



## LETTER TO THE EDITOR

### Saline, balanced solutions and Thomas Bayes



### Suero salino, soluciones balanceadas y Thomas Bayes

Dear Editor:

Since the publication of the study “SMART: Is saline on the tightrope?”<sup>1</sup>, several authors have worked with the hypothesis that the infusion of balanced solutions in critical patients improves the outcomes in terms of renal function and mortality (Table 1). No studies have evidenced benefit from the use of saline solution; in the best of cases, performance has been reported to be equivalent<sup>2</sup>.

A recent systematic review has been made of randomized clinical trials comparing balanced crystalloids with saline solution in adult critical patients, with 90-day mortality as the primary endpoint. The frequency statistics analysis revealed no significant differences. However, Bayesian analysis showed the posterior probability that balanced crystalloids reduce mortality to be 89.5%<sup>3</sup>.

Physicians naturally use the Bayes theorem in decision-making referring to patient diagnosis, prognosis and treatment. Based on an effect, we decide on the cause of the effect and intuitively assign a probability to the cause we are considering. Different information sources added in sequence – development of hyperchloremia, acidosis, renal failure – define in an increasingly precise way the probability of a certain cause, and always on an intuitive basis<sup>4</sup>. However, when considering research methodology, priority is given to the simplicity of being able to decide whether a treatment, a diagnostic method or a procedure is effective or not, based on a pre-established  $p < 0.05$ . The problem is that the p-value, which is no more than a tool used to quantify such uncertainty, is too often overvalued and misinterpreted.

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**Table 1** Principal characteristics of randomized controlled studies comparing 0.9% saline solution versus balanced solutions in critical patients after 2018.

Author, year	Name of study	Country	Patients randomized to SS 0.9%	Patients randomized to BS	Type of balanced solution	Follow-up
Semler, 2018	SMART	USA	1169	1167	RL or ABS	30 days
Pagano, 2020		Italy	49	35	RL	–
Golla, 2020		India	80	80	RL	30 days
Zampieri, 2021	BaSICS	Brazil	1017	1987	ABS	90 days
Finfer, 2022	PLUS	Australia and New Zealand	1026	1068	ABS	90 days

RL: Ringer lactate; BS: balanced solution; ABS: acetate balanced solution; SS 0.9%: 0.9% saline solution

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## Reply: Pulmonary aspergillosis in the Intensive Care Unit. An underdiagnosed disease? Active search protocol for pulmonary aspergillosis associated with COVID-19 pneumonia



### Respuesta: Aspergilosis pulmonar en la unidad de cuidados intensivos: ¿una enfermedad infradiagnosticada? Protocolo búsqueda activa aspergilosis pulmonar asociado a neumonía COVID-19

We have read the interesting editorial by Estella<sup>1</sup> and agree with the author on the need to “look for in order to find”. Invasive pulmonary aspergillosis in particular constitutes an important complication in patients with acute respiratory distress syndrome (ARDS), particularly when secondary to influenza virus or SARS-CoV-2 pneumonia. Furthermore, as we have seen in recent years, the situation is no longer limited to oncohematological, transplant or immune suppressed patients. The mortality rate among patients presenting criteria of COVID-19-associated pulmonary aspergillosis (CAPA) is 44% versus 19% among non-CAPA patients, according to the study published by Bartoletti et al.<sup>2</sup>

In our Department, since August 2020, we have implemented an early active search protocol for pulmonary aspergillosis in patients with pneumonia due to SARS-CoV-2 and subjected to invasive mechanical ventilation.

The active search protocol consists of weekly serum galactomannan (GM) testing, calcofluor staining and bronchial aspirate (BAS) fungal culture in all SARS-CoV-2 pneumonia patients subjected to mechanical ventilation. Fibrobronchoscopy with fungal culture and GM determination in bronchoalveolar lavage (BAL) is performed if any of the above prove positive, or in the event of clinical worsening of the patient. The definition of CAPA is established retrospectively with the ECMM/ISHAM criteria<sup>3</sup>.

In the post-implementation analysis of this protocol in our series of 345 subjects admitted over a period of 16 months and diagnosed with SARS-CoV-2 pneumonia, a total of 90% of the patients were seen to require mechanical ventilation. The mean age was 60 years, and 69% were males. With regard to the severity scales, the mean SOFA score upon

admission was 6.4, with an APACHE II score of 16.5 and a SAPS II score of 19.5. A total of 8.7% ( $n=30$ ) met the criteria of probable CAPA. Ninety percent of these subjects tested positive for GM in BAL, and 70% had positive culture and positive GM in BAL. The mortality rate in these patients was 23.3% versus 15.7% in the non-CAPA patients ( $p = 0.3$ , chi-square test)<sup>4</sup>.

We consider that this active search strategy has facilitated the diagnosis of CAPA, allowing early treatment and having a direct impact on the clinical course and prognosis of the disorder. In this respect, we detected two CAPA outbreaks in our Department, implementing a series of effective control measures that included the prophylactic administration of inhaled amphotericin B lipid complex in all patients during the outbreak<sup>5</sup>. Further, well-designed studies are needed to validate the active search and early intervention strategy on a protocolized and validated basis, to secure benefits in terms of morbidity-mortality among patients with CAPA.

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### Conflicts of interest

The authors declare that they have no conflicts of interest

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