and Jorge Menedez for providing training and guidance in ultrasound measurements.

Declaration of generative AI and AI-assisted technologies in the writing process:

Throughout the preparation of this work, the authors utilised ChatGPT 3.5 to enhance writing quality and conciseness. Subsequently, the authors thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.medine.2024.06.006.

References

1. Mauri T, Turrini C, Eronia N, Grasselli G, Volta CA, Bellani G, et al. Physiologic effects of high-flow nasal cannula in acute hypoxemic respiratory failure. Am J Respir Crit Care Med. 2017;195(9):1207–15, http://dx.doi.org/10.1164/rccm.201605-0916OC.
2. Egbers PH, Sutt AL, Petersson JE, Bergström L, Sundman E. High-flow via a tracheostomy tube and speaking valve during weaning from mechanical ventilation and tracheostomy. Acta Anaesthesiol Scand. 2023;67(10):1403–13, http://dx.doi.org/10.1111/aas.14305.
3. Corley A, Edwards M, Spooner AJ, Dunster KR, Anstey C, Fraser JF. High-flow oxygen via tracheostomy improves oxygenation in patients weaning from mechanical ventilation: a randomised crossover study. Intensive Care Med. 2017;43(3):465–7, http://dx.doi.org/10.1007/s00134-016-4634-7.
4. Vadi S, Phadtare S, Shetty K. High-flow oxygen therapy via tracheostomy to liberate COVID-19-induced ARDS from invasive ventilation: a case series. Indian J Crit Care Med. 2021;25(6):724–8, http://dx.doi.org/10.5005/jp-journals-10071-23858.
5. Serrano DAR, Terán PP, Blancas R, Arroyo M. Pleuropulmonary and diaphragmatic ultrasound in intensive care medicine. Med Intensiva. 2023;47(10):594–602, http://dx.doi.org/10.1016/j.medine.2023.06.009.
6. Zapata L, Blancas R, Conejo-Márquez I, García-de-Acilu M. Role of ultrasound in acute respiratory failure and in the weaning of mechanical ventilation. Med Intensiva. 2023;47(9):529–42, http://dx.doi.org/10.1016/j.medine.2023.03.018.
7. Lersritwimanmaen P, Rittayamai N, Tscheikuna J, Brochard L. High-flow oxygen therapy in tracheostomized subjects with prolonged mechanical ventilation: a randomized crossover physiologic study. Respir Care. 2021;66(5):806–13, http://dx.doi.org/10.4187/respcare.08585.
8. Stripoli T, Spadaro S, Di Mussi R, Volta CA, Trerotoli P, De Carlo F, et al. High-flow oxygen therapy in tracheostomized patients at high risk of weaning failure. Ann Intensive Care. 2019;9(1):4, http://dx.doi.org/10.1186/s13613-019-0482-2.
9. Natalini D, Grieco DL, Santantonio MT, Mincione L, Toni F, Anzellotti GM, et al. Physiological effects of high-flow oxygen in tracheostomized patients. Ann Intensive Care. 2019;9(1):114, http://dx.doi.org/10.1186/s13613-019-0591-y.
10. Thomas M, Joshi R, Cave G. How much PEEP does high flow deliver via tracheostomy? A literature review and benchtop experiment. Crit Care Res Pract. 2021;2021:6036891, http://dx.doi.org/10.1155/2021/6036891.

Ignacio Fernández Ceballos[a,b,*], Ivan Alfredo Huespe[a], María Sofía Venuti[a], Bruno Leonel Ferreyro[c], José María Dianti[d,e], Romina Famiglietti[a], Ana Montserrat Rivera[a], Indalecio Carboni Bisso[a], Marcos Jose Las Heras[a]

[a] *Critical Care Department, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina*
[b] *Critical Care Department, Hospital Italiano de San Justo Agustín Roca, Buenos Aires, Argentina*
[c] *Department of Medicine, Division of Respirology, Sinai Health System and University Health Network, Toronto, Canada*
[d] *Interdepartmental Division of Critical Care Medicine, University of Toronto, Toronto, Ontario, Canada*
[e] *Adult Intensive Care Unit, CEMIC, Buenos Aires, Argentina*

* Corresponding author.
E-mail address: ignacio.fernandez@hospitalitaliano.org.ar (I. Fernández Ceballos).

