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[Intervention Review]

Selenium supplementation for critically ill adults

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ABSTRACT

Background

Selenium is a trace mineral essential to health and has an important role in immunity, defence against tissue damage and thyroid function. Improving selenium status could help protect against overwhelming tissue damage and infection in critically ill adults. This Cochrane review was originally published in 2004 updated in 2007 and again 2015.

Objectives

The primary objective was to examine the effect of nutrition supplemented with selenium or ebselen on mortality in critically ill patients.

The secondary objective was to examine the relationship between selenium or ebselen supplementation and number of infections, duration of mechanical ventilation, length of intensive care unit stay and length of hospital stay.

Search methods

In this update, we searched the current issue of the Cochrane Central Register of Controlled Trials, the Cochrane Library (2014, Issue 5); MEDLINE (Ovid SP, to May 20, 2014), EMBASE (Ovid SP, to May 20, 2014), CAB, BIOSIS and CINAHL. We handsearched the reference lists of the newest reviews and cross-checked with our search in MEDLINE. We contacted the main authors of included studies to request any missed, unreported or ongoing studies. The latest search was performed up to 21 May 2014. The search is now from inception until 21 May 2014.

Selection criteria

We included randomized controlled trials (RCTs) irrespective of publication status, date of publication, blinding status, outcomes published or language. We contacted the trial investigators and authors in order to retrieve relevant and missing data.

Data collection and analysis

Two review authors independently extracted data and we resolved any disagreements by discussion. Our primary outcome measure was all-cause mortality. We performed several subgroup and sensitivity analyses to assess the effects of selenium in critically ill patients. We presented pooled estimates of the effects of intervention as risk ratios (RRs) with 95% confidence intervals (CIs). We assessed the risk of bias through assessment of trial methodological components and the risk of random error through trial sequential analysis.

Main results

We included six new RCTs in this review update. In total we included 16 RCTs (2084 participants) in this review. Most trials were at high risk of bias. The availability of outcome data was limited and trials involving selenium supplementation were, with the exception of one trial, small regarding sample size. Thus the results must be interpreted with caution.



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Thirteen trials of intravenous sodium selenite showed a statistically significant reduction in overall mortality (RR 0.82, 95% CI 0.72 to 0.93, 1391 participants, *very low quality of evidence*). However, the overall point estimate on mortality is primarily influenced by trials of high risk of bias. Meta-analysis of three trials of ebselen had a RR of 0.83 (95% CI 0.52 to 1.34, 693 participants, *very low quality of evidence*).

Nine trials of intravenous sodium selenite were analysed for 28 days mortality with no statistically significant difference (RR 0.84, 95% CI 0.69 to 1.02, 1180 participants, *very low quality of evidence*) while three trials were analysed for 90 days mortality with similar findings (RR 0.96, 95% CI 0.78 to 1.18, 614 participants, *very low quality of evidence*).

Two trials of ebselen were analysed for 90 days mortality and were not found to yield any benefit (RR 0.72, 95% Cl 0.42 to 1.22, 588 participants, *very low quality of evidence*).

For mortality among intensive care patients selenium supplementation failed to indicate any statistically significant advantage (RR 0.88, 95% CI 0.77 to 1.01, nine trials, 1168 participants, *very low quality of evidence*).

Six trials of intravenous sodium selenite found no statistically significant difference for participants developing infection (RR 0.96, 95% CI 0.75 to 1.23, 934 patients, *very low quality of evidence*). Similarly, three trials of ebselen provided data for participants developing infections (pyrexia, respiratory infections or meningitis) with no obvious benefit (RR 0.60, 95% CI 0.36 to 1.02, 685 participants, *very low quality of evidence*).

Our analyses showed no effect of selenium or ebselen on adverse events (Selenium: RR 1.03, 95% Cl 0.85 to 1.24; six trials, 925 participants; Ebselen: RR 1.16, 95% Cl 0.40 to 3.36; two trials, 588 participants, *very low quality of evidence*).

No clear evidence emerged in favour of selenium supplementation for outcomes such as number of days on a ventilator (mean difference (MD) -0.86, 95% CI -4.39 to 2.67, four trials, 191 participants, *very low quality of evidence*), length of intensive care unit stay (MD 0.54, 95% CI -2.27 to 3.34, seven trials, 934 participants, *very low quality of evidence*) or length of hospital stay (MD -3.33, 95% CI -5.22 to -1.44, five trials, 693 participants, *very low quality of evidence*).

The quality of trial methodology was low. Due to high risk of bias in the included trials, results must be interpreted with caution.

Authors' conclusions

Despite publication of a number of trials, the current evidence to recommend supplementation of critically ill patients with selenium or ebselen remains disputed. Trials are required which overcome the methodological inadequacies of the reviewed studies, particularly in relation to sample size, design and outcomes.

PLAIN LANGUAGE SUMMARY

Selenium supplements for adults who are critically ill

Selenium is a mineral that is essential to health. It has an important role in defence against tissue damage and disease. Improving selenium status could help protect adults with serious illness.

In this updated review, Cochrane researchers assessed the effects of additional selenium supplementation for adults recovering from critical illness. We investigated whether the number of people who died changed by giving a selenium supplement during their treatment. Also we checked the impact of such a strategy on the rate of infections and other diseases for these patients while in hospital. We also examined whether selenium affected the duration of respiratory assistance for patients on ventilators and the length of their stay in the intensive care unit and the hospital.

We included 16 trials with 2084 participants. Thirteen trials carried out tests with selenium while three trials examined selenium-containing compound ebselen. Overall quality of the included trials was poor, with little information on quality indicators. The results were limited and these trials involving selenium supplementation were mostly small. In most trials, there was a high risk of poor or even incorrect information. Thus the results must be interpreted with caution. The evidence is current to 21 May 2014.

Thirteen trials of intravenous sodium selenite showed a statistically significant effect on death. Three trials of the selenium-containing compound ebselen showed no effect on death. No effects on infections or secondary diseases were observed.

No clear evidence emerged for the benefits of selenium or ebselen supplementation for days on a respirator, length of intensive care unit stay, length of hospital stay or quality of life. Due to the quality of included trials, one must be cautious when interpreting the strength of the evidence in favour of selenium supplementation despite a statistically significant finding.

Overall, there was low quality evidence from the studies for the all results. Trials are required which overcome the statistical uncertainty of the reviewed studies, particularly in relation to sample size, design and outcomes.