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<tr><th></th><th colspan="3">Background</th></tr>
<tr><td>Article</td><td colspan="3">Balanced Multielectrolyte Solution versus Saline in Critically Ill Adults[1]</td></tr>
<tr><td>Objective/Purpose</td><td colspan="3">To determine if a balanced multielectrolyte solution (BMES) was associated with less mortality at 90-days among critically ill adult patients compared to saline.</td></tr>
<tr><td>Brief Background</td><td colspan="3">The use of intravenous fluids remains a critical tool used to manage patients in intensive care units (ICUs).[2] Normal saline (NS) and lactated ringers are two common crystalloid solutions typically used for fluid resuscitations in ICU patients. Plasma-Lyte 148 is a crystalloid, BMES with similar physiochemical properties to plasma.[3] Previous studies evaluating ICU outcomes with the use of either BMES or NS have yielded mixed results.[4,5]</td></tr>
<tr><th></th><th colspan="3">Methods</th></tr>
<tr><td>Outcome Measures</td><td colspan="3">Mortality from any cause 90-days after randomization.</td></tr>
<tr><td>Study Design</td><td colspan="3">Randomized, double-blind, parallel-group study that was conducted at 53 ICUs in Australia and New Zealand from September 2017 to December 2020.</td></tr>
<tr><td>Target Population & Enrollment</td><td>Inclusion Criteria:</td><td colspan="2">Exclusion Criteria:</td></tr>
<tr><td></td><td>• Male and female patients aged 18 years and older<br>• Fluid resuscitation judged to be necessary with either BMES or saline considered equally appropriate<br>• Expected to be in the ICU on three consecutive days</td><td colspan="2">• Disqualifying fluid resuscitation (>500 mL of fluid prescribed and administered in the ICU)<br>• Imminent risk for death or preexisting life expectancy of less than 90 days<br>• Traumatic brain injury or at risk for cerebral edema</td></tr>
<tr><td>Treatment Groups</td><td colspan="3">Patients were randomized in a 1:1 fashion to receive the BMES or saline treatment for all fluid resuscitations within the ICU.<br>*When moved out of the ICU, patients were not restricted to trial regimens. While in the ICU, other crystalloid fluids could be used, preferably five percent glucose solution, could be used to dilute medications when not compatible with trial fluids.</td></tr>
<tr><td>Statistical Analysis</td><td colspan="3">Power was set at 90% requiring 5,000 patients and alpha set at 0.05.<br>Primary efficacy analysis was conducted in the intention-to-treat population (ITT) which included all patients who were randomized.<br>Logistic regression was used to analyze the primary outcome.<br>Odds ratios with 95% CIs were converted to adjusted risk differences with 95% CIs using Hummel and Wiseman method.</td></tr>
<tr><th></th><th colspan="3">Results</th></tr>
<tr><td>Enrollment & Subjects Characteristics</td><td colspan="3">2,515 were assigned to BMES<br>2,522 were assigned to saline<br>Total of 5,037 randomized. Primary outcome only available in 4,846 patients.</td></tr>
<tr><td>Summary of Primary & Secondary Outcomes</td><td colspan="3">
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<tr><th></th><th>BMES (n=2515)</th><th>Saline (n=2522)</th><th>Absolute Difference (95% CI)</th><th>Odds Ratio (95% CI)</th><th>P value</th></tr>
<tr><td>Death from any cause at 90 days (%)</td><td>530/2433 (21.8)</td><td>530/2413 (22.0)</td><td>-0.15 (-3.60 to 3.30)</td><td>0.99 (0.86 to 1.14)</td><td>0.90</td></tr>
<tr><td>- Adjusted</td><td>--</td><td>--</td><td>-0.17 (-3.51 to 3.16)</td><td>0.99 (0.86 to 1.14)</td><td>--</td></tr>
<tr><td>- Multiple imputation</td><td>--</td><td>--</td><td>-0.22 (-3.61 to 3.18)</td><td>0.99 (0.86 to 1.13)</td><td>--</td></tr>
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<tr><td>Safety</td><td colspan="3">Overall, both treatments were generally well tolerated with no significant differences between groups.</td></tr>
<tr><th></th><th colspan="3">Discussion</th></tr>
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| **Author's Conclusion** | The PLUS trial did not show that 90-day mortality was lower with the use of BMES instead of saline in ICU patients. |
| **Strengths** | Power set and met.<br>Regimen was appropriate.<br>Length or study was appropriate.<br>Inclusion and exclusion criteria were appropriate.<br>Blinding was present.<br>Randomization produced similar groups.<br>Biostatistical test was appropriate.<br>Authors' conclusion supported by results.<br>Trial patients received BMES or saline for longer duration and in greater volume than previous studies. |
| **Limitations** | Unavailable primary outcome data on 191 patients.<br>Reduction in the size of the recruitment target.<br>More than half of the patients in BMES group received 500 mL or more of saline in the ICU (primarily for delivery of medications).<br>Fluids received outside of the ICU were not recorded or controlled.<br>Primarily male. |
| **Presenter's Conclusion** | This was a Level I trial, interventional, double-blind, randomized trial that set and met power, with Minor Limitations. Overall, the use of BMES instead of saline for fluid resuscitation in ICU adult patients did not show a statistically significant difference with regards to mortality at 90 days. Although originally planned to randomize a larger number of patients, the uncertainty surrounding funding during the ongoing SARS-CoV-2 pandemic forced the investigators to decrease their enrollment target. Even though this trial met power, primary outcome information was missing for 191 patients; however, analysis of the primary outcome accounting for missing data showed similar results indicating that this is not a major concern. This trial establishes that BMES or saline are both generally well tolerated and can be used in ICU patients with similar mortality results. |
| **Recommendation** | I do not recommend the use of a BMES, particularly over saline in adult ICU patients for the following reasons:<br>• No statistically significant difference in mortality<br>• Greater than half of the patients in the BMES group received 500 mL or more of saline<br>• Adverse events were similar between groups<br>• Plasma-Lyte costs slightly more than normal saline[6]<br>  ○ $4.50 vs. $2.00 per liter |

**References:**


1. Finfer S, Micallef S, Hammond N, et al. Balanced Multielectrolyte Solution versus Saline in Critically Ill Adults. *N Engl J Med*. 2022;386(9):815-826. doi:10.1056/NEJMoa2114464
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4. Semler MW, Self WH, Wanderer JP, et al. Balanced Crystalloids versus Saline in Critically Ill Adults. *N Engl J Med*. 2018;378(9):829-839. doi:10.1056/NEJMoa1711584
5. Young P, Bailey M, Beasley R, et al. Effect of a Buffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the Intensive Care Unit: The SPLIT Randomized Clinical Trial. *JAMA*. 2015;314(16):1701-1710. doi:10.1001/jama.2015.12334
6. Kwong YD, Liu KD. In the Literature: Selection of Intravenous Fluids. *Am J Kidney Dis Off J Natl Kidney Found*. 2018;72(6):900-902. doi:10.1053/j.ajkd.2018.05.007