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Case report

Sevoflurane as adjuvant for sedation during mechanical ventilation in intensive care unit medical patients: Preliminary results of a series of cases[☆]



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ABSTRACT

Objective: To disclose our preliminary experience in inhalation sedation with sevoflurane in a standardized manner using the Anesthetic Conserving Device in intubated, critically ill patients in our ICU.

Patients: It has been used in nine cases of adult patients, six men and three women, over 24 months.

Results: A proper implementation of the protocol by physicians and the nursing staff has been achieved, meeting the goals established for sedation (RASS 0, -2) free of hepatic or renal adverse outcomes or side effects.

Conclusions: In our limited experience, adjuvant inhalation sedation with sevoflurane in the ICU is safe and complementary to the use of intravenous drugs such as propofol, remifentanyl and midazolam, which are currently commonly used to achieve goal-directed sedation.

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Sevoflorano como coadyuvante en la sedación durante ventilación mecánica en pacientes médicos de Unidad de Cuidados Intensivos: resultados preliminares en una serie de casos

R E S U M E N

Palabras clave:

Anestesia por inhalación
Midazolam
Cuidados intensivos
Respiración artificial
Sedación consciente

Objetivo: Explicar nuestra experiencia preliminar en la utilización de sedación inhalatoria de manera estandarizada con sevoflorano mediante dispositivo Anesthetic Conserving Device en pacientes críticos intubados en nuestra UCI.

Pacientes: se ha utilizado en 9 casos, en pacientes adultos, 6 hombres y 3 mujeres, durante un periodo de 24 meses.

Resultados: se ha conseguido una adecuada implantación del protocolo por parte de médicos y personal de enfermería, logrando los objetivos de sedación fijados en un primer momento (RASS 0, -2) y sin obtener resultados adversos ni efectos secundarios a nivel hepático y/o renal.

Conclusiones: en nuestra limitada experiencia, la sedación inhalatoria con sevoflorano coadyuvante en UCI es una técnica segura y complementaria al uso de fármacos intravenosos, como propofol, remifentanilo y midazolam, utilizados habitualmente, para lograr una sedación guiada por objetivos.

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Introduction

Sedation is required to ensure adequate comfort and safety to ICU patients, lowering their anxiety, restlessness, and pain,¹ and facilitating mechanical ventilation. Notwithstanding the availability of consensus guidelines in patients admitted to the ICU, the clinical practice is quite variable.² Midazolam and propofol are two of the most commonly used agents for this purpose; however, these drugs exhibit pharmacological characteristics that make them less than an ideal sedative.³

Inhalation sedation using halogenated anesthetics embodies some of the characteristics of the ideal sedative: minimal accumulation, organ-independent metabolism, insignificant side effects, shorter time to awakening, and hemodynamic stability.⁴ Another advantage is that the drug concentration at the end of expiration may be monitored continuously to allow for adjustments in the depth of sedation. Moreover, it provides cardio and neuroprotection, in addition to bronchodilatation.⁵

In 2005, the AnaConDa® (AnaConDa® Sedana Medical, Uppsala, Sweden) device (Fig. 1) the acronym for Anesthetic Conserving Device (ACD), was marketed and allowed for the safe administration of inhaled agents (isoflurane and sevoflurane) with standard ICU ventilators.

To this date, there is evidence of the safe use and the existence of some advantages of inhalation sedation versus the conventional intravenous sedation, particularly for postsurgical patients.

The purpose of this paper is to disclose our results following the use of inhalation sedation for a maximum of 72 h with sevoflurane, using the ACD device in intubated critically ill patients, in our ICU, with a RASS⁶ objective of 0-2. And further, to evaluate the effect on renal and liver function in these patients.



Fig. 1 – AnaConDa® device (AnaConDa® Sedana Medical, Uppsala, Sweden).
Source: Authors.

Patients and method

The protocol illustrated in Fig. 2 has been implemented in the usual clinical practice in our ICU since early in 2012 and it is still used. The approval by an ethics committee was not required in view of the characteristics of the trial and pursuant to the local legislation.

Upon drafting the protocol and reaching a consensus among physicians, educational sessions were organized for the nursing team, resident physicians and the rest of the healthcare staff with the aim of explaining the protocol, educating on the proper use of the equipment and responding to any questions.