Reasons for refusal of admission to the ICU in oncological population and their association with 6-month mortality

Motivos de rechazo de ingreso en UCI en población oncológica y su asociación con la mortalidad a seis meses

The incorporation of innovation, both technological and pharmacological, into the world of medicine has substantially modified the diagnostic and therapeutic processes for so many diseases.

With the development of new molecules, the prognosis of many neoplasms has drastically changed in recent years, showing an increase in survival. This situation poses a challenge when considering the admission of these patients to intensive care units. It is necessary to avoid grouping all cancer patients into a single category and start individualizing treatment.[1]

Regardless of the reason for ICU admission, this subgroup of patients can benefit from the creation of multidisciplinary teams for their management. This involves strengthening ties among different specialties involved in both the acute process at the ICU setting and their subsequent follow-up in conventional hospitalization wards. Indeed, a growing trend is management by multiple professionals in wards, with close monitoring through alert systems.[2]

DOI of refers to article: https://doi.org/10.1016/j.medin.2024.05.005

Table 1 General characteristics and their association with ICU admission.

		ICU admission						
Variable	Category	Total cohort	No	Yes	p	a/n	Adjusted OR (95%CI)	p
Age, mean (SD)		66.30 (10.30)	68.68 (9.72)	65.72 (10.38)	0.095		0.97 (0.93–1.01)	0.103
Sex, n (%)	Female	76 (35.35)	21 (50.00)	55 (31.79)	0.027	55/76	1 (ref)	
	Male	139 (64.65)	21 (50.00)	118 (68.21)		118/139	2.62 (1.10–6.23)	0.029
Hypertension, n (%)		111 (51.63)	22 (52.38)	89 (51.45)	0.913	89/111	1.66 (0.66–4.17)	0.279
Dyslipidemia, n (%)		61 (28.37)	8 (19.05)	53 (30.64)	0.135	53/61	2.01 (0.72–5.61)	0.185
Diabetes mellitus, n (%)		34 (15.81)	6 (14.29)	28 (16.18)	0.762	28/34	1.41 (0.44–4.48)	0.561
Smoking, n (%)		47 (21.86)	12 (28.57)	35 (20.23)	0.241	35/47	0.27 (0.09–0.80)	0.018
Alcohol, n (%)		33 (15.35)	5 (11.90)	28 (16.18)	0.490	28/33	1.22 (0.35–4.17)	0.756
