

[Intervention Review]

# Liberal versus conservative fluid therapy in adults and children with sepsis or septic shock

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## ABSTRACT

### Background

Sepsis and septic shock are potentially life-threatening complications of infection that are associated with high morbidity and mortality in adults and children. Fluid therapy is regarded as a crucial intervention during initial treatment of sepsis. Whether conservative or liberal fluid therapy can improve clinical outcomes in patients with sepsis and septic shock remains unclear.

### Objectives

To determine whether liberal versus conservative fluid therapy improves clinical outcomes in adults and children with initial sepsis and septic shock.

### Search methods

We searched CENTRAL, MEDLINE, Embase, intensive and critical care conference abstracts, and ongoing clinical trials on 16 January 2018, and we contacted study authors to try to identify additional studies.

### Selection criteria

We planned to include all randomized controlled trials (RCTs), quasi-RCTs, and cluster RCTs comparing liberal fluid therapy versus conservative fluid therapy for adults and children with sepsis or septic shock.

### Data collection and analysis

We used the standard methodological procedures expected by Cochrane. We assessed risk of bias of all included trials by using the Cochrane risk of bias tool. When appropriate, we calculated risk ratios (RRs) and 95% confidence intervals (CIs) for dichotomous outcomes, and mean differences (MDs) and 95% CIs for continuous outcomes. Our primary outcomes were all-cause mortality in hospital and at follow-up. Secondary outcomes included adverse events (organ dysfunction, allergic reaction, and neurological sequelae). We used GRADE to assess the quality of evidence for each outcome.

### Main results

We identified no adult studies that met our selection criteria.

This review included three paediatric RCTs (N = 3402), but we were able to extract data from only two of the three trials (n = 3288). These trials were conducted in India (two studies) and Africa. Participants were children from one month to 12 years old with sepsis or septic

shock. All three included trials investigated liberal versus conservative fluid therapy, although definitions of liberal and conservative fluid therapy varied slightly across included studies. Results of the two trials included in the analyses show that liberal fluid therapy may increase risk of in-hospital mortality by 38% (2 studies; N = 3288; RR 1.38, 95% CI 1.07 to 1.77; number needed to treat for an additional harmful outcome (NNTH) = 34; moderate-quality evidence) and may increase risk of mortality at follow-up (at four weeks) by 39% (1 study; N = 3141; RR 1.39, 95% CI 1.11 to 1.74; NNTH = 29; high-quality evidence). The third study reported inconclusive results for in-hospital mortality (very low-quality evidence).

We are uncertain whether there is a difference in adverse events between liberal and conservative fluid therapy because the single-study results are imprecise (organ dysfunction - hepatomegaly: RR 0.95, 95% CI 0.60 to 1.50; n = 147; low-quality evidence; organ dysfunction - need for ventilation: RR 1.17, 95% CI 0.83 to 1.65; n = 147; low-quality evidence; allergic reaction: RR 1.74, 95% CI 0.36 to 8.37; n = 3141; low-quality evidence; neurological sequelae: RR 1.03, 95% CI 0.61 to 1.75; n = 2983; low-quality evidence). Results are also uncertain for other adverse events such as desaturation, tracheal intubation, increased intracranial pressure, and severe hypertension.

### Authors' conclusions

No studies compared liberal versus conservative fluid therapy in adults. Low- to high-quality evidence indicates that liberal fluid therapy might increase mortality among children with sepsis or septic shock in hospital and at four-week follow-up. It is uncertain whether there are any differences in adverse events between liberal and conservative fluid therapy because the evidence is of low quality. Trials including adults, patients in other settings, and patients with a broader spectrum of pathogens are needed. Once published and assessed, three ongoing studies may alter the conclusions of this review.

## PLAIN LANGUAGE SUMMARY

### Different fluid therapy strategies for sepsis and septic shock

#### Review question

We aimed to investigate whether liberal fluid therapy can lead to more beneficial or harmful effects compared to conservative fluid therapy for adults and children with severe sepsis or septic shock. We mainly evaluated the different effects of these two interventions on risk of death and occurrence of adverse events.

#### Background

Sepsis and septic shock are complications of infection. Patients in the intensive care unit (ICU) are more likely than others to be affected by this condition. Once affected, patients experience organ dysfunction, which in some cases may lead to death. Fluid therapy is often used as an important intervention for initial treatment of sepsis in adults and children.

#### Results

We searched the electronic databases on 16 January 2018. We identified no adult trials that met our inclusion criteria. We included three trials involving 3402 children. We identified three 'ongoing' trials that have not yet been published. Pooled results from two trials (involving 3288 children) show that liberal fluid therapy may increase risk of in-hospital death by 38%, and risk of death at four-week follow-up by 39%. This means that for every 34 children receiving fluid therapy, one more in-hospital death will occur in the liberal fluid therapy group than in the conservative fluid therapy group. Similarly, at four-week follow-up, one more death will occur in the liberal fluid therapy group than in the conservative fluid therapy group for every 29 children receiving fluid therapy. One small study reported inconclusive results on risk of in-hospital death. We are uncertain whether there is a difference in adverse events (i.e. hepatomegaly, need for ventilation, allergic reaction, and neurological sequelae) between patients receiving liberal versus conservative fluid therapy.

One trial (involving 101 children) reported that conservative fluid therapy can shorten ICU stay and the duration of ventilation. However, we have very little confidence in this finding owing to the small sample size. We found no studies investigating adults with sepsis or septic shock.

#### Conclusion

Low- to high-quality evidence shows that liberal fluid therapy may increase the death rate for children with sepsis or septic shock. Except for this finding, we are uncertain about the effects of liberal versus conservative fluid therapy on the risk of adverse events. We are also uncertain about the effects of these two interventions for adults with sepsis or septic shock due to lack of data. Future trials focusing on adult sepsis or septic shock in other settings, with a wider range of pathogens, are expected. Once published and assessed, the three 'ongoing' studies identified may alter the conclusions of this review.