2.0 vs 0.0; p=0.01) -There was no difference in pain scores between both groups -There was no difference on the SERSDA scale for 8 of the variables measured (headache, fatigue, dizziness, hearing, vision, mood change, discomfort, hallucination)

Conclusions

While sub-dissociative dose ketamine can be administered as an IV push, it may not be in the patient's best interest to do so. IV push ketamine is associated with more moderate-severe adverse effects to include increased feeling of unreality and hallucinations. Studies recommend administration via slow infusion to reduce these unpleasant side effects, and our current practice here reflects this technique.

References

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