COPD, n (%)		34 (15.81)	5 (11.90)	29 (16.76)	0.439	29/34	1.25 (0.37–4.22)	0.716
Heart disease, n (%)		37 (17.21)	12 (28.57)	25 (14.45)	0.030	25/37	0.62 (0.21–1.83)	0.391
Renal failure, n (%)		9 (4.19)	5 (11.90)	4 (2.31)	0.005	4/9	0.21 (0.03–1.39)	0.105
Type of tumor, n	CNS	16 (7.44)	2 (4.76)	14 (8.09)	0.519	14/16	1 (ref)	
(%)	HN	23 (10.70)	6 (14.29)	17 (9.83)		17/23	0.36 (0.04–3.10)	0.352
	Respiratory	42 (19.53)	12 (28.57)	30 (17.34)		30/42	0.37 (0.05–2.76)	0.334
	Digestive	75 (34.88)	14 (33.33)	61 (35.26)		61/75	0.68 (0.10–4.72)	0.698
	Renal	3 (1.40)	0 (0.00)	3 (1.73)		3/3	1.00 (1.00–1.00)	
	Genitourinary	55 (25.58)	8 (19.05)	47 (27.17)		47/55	0.89 (0.12–6.66)	0.912
	Cutaneous	1 (0.47)	0 (0.00)	1 (0.58)		1/1	1.00 (1.00–1.00)	
Tumor stage, n (%)	I	129 (60.00)	2 (4.76)	127 (73.41)	<0.001	127/129	1 (ref)	
	II	73 (33.95)	31 (73.81)	42 (24.28)		42/73	0.03 (0.01–0.16)	<0.001
	III	13 (6.05)	9 (21.43)	4 (2.31)		4/13	0.02 (0.00–0.13)	<0.001
Tumor spread, n	Metastasis	115 (53.49)	18 (42.86)	97 (56.07)	0.124	97/115	1 (ref)	
(%)	Locoregional	100 (46.51)	24 (57.14)	76 (43.93)		76/100	0.97 (0.42–2.24)	0.942
Oncological	No treatment	47 (21.86)	14 (33.33)	33 (19.08)	0.009	33/47	1 (ref)	
treatment	Surgical	65 (30.23)	5 (11.90)	60 (34.68)		60/65	5.94 (1.59–22.15)	0.008
received, n (%)	RT	8 (3.72)	1 (2.38)	7 (4.05)		7/8	3.37 (0.23–49.12)	0.375
	RT + CT	16 (7.44)	4 (9.52)	12 (6.94)		12/16	1.54 (0.31–7.65)	0.595
	Neoadjuvant	7 (3.26)	0 (0.00)	7 (4.05)		7/7	1.00 (1.00–1.00)	
	Surgical + adjuvant	46 (21.40)	8 (19.05)	38 (21.97)		38/46	2.14 (0.61–7.51)	0.237
	Palliative	1 (0.47)	1 (2.38)	0 (0.00)		0/1	1.00 (1.00–1.00)	
	CT	21 (9.77)	7 (16.67)	14 (8.09)		14/21	1.01 (0.24–4.27)	0.992
	Immunotherapy	4 (1.86)	2 (4.76)	2 (1.16)				
State of the	Induction	108 (50.23)	9 (21.43)	99 (57.23)	<0.001	99/108	1 (ref)	
oncological	Progression	68 (31.63)	31 (73.81)	37 (21.39)		37/68	0.14 (0.05–0.39)	<0.001
disease, n (%)	Remission	30 (13.95)	2 (4.76)	28 (16.18)		28/30	2.06 (0.34–12.44)	0.429
	Cure	8 (3.72)	0 (0.00)	8 (4.62)		8/8	1.00 (1.00–1.00)	
	Unknown	1 (0.47)	0 (0.00)	1 (0.58)		1/1	1.00 (1.00–1.00)	

