CME

Cochrane for Clinicians

Corticosteroids for Treating Sepsis in Children and Adults

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Author disclosure: No relevant financial relationships.

CLINICAL QUESTION

Do systemic corticosteroids reduce 28-day mortality for hospitalized children and adults with sepsis?

EVIDENCE-BASED ANSWER

Systemic corticosteroids probably reduce 28-day mortality for adults (18 years and older) hospitalized with sepsis. Furthermore, systemic corticosteroids may decrease length of hospitalization, probably reduce in-hospital mortality, and may reduce 90-day all-cause mortality for children and adults hospitalized with sepsis. However, they have little to no effect on long-term (ie, 90 days to 1 year) all-cause mortality.[1] (Strength of Recommendation: B, inconsistent or limited-quality patient-oriented evidence.)

PRACTICE POINTERS

Sepsis, broadly defined as a dysregulated immune response to an infection, is a common pathologic syndrome in hospitalized children and adults. Each year, 1.7 million adults and up to 72,000 children develop sepsis in the United States.[2,3] The in-hospital mortality rate associated with sepsis is high at an estimated 17% to 33%.[4,5]

This Cochrane review included 87 randomized controlled trials with 24,336 participants who had sepsis between 1976 and 2024 across 5 continents.[1] Sepsis was defined by the Sepsis 3 criteria or the presence of an infectious source with two symptoms of systemic inflammatory response syndrome and a sign of organ dysfunction. Of these trials, six included only children (excluding neonates), two included children and adults, and 79 included adults only. Steroid administration was compared with placebo or usual care. Any systemic corticosteroid was considered in the intervention groups (eg, cortisone, fludrocortisone, hydrocortisone, methylprednisolone, betamethasone, dexamethasone). This included continuous or bolus dosing of all dose ranges and treatment durations.

The primary outcome for this review was 28-day mortality. Secondary outcomes included length of hospitalization, long-term (ie, 90 days to 1 year) mortality, in-hospital mortality, and incidence of adverse effects (eg, superinfection, hyperglycemia, hypernatremia, neuropsychiatric effects [eg, delirium, confusion], muscle weakness, cardiac events, gastroduodenal bleeding).[1]

Systemic corticosteroid administration probably improves 28-day mortality in children and adults compared with usual care (risk ratio [RR] = 0.89; 95% CI, 0.84-0.95; 72 trials; n = 22,915; number needed to treat = 36; moderate-certainty evidence). Subgroup analysis further demonstrated that systemic corticosteroids seem to improve 28-day mortality in adults (RR = 0.89; 95% CI, 0.83-0.95; 62 trials; n = 21,851) but do not have a significant effect on 28-day mortality in children.[1]

In children and adults, systemic corticosteroids may reduce length of hospitalization (mean difference = –1.09 days; 95% CI, –1.85 to –0.34; 31 trials; n = 16,954; low-certainty evidence), may decrease intensive care unit length of stay (mean difference = –0.86 days; 95% CI, –1.67 to –0.05; 25 trials; n = 8,069; low-certainty evidence), probably decrease in-hospital mortality (RR = 0.9; 95% CI, 0.84-0.97; 40 trials; n = 17,459; moderate-certainty evidence), and may decrease 90-day all-cause mortality (RR = 0.89; 95% CI, 0.82-0.97; 13 studies; n = 8,360; low-certainty evidence). Corticosteroid use in patients with sepsis had no significant effect on long-term mortality.[1]

Regarding adverse effects, systemic corticosteroids compared with placebo or usual care appear to increase the risk of hyperglycemia and hypernatremia.[1] These terms were not well defined, and the data were presented heterogeneously; therefore, the clinical implications of these findings are unclear. Compared to placebo or usual care, corticosteroids have little to no effect on the incidence of superinfection, gastroduodenal bleeding, or neuropsychiatric events, and it is unclear if they cause any increased risk of muscle weakness, cardiac events, or stroke. Because subgroup analyses distinguishing children vs adults were not reported in the meta-analysis, it is unclear whether these conclusions are true for each subgroup. Subgroup analyses distinguishing corticosteroid type, dose, duration, or mode of delivery did not show any differences in 28-day mortality among groups.

The results of this meta-analysis are consistent with a recent meta-analysis that also showed a possible short-term mortality benefit from systemic corticosteroids for patients with septic shock and a 2013 meta-analysis that showed no improvement in mortality in children with sepsis who were treated with systemic corticosteroids.[6,7] The Society of Critical Care Medicine recommends that patients with septic shock, defined as sepsis with hypotension unresponsive to intravenous fluids requiring vasopressors, receive high-dose intravenous corticosteroids (eg, hydrocortisone, 400 mg/day) for up to 3 days, but it does not make a recommendation regarding sepsis without shock.[8] Further study is necessary, particularly regarding the use of systemic corticosteroids in children with sepsis.

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Wrist Acupuncture to Prevent Postoperative Nausea and Vomiting

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Author disclosure: No relevant financial relationships.

CLINICAL QUESTION

Is stimulation of the wrist at the pericardium 6 (PC6; also known as Master of the Heart 6 or Neiguan) acupuncture point (acupoint) effective in preventing postoperative nausea and vomiting?

EVIDENCE-BASED ANSWER

Invasive traditional percutaneous needling and noninvasive acupressure stimulation of acupoint PC6 reduce postoperative nausea compared with sham interventions.[1] (Strength of Recommendation [SOR]: B, inconsistent or limited-quality patient-oriented evidence.) Invasive and noninvasive PC6 acupoint stimulation reduce postoperative vomiting compared with sham interventions. (SOR: B, inconsistent or limited-quality patient-oriented evidence.)

