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LETTER

Volatile sedation practices in patients with severe acute respiratory distress syndrome under VV-ECMO support

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Dear Editor,

Veno-venous extracorporeal membrane oxygenation (VV-ECMO) in severe acute respiratory distress syndrome (ARDS) can be lifesaving [1]. In these cases, the complex brain-lung crosstalk might lead to a form of acute brain injury that can pose a challenge on sedation strategies [2]. Furthermore, the pharmacokinetic alterations related to the VV-ECMO therapy can lower plasma drug concentrations, making the dose–response relationship of sedatives unpredictable [3]. Complex sedation scenarios in VV-ECMO ARDS patients are thus not rare. Volatile sedation (VS) is a novel therapy in the critical care setting. Different studies demonstrate that VS induces light to deep sedation and is associated with shorter awakening times. Moreover, it could improve oxygenation and decrease the production of alveolar cytokines even in situations where lung mechanics are deeply affected [4].

This retrospective study (January-2021/March-2023), performed in eleven Spanish ECMO centers, included patients with ARDS and VV-ECMO therapy who received concomitant VS for at least 24 h. Patients under 18 years and those who were pregnant were excluded. As the primary objective, we analyzed whether VS led to decreased intravenous (IV) sedation needs. As secondary objectives, we investigated the repercussions of VS in sedation depth and opioid usage, VS practices, and its impact on oxygenation and mechanical ventilation (MV)/ECMO parameters. Data were evaluated before the start of VS (D0), at 24 h (D1), and at 72 h (D3) after its initiation.

Sixty-six patients were included. The patients' general characteristics, main VV-ECMO indications, and VS features are shown in supplementary Table 1S. On D0, patients received a median of 2 (1;2) IV sedatives to achieve a Richmond Agitation Sedation Scale (RASS) score of −4 (−4; −5) and a bispectral index (BIS) level of 45 (40;60). Table 1 summarizes changes in practice after VS. On D1 and D3, there was a decrease in the number of IV sedatives required per patient [2 (1;2) at D0 vs. 1 (0;2) at D1 p = 0.00; 2 (1;2) at D0 vs. 0 (0;1) at D3 p = 0.00] with no significant changes in sedation depth as shown by the BIS [45 (40;60) at D0 vs. 42.5 (39.5;52) at D1 p = 0.32; 45 (40;60) at D0 vs. 50 (40;65) at D3 p = 0.22] and RASS [−4 (−4; −5) at D0 vs. −5 (−4; −5) at D1 p = 0.09; −4 (−4; −5) at D0 vs. −4 (−4; −5) at D3 p = 0.48] values. Daily doses of propofol, midazolam and opioids, excluding remifentanil, remained stable on D3, but the number of patients needing IV sedatives or neuromuscular blockade (NMB) diminished (supplementary Table 2S and Fig. 1S). A slight increase in tidal volume and PaO_2/FiO_2 ratio (supplementary Fig. 2S) and a decrease in positive end-expiratory pressure (PEEP) were found.

This multicenter study describes VS usage in ARDS patients undergoing VV-ECMO and ultraprotective MV. This study, like the single-center study by Graselli et al.,

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Table 1 Changes in practice after introducing volatile sedation

Categorical variables								
	D0		D1			D3		
Variable (YES)	N (%)	OR (95%CI)	N (%)	OR (95%CI)	p value	N (%)	OR (95%CI)	p value
Propofol	52 (78.8)	RC	26 (39.4)	0.05 (0.01; 0.24)	0.00	18 (27.3)	0.02 (0; 0.11)	0.00
MDZ	45 (68.2)	RC	24 (36.4)	0.1 (0.03; 0.37)	0.00	13 (19.7)	0.02 (0;0.11)	0.00
Ketamine	5 (7.6)	RC	7 (10.6)	0.27 (0.02; 3.16)	0.27	4 (6.1)	0.12 (0; 1.92)	0.14
DXMD	6 (9.1)	RC	4 (6.1)	0.3 (0.06; 1.53)	0.15	4 (6.1)	0.30 (0.06; 1.53)	0.15
Clonidine	5 (7.6)	RC	6 (9.1)	2.73 (0.15; 50.25)	0.5	5 (7.6)	2.73 (0.15; 50.25)	0.5
Remifentanil	22 (33.3)	RC	27 (40.9)	7.86 (0.81; 76.1)	0.07	26 (39.4)	3.3 (0.51; 21.42)	0.21
Fentanyl	26 (39.4)	RC	21 (31.8)	0.19 (0.03;1.16)	0.07	19 (28.8)	0.19 (0.03; 1.16)	0.07
Morphine	16 (24.2)	RC	19 (28.8)	2.38 (0.5; 11.26)	0.27	20 (30.3)	5.26 (0.86; 32)	0.07
cNMB	32 (48.5)	RC	20 (30.3)	0.26 (0.09; 0.71)	0.00	18 (27.3)	0.23 (0.08; 0.66)	0.01
CATECH	39 (59.1)	RC	46 (69.7)	1.8 (0.69; 4.76)	0.23	44 (66.7)	1.72 (0.64; 4.62)	0.28
Numerical variables								
	D0		D1			D3		
Variable	Median (p25;p75)	Coeff (95%CI)	Median (p25;p75)	Coeff (95%CI)	p value	Median (p25;p75)	Coeff (CI95)	p value
Nº IV SED	2 (1; 2)	RC	1 (0; 2)	− 0.8 (− 1; − 0.6)	0.00	0 (0; 1)	− 1.1 (− 1.3; − 0.9)	0.00
BIS value	45 (40; 60)	RC	42.5 (39.5; 52)	− 2.6 (− 7.8; 2.6)	0.32	50 (40; 65)	3.3 (− 2; 8.7)	0.22
RASS value	− 4 (− 5; − 4)	RC	− 5 (− 5; − 4)	− 0.3 (− 0.63; 0.05)	0.09	− 4 (− 5; − 4)	0.1 (− 0.22; 0.5)	0.48

MDZ midazolam, *DXMD* dexmedetomidine, *cNMB* continuous infusion of neuromuscular blocking agents, *CATECH* catecholamines, *Nº IV SED* number of simultaneously needed IV sedatives to achieve target sedation levels, *BIS* bispectral index, *RASS* Richmond Agitation Sedation Scale. The RASS values presented correspond solely to the group of patients without cNMB (D0 n = 43; D1 n = 46; D3 n = 45). *CI* confidence interval, *OR* odds ratio, *RC* reference category

found that VS is feasible in this population and is associated with less need for IV sedatives without compromising the optimal level of sedation or MV efficacy [5]. The introduction of VS can help decrease the usage of continuous NMB and might lead to better oxygenation, although these findings need further study.

Supplementary Information

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Author Contribution
All authors contributed to the study's conception and design. Material preparation and data collection were performed by SAC, AdS, SC, JR, AB, AG, ST, MPT, CJM, MGS and ST. AR and SAC performed the analysis. SAC wrote the first draft of the manuscript, and all authors commented on previous versions. All authors read and approved the final manuscript.

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Data availability statement
All gathered date is available upon request from the authors.

Declarations

Conflicts of interest
SAC has received lecture fees from Sedana Medical and Orion Pharma. MGS has received lecture fees from Sedana Medical and Medtronic. SC, JMG, and ST have received lecture fees from Sedana Medical. All other authors have no conflicts of interest to declare.

Ethical statements
The study was approved by the Ethics Committee of Hospital Universitario Puerta de Hierro Majadahonda (Comité de Ética de Investigación con Medicamentos 143/22), and written informed consent was waived due to its retrospective design.

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