CNS: central nervous system, CT, chemotherapy; HN, head and neck, stage I, potential cure, stage II, not curable, stage III, palliative management, RT, radiotherapy.

Table 2 ICU admission denial characteristics associated with 6-month mortality.

6-month mortality							
Variable	Category	No	Yes	p	a/n	Adjusted OR (95%CI)	p
Reason for ICU non-admission, n (%)	Age	No	6 (100.00)	30 (83.33)	0.280	30/36	1 (ref)
		Yes	0 (0.00)	6 (16.67)		6/6	1.00 (1.00–1.00)
	Severe chronic disease	No	4 (66.67)	20 (55.56)	0.611	20/24	1 (ref)
		Yes	2 (33.33)	16 (44.44)		16/18	1.62 (0.18–14.68)
	Previous functional limitation	No	4 (66.67)	12 (33.33)	0.120	12/16	1 (ref)
		Yes	2 (33.33)	24 (66.67)		24/26	3.96 (0.32–49.08)
	Poor estimated quality of life	No	1 (16.67)	3 (8.33)	0.520	3/4	1 (ref)
		Yes	5 (83.33)	33 (91.67)		33/38	5.32 (0.29–97.67)
	Futility of treatment	No	3 (50.00)	8 (22.22)	0.152	8/11	1 (ref)
		Yes	3 (50.00)	28 (77.78)		28/31	6.35 (0.71–57.22)
	Living will	No	6 (100.00)	35 (97.22)	0.679	35/41	1 (ref)
		Yes	0 (0.00)	1 (2.78)		1/1	1.00 (1.00–1.00)
	Patient refusal	No	6 (100.00)	34 (94.44)	0.554	34/40	1 (ref)
		Yes	0 (0.00)	2 (5.56)		2/2	1.00 (1.00–1.00)
Patient informed, n (%)	Yes	5 (83.33)	35 (97.22)	0.139	35/40	1 (ref)	
	Unknown	1 (16.67)	1 (2.78)		1/2	0.25 (0.01–8.14)	0.438
Family informed, n (%)	No	1 (16.67)	1 (2.78)	0.137	1/2	1 (ref)	
	Yes	3 (50.00)	30 (83.33)		30/33	3.51 (0.06–202.07)	0.543
	Unknown	2 (33.33)	5 (13.89)		5/7	1.44 (0.01–141.18)	0.876
Included in the medical history, n (%)	No	1 (16.67)	3 (8.33)	0.520	3/4	1 (ref)	
	Yes	5 (83.33)	33 (91.67)		33/38	0.68 (0.03–15.29)	0.810
Disagreement with family, n (%)	No	3 (50.00)	31 (86.11)	0.037	31/34	1 (ref)	
	Unknown	3 (50.00)	5 (13.89)		5/8	0.24 (0.03–1.88)	0.176
Disagreement with consulting physician, n (%)	No	3 (50.00)	30 (83.33)	0.057	30/33	1 (ref)	
	Yes	3 (50.00)	4 (11.11)		4/7	0.04 (0.00–0.72)	0.028
	Unknown	0 (0.00)	2 (5.56)		2/2	1.00 (1.00–1.00)	

We conducted a prospective cohort study was conducted in the ICU of a tertiary referral center. All adult patients with solid organ tumors who experience an acute event (whether medical or surgical) and require assessment by the intensive care service for potential ICU admission were consecutively recruited over a period of 2 years. A total of 215 patients were consecutively recruited, with no losses to follow-up. A total of 173 of these patients were admitted to the ICU and 42 were denied admission as a measure of life support limitation. Within the group of patients who were denied admission, the reasons for ICU admission denial given by the intensivist and their association with the 6-month mortality rate were evaluated. These reasons for rejection were drawn from the ADENI-UCI trial[3] since there are no specific studies in this population. The study received approval from Cantabria Research Ethics Committee (CEI). Since no intervention was required, informed consent was deemed unnecessary.

The general characteristics of the sample and their association with ICU admission are detailed in Table 1.

A total of 173 out of all the patients from our sample were admitted to the ICU, with a mean age of 65.72 years (SD, 10.38) (p = 0.095). A significant correlation was seen between ICU admission and the sex of the patients. We found a higher probability of admission in men vs women (OR, 2.62, [95%CI, 1.10–6.23]) and a lower probability of admission if the patient was a smoker (OR 0.27, [95%CI, 0.09–0.80]).

Among the comorbidities studied, heart disease and renal failure showed different behaviors between patients admitted to the ICU and those who were not. A total of 28.57% (n = 12) of patients with heart disease were not admitted to the ICU, as opposed to 14.45% (n = 25) of those who were actually admitted. Also, the rate of former smokers was not the same, with 11.90% (n = 5) were not admitted to the ICU, while 27.17% (n = 47) were actually admitted.

Regarding the type of primary tumor, a heterogeneous distribution was noted. In the entire cohort, digestive tumors were predominant at 34.88% (n = 75), followed by genitourinary tumors at 25.58% (n = 55).

Regarding the tumor stage, we found that patients in stage II and stage III reduced the risk of ICU admission by 97%–98% vs patients in stage I (OR, 0.03 [95%CI, 0.01–0.16] for stage II) and III (OR 0.02 [95%CI, 0.00–0.13]). Patients in the progression stage were 86% less likely to be admitted to the ICU than those in the induction stage (OR, 0.14, [OR, 5.94, [95%CI, 0.05–0.39]).