Invasive and noninvasive PC6 acupoint stimulation also reduce the need for rescue drug therapy to treat postoperative nausea and vomiting compared with sham interventions.[1] (SOR: B, inconsistent or limited-quality patient-oriented evidence.) No serious adverse events were reported with PC6 acupoint stimulation. (SOR: B, inconsistent or limited-quality patient-oriented evidence.)

PRACTICE POINTERS

Postoperative nausea and vomiting are common complications after general anesthesia, affecting up to 80% of patients.[1] These symptoms not only impair recovery and patient satisfaction but also contribute to prolonged postanesthesia care unit stays, unanticipated hospital admissions, and increased health care costs.[2] Antiemetics are only partially effective in preventing or treating postoperative nausea and vomiting.[3]

Among various nonpharmacologic approaches, PC6 acupoint stimulation has been evaluated in many clinical trials.[4-6] The PC6 acupoint lies between the tendons of palmaris longus and flexor carpi radialis muscles, 4 cm proximal (2-3 fingerbreadths) to the wrist crease. Stimulation using invasive percutaneous traditional acupuncture needling or noninvasive acupressure can be performed on this site. The authors of this Cochrane review sought to determine if PC6 acupoint stimulation is effective in preventing postoperative nausea and vomiting.[1]

The review included 77 randomized controlled trials with 9,847 participants, mostly adults, across several countries (eg, United States, South Korea, India, China, Turkey, Iran).[1] The studies compared PC6 acupoint stimulation with sham treatment or antiemetic drugs. Sham treatment was defined as a device applied in a non-PC6 location, any attempt to imitate PC6 acupoint stimulation, or the use of placebo (saline) antiemetic drugs. Antiemetics included serotonin ($5\text{-}HT_3$) receptor antagonists, D_2 dopamine receptor antagonists, corticosteroids, and antihistamines. The duration of follow-up was 0 to 24 hours after surgery.

Outcomes were measured as occurrence of nausea, vomiting, or the need for rescue medications (binary outcomes) rather than severity of symptoms. Risk ratios (RRs) with 95% CIs were reported with frequentist network meta-analysis, a statistical analysis that compares more than two treatments by combining direct and indirect evidence from multiple studies. A beneficial effect of treatment was defined as the upper end of the 95% CI being below an RR of 0.80 compared with sham treatment. The review was current as of June 2025.

In 63 studies (n = 7,534), five comparisons were analyzed regarding postoperative nausea: invasive PC6, noninvasive PC6, antiemetics, invasive PC6 plus antiemetics, and noninvasive PC6 plus antiemetics.[1] Each decreased the likelihood of nausea compared with sham (invasive PC6: RR = 0.49; 95% CI, 0.38-0.64; number needed to treat [NNT] to reduce incidence of nausea = 5; low-certainty evidence; noninvasive PC6: RR = 0.67; 95% CI, 0.58-0.76; NNT = 7; low-certainty evidence; antiemetics: RR = 0.73; 95% CI, 0.59-0.91; NNT = 8; very low-certainty evidence; invasive PC6 plus antiemetics: RR = 0.21; 95% CI, 0.10-0.45; NNT = 3; moderate-certainty evidence).

In 75 studies (n = 8,627), five comparisons were analyzed regarding postoperative vomiting: invasive PC6, noninvasive PC6, antiemetics, invasive PC6 plus antiemetics, and noninvasive PC6 plus antiemetics.[1] Each decreased the likelihood of vomiting compared with sham (invasive PC6: RR = 0.47; 95% CI, 0.34-0.64; NNT = 6; low-certainty evidence; noninvasive PC6: RR = 0.58; 95% CI, 0.49-0.70; NNT = 8; low-certainty evidence; antiemetics: RR = 0.62; 95% CI, 0.47-0.81; NNT = 9; very low-certainty evidence; invasive PC6 plus antiemetics: RR = 0.37; 95% CI, 0.18-0.76; NNT = 5; low-certainty evidence; noninvasive PC6 plus antiemetics: RR = 0.52; 95% CI, 0.33-0.83; NNT = 7; very low-certainty evidence).

In 55 studies (n = 6,614), five comparisons were analyzed regarding the need for rescue antiemetics when prophylactic techniques were inadequate; only the combination of invasive PC6 and antiemetics was not effective.[1] Invasive PC6, noninvasive PC6, antiemetics, and noninvasive PC6 plus antiemetics each decreased the need for rescue medication compared with sham: antiemetics: RR = 0.56; 95% CI, 0.40-0.80; NNT = 8; very low-certainty evidence; noninvasive PC6: RR = 0.60; 95% CI, 0.51-0.70; NNT = 8; low-certainty evidence; invasive PC6: RR = 0.61; 95% CI, 0.44-0.84; NNT = 8; low-certainty evidence; noninvasive PC6 plus antiemetics: RR = 0.44; 95% CI, 0.28-0.70; NNT = 6; moderate-certainty evidence.

The treatments were not compared with one another for any outcome.[1] No serious or long-term complications were reported in the studies. Minor self-limiting adverse effects (eg, skin irritation, redness, swelling) were occasionally reported with PC6 acupoint stimulation.

The Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting recommend risk-based, multimodal management.[7] Patients with two or more risk factors should receive at least two prophylactic antiemetics from different classes. Although PC6 acupoint stimulation has been shown to reduce the risk of postoperative nausea and vomiting, the consensus guidelines call for additional study of acupuncture as a prevention or treatment modality.[6] More high-quality studies are needed to investigate the combined PC6 acupoint stimulation with antiemetics.

Editor's Note: The numbers needed to treat reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review.

The practice recommendations in this activity are available at https://www.cochrane.org/CD003281.

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