

Use of the Intranasal Route for Administration of Ketamine by Special Operations Medical Personnel During Training Mishaps

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Dear Editor,

We read with great interest the study by Fisher et al. advocating the use of ketamine by Special Operations medical personnel during training mishaps.¹ We fully agree with the different points of the article highlighting the benefit of the use of ketamine for analgesia in austere settings. Indeed, the optimal management of analgesia is a key point in combat casualty care.²⁻⁴ Among the various drugs available for combat analgesia, ketamine appears as a suitable drug on the battlefield, well known by military physicians, reliable and effective in controlling casualties' acute pain, with a large therapeutic window.⁵ Interestingly, in the study by Fisher et al.,¹ a total of eight patients (23.5%) received ketamine using the intranasal (IN) route. Recent studies have shown a growing interest in the IN route for administration of ketamine during analgesia procedures.^{6,7} The average bioavailability of ketamine delivered via the IN route is 40%.⁷ Based on the French Military Medical Service experience, recent analgesia procedures proposed to extend the use of IN route for analgesia into combat zones. Military physicians from the First Special Operation Medical Unit (1^{ère} Antenne Médicale Spécialisée), supporting the Groupe d'Intervention de la Gendarmerie Nationale, a French military tactical unit, use a dedicated analgesia protocol for administering sufentanil and ketamine via the IN route.⁸ Cazes et al. reported the case of a French soldier wounded in operations who received multimodal analgesic at the point of care, including 50µg/kg IN sufentanil, and the authors also highlighted the interest of the use of IN ketamine on the battlefield.⁹ Sufentanil is more lipophilic than ketamine and, consequently, is absorbed better by the nasal mucosa. The average bioavailability of sufentanil delivered via the IN route is 78%.¹⁰ The current US military and civilian standards of analgesia do not include the use of IN sufentanil. However, this analgesia option is under investigation in Europe although there is with sparse information on efficacy and safety.¹¹⁻¹³ Other French military medical teams reported the use of IN ketamine to manage acute pain during deployment in overseas military operations. Dubecq et al. reported a cohort of 73 combat casualties who received 0.5mg/kg IN ketamine, with high efficacy and rare side effects. Indeed, the authors reported only one case of psychodyslepsy, which ended after

another dose of 25mg of ketamine IN.¹⁴ (R,S)-Ketamine is a phenylcyclohexylamine derivative consisting of its two optical enantiomers, (S)- and (R)-ketamine. Racemic mixture is usually used, but (R)-ketamine does not exhibit psychoactive effects.¹⁵ Currently, French military physicians have access to only a racemic mixture of ketamine.

Moreover, a recent cross-sectional survey, investigating the use of IN analgesia in military setting, aimed to evaluate the medical practice of the French Military Medical Service physicians regarding the current understanding and use of IN analgesia. The surveyed population involved physicians of the French Military Medical Service. Of the 259 responses collected, 77.6% of physicians reported being familiar with the IN route for analgesia. However, only 18.4% had already used it. The most common drug used was ketamine (51%).

Finally, a ketamine pulverization device for IN analgesia is being developed currently by the Central Pharmacy of the French Military Medical Service. Such a dedicated device, deployed in all medical kits, could allow auto-administration of IN ketamine for all servicemen and women, in addition to or instead of the administration of a syrette of morphine.¹⁶ To conclude, the IN route seems to allow rapid and effective pain control on the battlefield, before obtaining intravenous (IV) or intraosseous (IO) access, which currently remains the gold standard for analgesia. We believe that having been the subject of numerous ongoing studies in civilian and military settings, and illustrated by Fisher et al.'s study, IN ketamine seems to be a promising solution for analgesia procedures performed in remote and austere environments.

Author Contributions

All authors read and approved the final manuscript.

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