All patients on neoadjuvant therapy were admitted to the ICU compared with 0 patients on palliative treatment. Patients who underwent prior surgical treatment were nearly 6 times more likely to be admitted to the ICU vs those with no oncological treatment.

The association between the characteristics associated with ICU admission denial and the 6-month mortality rate is shown in Table 2.

No significant differences were found in the 6-month mortality rate and the various reasons for ICU admission denial.

Regarding the information given to the patient, no significant differences were observed. However, it was noted that 86.11% (n = 31) of patients who did not disagree with the family was found died (p = 0.037). Similarly, a total of 83.33% (n = 30) of patients who did not disagree with the consulting physician was found died, although with borderline significance (p = 0.057).

Analyzing the group of patients who were denied access to the ICU, we found that those who disagreed with the consulting physician had fewer chances of dying (OR, 0.04 [95%CI, 0.00–0.72]).

Intensivists are the specialists best trained to address the patient's life support, but the patient's regular oncologist or hematologist is the one who best knows the underlying neoplasm and the available therapeutic options. We believe that the creation of multidisciplinary teams[4,5] for making these types of decisions is essential. These teams should provide comprehensive knowledge of the patient, balance the benefits and negative aspects of ICU admission, establish effective communication with the patient and family, and ensure continuity of care.

In conclusion, future studies are necessary to analyze the reasons for ICU admission denial in this population and examine the degree of agreement between the consulting physician and the consulted physician.

Funding

No funding has been received.

Conflicts of interest

None declared.

References

1. Carmona-Bayonas A, Gordo F, Beato C, Castaño Pérez J, Jiménez-Fonseca P, Virizuela Echaburu J, et al. Intensive care in cancer patients in the age of immunotherapy and molecular therapies: commitment of the SEOM-SEMICYUC. Med Intensiva (Engl Ed). 2018;42(6):363–9, http://dx.doi.org/10.1016/j.medin.2018.01.008.
2. Gordo F, Molina R. Evolution to the early detection of severity. Where are we going? Med Intensiva (Engl Ed). 2018;42(1):47–9, http://dx.doi.org/10.1016/j.medin.2017.06.008.
3. Escudero-Acha P, Leizaola O, Lázaro N, Cordero M, Cossío AM, Ballesteros D, Recena, et al. ADENI-UCI study: analysis of non-income decisions in ICU as a measure of limitation of life support treatments. Med Intensiva (Engl Ed). 2020;46:192–200, http://dx.doi.org/10.1016/j.medin.2020.11.003.
4. García-de-Lorenzo A, Jiménez V, Feliu J, Asensio MJ, Civantos B, Añón JM. Rondas multidisciplinares en oncología y hematología: ¿son superiores a los equipos de respuesta rápida? Multidisciplinary rounds in oncology and hematology: are they superior to rapid response teams? Rev Med Clin. 2021;45(2):127–8, http://dx.doi.org/10.1016/j.medin.2020.01.011.
5. Civantos B, Añón JM, Yus S, Asensio MJ, García-de-Lorenzo A. Outcomes of hospitalized hematologic oncology patients

receiving rapid response system activation for acute deterioration: another time, another way. Crit Care. 2019;23:419, http://dx.doi.org/10.1186/s13054-019-2714-0.

Elena Cuenca Fito[a,*], Alejandro González Castro[b], Inés Gómez Acebo[c]

[a] *Servicio de Medicina Intensiva Hospital Universitario de Ourense, Spain*

[b] *Servicio Medicina Intensiva Hospital Universitario Marqués de Valdecilla, Spain*

[c] *Departamento Ciencias médicas y quirúrgicas de la Universidad de Cantabria, Spain*

* Corresponding author.
E-mail address: ecuencafito@gmail.com (E. Cuenca Fito).

2173-5727/

Meropenem for the management of valproic acid intoxication: a case report and a review of the literature

Uso de meropenem para el manejo de la intoxicación por valproico: descripción de un caso y revisión de la literatura

Valproic acid is a broad-spectrum antiepileptic drug used in the treatment of epilepsy and commonly used in other conditions such as bipolar disorder, schizophrenia and migraine.

