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Early Use of Norepinephrine in Septic Shock Resuscitation (CENSER) : A Randomized Trial.

Permpikul C[1], Tongyoo S[2], Viarasilpa T[1], Trainarongsakul T[1], Chakorn T[3], Udompanturak S[4].

Author information

Abstract

RATIONALE: Recent retrospective evidence suggests the efficacy of early norepinephrine administration during resuscitation; however, prospective data to support this assertion are scarce.

OBJECTIVES: To conduct a Phase II trial evaluating the hypothesis that early low-dose norepinephrine in adults sepsis with hypotension increases shock control by six hours compared with standard care.

METHODS: This single-center, randomized, double-blind, placebo-controlled clinical trial was conducted at Siriraj Hospital, Bangkok, Thailand. The study enrolled 310 adults diagnosed with sepsis with hypotension. The patients were randomly divided into two groups: early norepinephrine (n=155) and standard treatment (n=155). The primary outcome was shock control rate (defined as achievement of mean arterial blood pressure >65mmHg, with urine flow >0.5mL/kg/h for 2 consecutive hours, or decreased serum lactate >10% from baseline) by 6 hours after diagnosis.

MEASUREMENTS AND MAIN RESULTS: The patients in both groups were well matched in background characteristics and disease severity. Median time from emergency room arrival to norepinephrine administration was significantly shorter in early norepinephrine group (93 vs.192min;P<0.001). Shock control rate by 6 hours was significantly higher in early norepinephrine group (118/155[76.1%] vs.75/155[48.4%];P<0.001). 28 day mortality was not different between groups: 24/155(15.5%) in the early norepinephrine group versus 34/155(21.9%) in the standard treatment group (P=0.15). The early norepinephrine group was associated with lower incidences of cardiogenic pulmonary edema (22/155[14.4%] vs. 43/155[27.7%]; P=0.004) and new-onset arrhythmia (17/155[11%] vs. 31/155[20%]; P=0.03).

CONCLUSIONS: Early norepinephrine was significantly associated with increased shock control by 6 hours. Further studies are needed before this approach is introduced in clinical resuscitation practice. Clinical trial registration available at www.clinicaltrials.gov, ID NCT01945983.