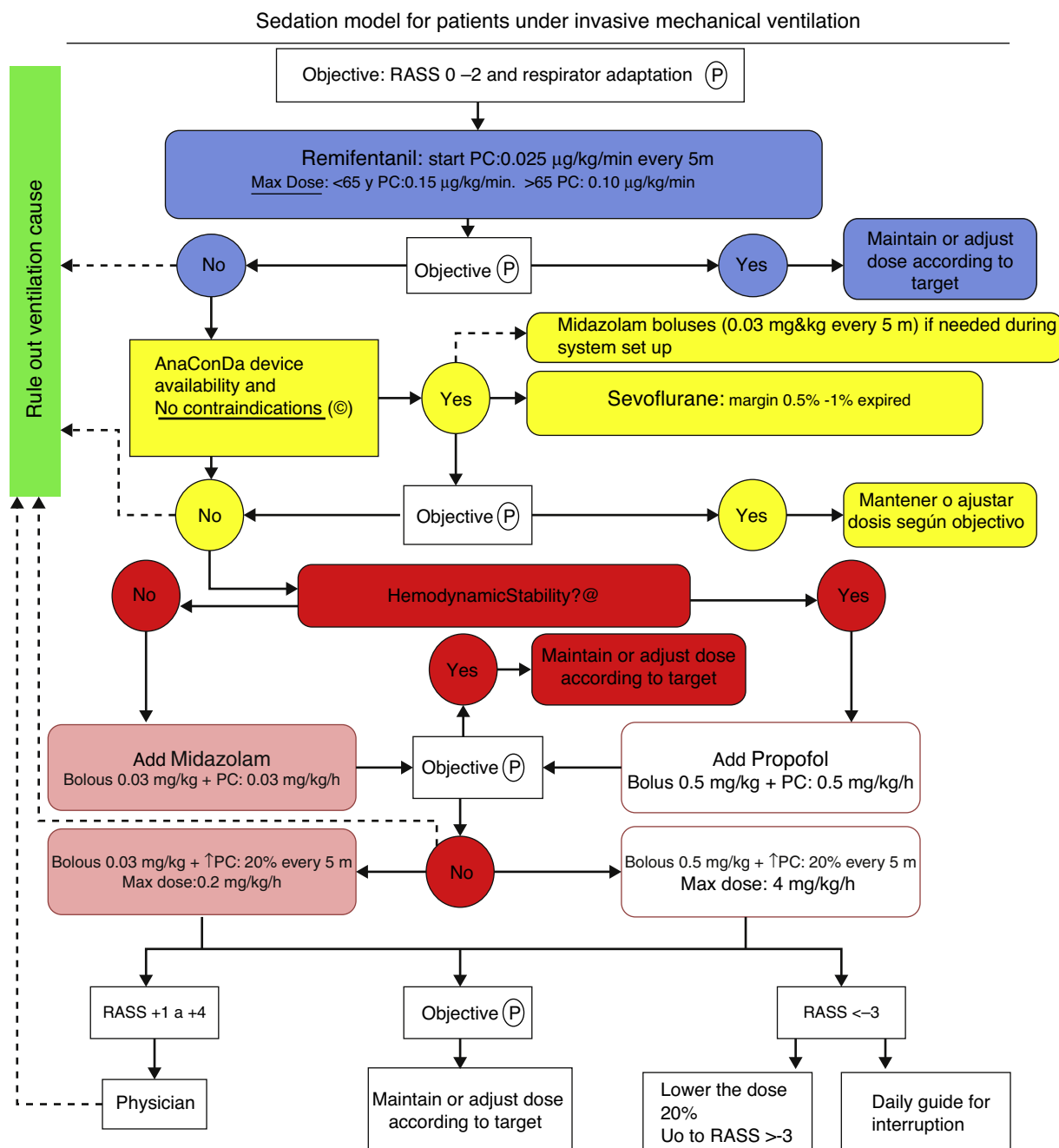


Fig. 2 – Sedation model for patients under invasive mechanical ventilation.

Source: Authors.

The protocol has been used in nine adult patients, six males and three females. Six of the nine patients had a diagnosis of acute respiratory failure and three had a diagnosis of acute over chronic respiratory failure.

Sevoflurane is used as an adjuvant when the maximum dose of remifentanyl is insufficient for proper adaptation of the patient to mechanical ventilation or with a RASS score between +2 and +4. Sevoflurane is contraindicated whenever there is a history or suspicion of malignant hyperthermia and hypersensitivity to sevoflurane. We have not used Sevo in pregnant women or in patients with intracranial

hypertension, since safety has not been established under these circumstances.