Valproic acid intoxication is associated with remarkable morbidity and potential life-threatening complications. Current management options for valproate toxicity are limited and often associated with challenges such as delayed elimination and increased half-life.

We describe the case of a patient in which we used meropenem as an adjunct therapy in the management of valproic acid toxicity.

In April 2023, a 59-year-old woman, with a medical history of Schizoaffective disorder and a previous suicide attempt through intentional overdose in 2004, was found by her family at home with low level of consciousness following a drug overdose. The time of ingestion was unknown.

She presented to the emergency department with a persistently low Glasgow Coma Scale of 4/15, miotic pupils, tachycardia and difficulty of breathing. The patient was administered 50 mg of activated charcoal via nasogastric tube, 0.4 mg of naloxone, and 1 mg of flumazenil. However, there was a minimal response to the latter, characterized by a flexor response of the limbs and the emission of guttural sounds upon painful stimulation. A flumazenil 0.4 mg/h continuous infusion was initiated but the Glasgow Coma Scale did not improve, leading to her prompt intubation for airway protection. She was then transferred to the Intensive Care Unit while remaining hemodynamically stable and sedated.

The initial laboratory tests showed an increased anion gap metabolic acidosis, with lactic acid concentration of 3.4 mmol/L, pH 7.33, ammonia concentration of 315.55 μg mol/L, valproic acid concentration of 503.06 μg/mL (normal range 50—100 μg/mL) and an olanzapine concentration of 175 ng/mL (normal range 20—80 ng/mL). Benzodiazepines were also detected in the urine. The patient was administered levocarnitine to prevent and reverse valproate-related metabolic disorders. A 12-lead electrocardiogram revealed an initial QTc of 464 msec, a chest X-ray indicated no signs of aspiration pneumonia. However, it was decided to begin empiric antibiotic therapy with amoxicillin/clavulanic acid.

The patient's valproic acid concentrations subsequently decreased to 296.85 μg/mL and 282.06 μg/mL at 2 and 10 h after admission, respectively. We calculated the individual pharmacokinetics parameters using the Bayesian forecasting model that contains a population model (14–70 years) of valproic acid (Abbottbase pharmacokinetic system PKS®, Abbott Laboratories, PKS, Chicago, IL, USA). The maximum serum concentrations of valproic acid allowed in this model were 250.00 μg/mL. Accepting this adjustment, the predicted valproate serum concentrations in our patient at 36 h of admission were still above the normal range (118.15 μg/mL).

After that, it was decided to prescribe a single dose of 1 g of meropenem. Following meropenem administration, 15 h later (36 h after admission), serum valproic acid concentrations declined to 13.9 μg/mL, below subtherapeutic concentrations. Her ammonia concentration reached normal range and the patient showed increased alertness and started responding to commands. The patient was transferred out of the Intensive Care Unit on the 3rd day of hospitalization and ultimately discharged to inpatient psychiatry.

Valproic acid exhibits a complex nonlinear pharmacokinetic profile and is highly bound to albumin. The unbound fraction of valproic acid in the serum varies between 6% and 10%. However, this percentage is influenced by factors such as serum albumin concentration, serum VPA concentration, age, and the presence of end-organ failure. Therefore, relying solely on the total serum concentration of valproic acid can sometimes be misleading.[1]

The pharmacological mechanisms underlying the interaction between valproic acid and carbapenem antibiotics, such as meropenem, are complex and not well defined. Evidence suggests that carbapenems may influence valproic acid absorption, distribution, and metabolism, leading to a rapid and pronounced reduction in serum valproate concentrations, and increasing the risk of seizures in epileptic patients.[2] Because of this interaction, it is generally recommended to avoid the use of these two medications concurrently. However, based on various cases published in the literature[3–8] we intentionally used a carbapenem to decrease valproic acid concentrations in our patient. Table 1 summarizes all the published studies regarding inten-

DOI of refers to article: https://doi.org/10.1016/j.medin.2024.05.023