Ketamine inhalation

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Editor—Usually, ketamine is dissolved in saline and administered i.v. or i.m. Alternative routes, such as oral, nasal, and rectal administration, have been described for less resource-consuming and painless administration.[1 2] We explored the safety and feasibility of delivery of ketamine by inhalation. Advantages of this route include rapid delivery and absorption into the systemic circulation and the possibility of ketamine administration outside the hospital setting because no i.v. access line is required. The study was performed in healthy volunteers of either sex (aged 18–40 yr, BMI <30 kg m^{-2}) after approval by the local human ethics committee and after receiving written informed consent from participants. The study was registered at the Dutch trial registry (NTR 5358).

Volunteers inhaled three increasing doses of preservative-free S-ketamine (dose 0.35, 0.5, and 0.7 mg kg^{-1}; inhalation duration 20–40 min). Ketamine was inhaled through a nebulizer system (Aerogen Ultra; Medicare Uitgeest BV, Uitgeest, The Netherlands) that uses a palladium high-frequency vibrating mesh (Aerogen Solo Nebulizer) to aerosolize liquid ketamine and deliver the predefined quantity of drug to a spontaneously breathing subject. The main end point was safety of the procedure. Additionally, we measured psychedelic effects and arterial plasma concentrations of S-ketamine and S-norketamine.

Twelve volunteers were recruited and participated in the trial. One subject did not complete the study because of persistent nausea and vomiting. As a result of technical issues, the data from one subject were lost; hence, we report the data from the remaining 10 subjects.

All subjects indicated that inhalation from the nebulizer was tolerable and easy. None of the subjects was incapacitated or sedated to an extent that prevented use of the nebulizer. The inhalant tasted mildly bitter. There were no incidences of oropharyngeal irritation, hypersalivation, stridor, laryngospasm, cough, dry mouth, hoarseness, dyspnoea, tachypnoea, aspiration, cardiac dysrhythmias, or desaturations during or after ketamine administration. Adverse events were related to ketamine and not to the mode of administration, as follows: mild hypertension (n=10), nausea (n=3), vomiting (n=2), drug high (n=10), and psychedelic side-effects (n=10).

The duration of inhalation for complete aerosolization of S-ketamine was longer than expected. Mean (range) inhalation times were 22 (19–40), 33 (24–51), and 41 (30–54) min for 0.35, 0.5, and 0.7 mg kg^{-1} S-ketamine, respectively. We relate this to the high viscosity of the S-ketamine solution, which is three to four times greater than that of water. S-Ketamine and S-norketamine pharmacokinetic parameters are given in Table 1. S-Ketamine maximal concentration (C_{max}) values increased in a dose-dependent manner by 77% from the lowest to the highest inhalation dose; S-norketamine C_{max} values were about half those of S-ketamine.

Table 1 Pharmacokinetic data of the inhalation and infusion of S-ketamine. Values are the mean (SD), except where indicated. C_{max}, maximal concentration during or following inhalation or infusion; CV, coefficient of variation; T_{max}, time of C_{max} from the initiation of inhalation

Parameter	First inhalation	Second inhalation	Third inhalation
Dose (mg kg^{-1})	0.35	0.5	0.7
Duration of inhalation or infusion (min)	22 (7)	33 (8)	41 (7)
S-Ketamine			
C_{max} (ng ml^{-1})	128 (3)	180 (39)	227 (36)
Range (ng ml^{-1})	80–165	107–224	158–277
T_{max} (min)	22(7)	15 (0)	25 (0)
CV (%)	26	22	16
S-Norketamine			
C_{max} (ng ml^{-1})	52 (15)	97 (21)	153 (27)
Range (ng ml^{-1})	40–81	68–126	75–219
T_{max} (min)	63 (7)	48 (7)	41 (7)
CV (%)	27	22	20

In summary, in this small exploratory observational study we show that inhalation of preservative-free S-ketamine rapidly delivers a potentially active S-ketamine plasma concentration (>100 ng ml^{-1}).[3 4] Immediate adverse events were related to the inhaled compound, with serious nausea and vomiting in one subject (10%). In the other subjects, S-ketamine-related events were mild and did not interfere with operation of the inhalation device. Short-term inhalation of ketamine seems a valid alternative to i.v. ketamine administration without the need for i.v. access. Further studies are required to assess whether safety issues occur during and after longer-term inhalation of S-ketamine in clinical practice.

Declaration of interest

None declared.

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Appendix

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Direct laryngoscopy training is important for videolaryngoscopy skill acquisition

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Editor—It has been suggested that novice doctors or medical students can acquire tracheal intubation skills using a videolaryngoscope rather than conventional direct laryngoscopes even in difficult airways.[1 2] However, no one has validated how direct laryngoscopy training might affect the acquisition of videolaryngoscope skills. We used simulation training to assess the efficacy of direct laryngoscopy training for acquiring indirect laryngoscopy skills among medical students. This study was approved by the Research Ethics Committee of Osaka Medical College.

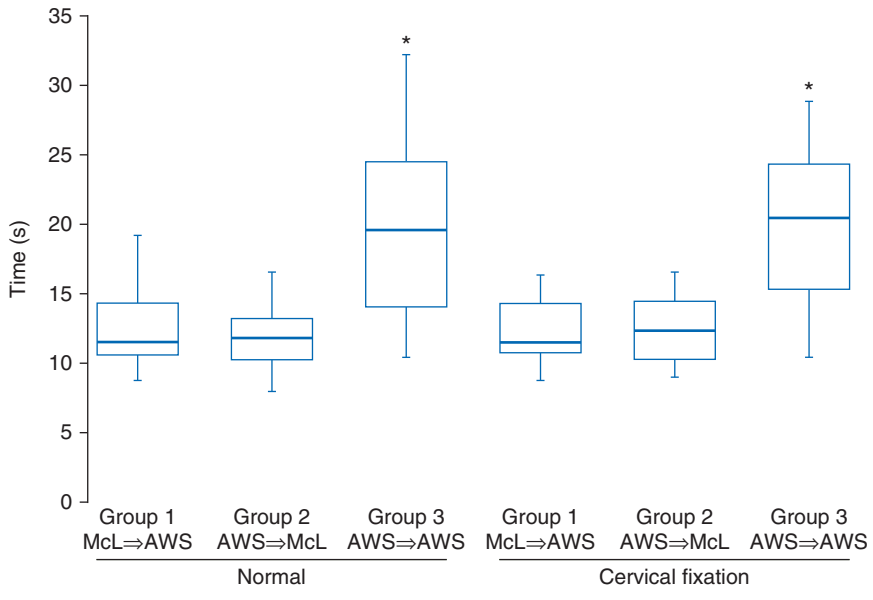

Fig 1 Intubation time with Pentax-AWS Airwayscope™ (AWS; HOYA, Japan) in normal and difficult airways (cervical fixation). *$P<0.05$ compared with Groups 1 and 2.