Our sedation objective is determined by the Richmond Agitation/Sedation Scale (RASS), with a target of 0 to -2. Every patient was evaluated according to RASS every 8 h.

We began IV continuous perfusion of remifentanyl sedation, titrating the dose depending on the age of the patient, starting with 0.025 mcg/kg/min and increasing the perfusion every 5 min until the maximum dose, if the target was not reached. When a new drug was required because of poor adaptation to the ventilator or failure to reach the RASS target,

Table 1 – Results of 9 patients.

Time	Parameter	1 H (65)	2 H (72)	3 M (66)	4 M (56)	5 H (69)	6 H (54)	7 M (63)	8 H (48)	9 H (73)
Basal	Urea	42	77	41	89	57	63	66	68	71
48 h	mg/dl	48	57	99	57	89	78	18	91	43
96 h	(10–50)	55	59	88	71	116	109	25	43	49
Basal	Plasma creatinine	0.53	1.25	0.89	3.79	1.48	1.83	0.90	1.08	1.39
48 h	mg/dl	0.71	0.67	1.16	2.42	1.30	2.13	0.64	1.30	0.87
96 h	(0.4–1.2)	0.71	0.73	0.88	2.41	1.36	1.92	0.66	0.76	0.93
Basal	Glomerular filtration	>60	59	60	15	52	37	>60	>60	39
48 h	ml/min/1.73	>60	>60	45	26.97	53	31	>60	>60	>60
96 h	(>60)	>60	>60	>60	26.71	57	36.9	>60	>60	>60
Basal	Total bilirubin	0.48	0.20	0.11	17.66	0.78	3.32	0.70	0.60	0.29
48 h	mg/dl	0.50	0.28	0.18	8.50	0.45	3.07	1.38	1.50	0.33
96 h	(0–1.2)	0.35	0.71	0.16	5.50	0.45	0.20	0.98	0.93	0.20
Basal	GOT	15	164	27	386	16	19	21	9	8
48 h	U/L	12	165	14	373	15	18	22	19	16
96 h	(5–31)	18	125	17	357	10	18	22	20	13
Basal	GPT	12	124	43	236	13	30	34	176	11
48 h	U/L	9	116	28	202	17	22	16	136	24
96 h	(5–31)	9	101	19	234	16	24	22	57	15
Basal	GGT	103	153	43	517	59	307	33	100	30
48 h	U/L	107	156	44	401	51	229	47	93	82
96 h	(7–32)	111	142	38	400	33	129	33	113	32
48 h	Fluor mcmol/L (<50)	97.1	0.47	30	36.57	260.8	224	0.7	1.89	82
Every 8 h from baseline	RASS –5, +4	+1, –2, –2 –2, –1, –2 0, –2, –1 –2, –2, –2	+1, –2, –2 –2, –2, –2 –2, –1, –2 –2, –1, –1	+2, –2, –2 –2, 0, –2 –2, –1, –1 –2, –1, –1	+2, –2, –1 –2, –2, –2 –2, –1, –1 –1, –2, –2	+1, –2, –2 –2, –2, –2 –2, –1, –1 –2, –2, –2	+2, –2, –2 –2, –2, –2 –2, –1, –1 –1, –1, –2	+2, –2, –2 –2, –2, –2 –2, –1, –1 –1, –1, –2	+1, –2, –2 –2, –2, –2 –2, –1, –1 –2, –2, –1	+2, –2, –2 –2, –2, –2 –2, –1, –1 –2, –1, –2

Analytical results of the nine patients at the time of initiating the ACD device (basal), at 48 h (after removal) and at 96 h. The RASS was determined every 8 h and is expressed in values ranging from –5 a +4. The plasma fluorine measurement was made 48 after the basal, except for patients 5 and 6, that were measured after 72 h of administering sevoflurane treatment. The values in parenthesis are the reference normal values. GFR was measured with MDRD. Males are represented as H and females as M, with the age in parenthesis

Source: Authors.

we used sevoflurane via an ACD device. Once the system was wet up, the sevoflurane end tidal % (Et sev %) was monitored, with a maximum allowance of 1%. The rate of continuous infusion of liquid sevoflurane ranges from 1 to 10 ml/h, with significant patient-to-patient variation. At the time of weaning, if a new drug needs to be added, the regime illustrated in Fig. 2 is used. The device was used for a maximum of 72 h, although in most patients it was only used for 48 h and then was removed; plasma fluoride levels were measured and continuous ventilation was maintained. However, in patients 5 and 6 ACD was used for 72 h, and then the determination was made. Additionally, serial analyses were completed for urea, plasma creatinine, GFR, total bilirubin, GOT, GPT and GGT for the assessment of renal and liver function a few hours before using the ACD device (basal), at the time of removal (after 48 h) and 48 h after removal (96 h).

