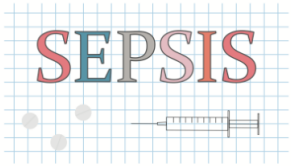
ICU MANAGEMENT & PRACTICE

Stronger evidence for vitamin C use in sepsis treatment



A new meta-analysis reveals a positive correlation between incorporating vitamin C in the treatment of sepsis and favourable patient outcomes. Results of the meta-analysis showed a marked reduction in mortality and duration of vasopressor administration in the group with the use of vitamin C, despite varying degrees of statistical significance between the original studies included in this analysis.

Sepsis is a severe condition with high mortality rates. Two recent publications by Sheikh and Horner and Teng et al. reviewed studies on incorporating vitamin C to treat septic patients. While the reviews offered insightful appraisals regarding the original studies and reported them in perspective, a meta-analysis was not produced and therefore aggregated quantitative results were not available for review.

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Jing Li, Santa Barbara Cottage Hospital (Santa Barbara, CA, USA), extended the above authors' work by performing a meta-analysis and demonstrating the pooled results. A search of EMBASE and PubMed similar to that of Sheikh and Horner was conducted on 8 June 2018, but no further full-text articles were found; therefore, the three papers reviewed by Sheikh and Horner were included in the meta-analysis.

Although all three studies looked at treating septic patients with vitamin C, Li points out that the quality of results varied due to differences in study design, inclusion criteria, and sample size. Two studies were randomised, double-blind, placebo-controlled clinical trials of small sample sizes, and the third one was a before-after study with propensity score adjustment. Three clinical outcomes were reported by at least two articles, which were mortality, intensive care unit length of stay (ICU-LOS), and vasopressor duration.

Li's meta-analysis was performed on these three outcomes using Comprehensive Meta-Analysis (version 3.3.070). Considering diversity in the study populations and differences in the treatments including varying doses of vitamin C, a random-effects model was used in all analyses. Mortality was considered the primary outcome for this meta-analysis, and a fail-safe N test was carried out to assess publication bias.

All three studies reported mortality rates between the experimental arm with the use of vitamin C and the control arm without vitamin C. Pooled analysis of all three studies revealed a marked reduction in mortality with the use of vitamin C (odds ratio (OR) = 0.17, 95% confidence interval (CI) 0.07–0.40; $p < 0.001$). No significant heterogeneity between studies was found ($I2 = 0$; $p = 0.40$ for Cochran's Q). Due to the strong effect size of two of the three studies, the computed fail-safe N would require nine null-finding studies to render this pooled result nonsignificant at $\alpha = 0.05$.

All three studies reported ICU-LOS, but one study was excluded in the meta-analysis as it did not provide either standard deviation (SD) for direct synthesis or the median for estimating SD. Pooled analysis favoured the use of vitamin C, but statistical significance was not reached (standardised mean difference (SMD) = –0.30, 95% CI –0.83 to 0.23; $p = 0.27$). Heterogeneity between these two studies was not significant ($I2 = 42.3\%$; $p = 0.19$ for Cochran's Q).

As regards the duration of vasopressor use, the meta-analysis excluded one study as this did not provide either SD for direct synthesis or the median for estimating SD, and the duration was summarised in days while the other two studies reported hours. Pooled analysis showed a significant reduction in duration of vasopressor administration in the group with vitamin C (SMD = –1.57, 95% CI –2.03 to –1.11; $p < 0.001$). Heterogeneity between these two studies was not significant ($I2 = 15.0\%$; $p = 0.28$ for Cochran's Q).

"Since this is a quantitative synthesis of a small number of studies, further randomised clinical trials are required to prove a causal relationship," Li notes. "If this relationship is confirmed, vitamin C has enormous potential to improve patient care and reduce mortality rates due to its low cost and wide availability."

Source: Critical Care
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