Results

The analytical results are presented in Table 1.

An adequate ventilator adaptation was achieved in all patients in whom ACD inhalation sedation was administered, with a RASS score between 0 and -2. Thus the sedation using the ACD device was appropriate and met the primary goal. As illustrate in the Table, at the time of establishing inhalation sedation, most patients were restless and agitated, anxious, with poor coordination and poorly adapted to the ventilator, as expressed by RASS scores over 0. This situation improved following the administration of inhaled sevoflurane.

Moreover, none of the patients exhibited a significant decline in the kidney or liver function, despite the fact that patients 5 and 6 exhibited elevated plasma fluoride levels, as shown in Table 1. These values are considered exclusively secondary to the use of inhaled sevoflurane, though we cannot rule out other underlying causes.

Discussion

The article discusses the preliminary results from the adjuvant use of inhalation sedation with sevoflurane in medical ICU patients, using the ACD device⁷ safely and explains how we have implemented a protocol in our unit. Currently there are no trials underway in our unit, although we continue to collect data to be able to undertake a study with a larger sample and stringent scientific rigor in the near future.

Until now inhalation sedation using the ACD device had mainly been used in post-surgical patients with good results.⁸ We present our experience using this type of sedation in an ICU where most patients are medical, with pathologies such as pneumonia, respiratory distress and septic shock.

Several papers have shown the benefit of using sevoflurane for ICU sedation using the ACD device. Röhm et al.⁹ showed a shorter time to extubation and hospital discharge, comparing sevoflurane versus propofol in patients undergoing heart surgery. Mesnil et al.¹⁰ showed that the quality of awakening was improved, with fewer episodes of hallucinations and agitation, when comparing sevoflurane, propofol and midazolam. These observations are consistent with our findings in terms of adaptation to the ventilator and the occurrence

of restlessness episodes, measured with RASS, as shown in Table 1. Although in our case we have not recorded the time to extubation – that was not the purpose of the study – we have observed however that patients adapt better to the ventilator and are less agitated under sevoflurane sedation; so very seldom a third sedative is needed. This is the reason why we consider sevoflurane particularly helpful in situations of considerable difficulty to adapt the ventilator to the patient either because of a high need of intravenous medication or because of persistent episodes of agitation. Using this type of sedation the patients are alert and calmed, without any restlessness or anxiety; they do not exhibit violent behaviors and are not fighting the ventilator (RASS 0, -2).

Following the analyses to measure renal and hepatic function, we have observed that there were no alterations as compared to the baseline status, notwithstanding the fact that some patients exhibited very high fluoride plasma levels. Volatile anesthetic agents such as sevoflurane, produce inorganic fluoride metabolites associated with renal dysfunction. A value of 50 mcmol/L has been postulated as a threat to develop renal failure¹¹ and it is believed to potentially cause liver failure as well.¹² However, although some of our patients exhibit significantly high levels, none of them has developed kidney or liver failure associated with this type of sedation, as established in further follow-up.

Notwithstanding the limitations of the studies so far completed, most of them show the superiority of volatile anesthetics against the traditional intravenous drugs for ICU sedation. Volatile agents reduce the time to extubation and discharge, and consequently reduce the risk of infection and complications, at a cost similar to that of intravenous agents. The excellent pharmacokinetics^{13,14} of volatile anesthetics makes them a good choice for ICU sedation based on the rapid patient evaluation and faster awakening, extubation, and discharge.

For all these reasons, we suggest the use of this sedation modality in conventional ICUs, stressing the importance of proper training of all the staff members involved in the care of these patients. Adjuvant sevoflurane is a safe sedation alternative to the current use of the regular intravenous agents and is a valid and effective option for the everyday ICU practice.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Conflicts of interest

The authors have no conflicts of interest to declare.

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