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 Journal Club
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P: In patients with sepsis

I: Is the empiric use of steroids

C: Compared to withholding steroids or checking cortisol levels

O: Associated with better outcomes

Clinical scenario: 65 yo female brought from the nursing home for “altered mental status” with temp-102.3, HR 116, BP 76/40, RR-30. Following the Surviving Sepsis Guidelines, you start IV fluids, empiric antibiotics and place a CVL. You start Levophed b/c the patient remains hypotensive despite IV fluids and wonder if you should begin hydrocortisone.

Author	Patient Group	Study Type	Outcomes	Key Results	Limitations
Annane, et al 2005 Cochrane Review	Patients with severe sepsis/septic shock given corticosteroid vs placebo/ supportive tx	15 trials of RCT or quasi-RCT of tx with	28-day all cause mortality ICU mortality Time to shock reversal Adverse effects (GI bleed, superinfxn, hyperglyc)	High dose-corticosteroids did not improve mortality Long course low dose steroids improved ICU and 28-day mortality, and decreased time to shock reversal	Results heavily based on Annane’s study
Annane, et al; JAMA, France, 2002	299 septic pts given corticotropin test; responders vs. nonresponders (RAI) random assign to placebo vs. hydrocort (50mg IV q 6) + fludrocort (50ug po BID) x 7 days	Placebo-controlled, randomized, double-blind, parallel-group 19 ICUs in France	28-day survival in pts with RAI 28-day survival in responders ICU, hospital, and 1 year mortality Time to vasopressor withdrawal Adverse events: steroids v. pressors v. invasive procedure	NR (229); deaths – 73 placebo v. 60 steroid (NNT 7) Pressor w/draw 10 vs. 7 days Responder (70); Placebo 18 deaths, steroid 22 deaths Pressor w/draw 7 vs. 9 days No signif diff ICU, hosp, 1-year mortality in all pts No diff in adverse events placebo v. steroids	Etomidate amendment 2yrs into study – falsely low cortisol and response? Unusually ill pt population Additional benefit of fludrocort?
Thomas, PharmD and	Key words: hydrocortisone,	MEDLINE articles from	Role of steroids in	Serum cortisol levels vary	

Fraser, PharmD al; 2007 Annals of Pharmacotherapy	adrenal insufficiency, acute respiratory distress syndrome, pneumonia, sepsis, and cortisol	1966-2007	sepsis, severe CAP, ARDS Accuracy stim test	hourly with no circadian pattern; 91% NR Stim test in measured by 3 diff immunoassay had <50% agreement RAI is 34% in etomidate-naïve pts (Annane was 77%) Discrepancy b/w free cortisol and total cortisol	
Sprung, et al; NEJM 2008	Multicenter, randomized, double-blind, placebo control	499 pts; 251 IV hydrocortisone vs. 248 placebo All given stim test	Death at 28 days in pts without response to corticotropin Death at 28 days in all pts Time to reversal of shock	233 pts NR (125 v. 108) No diff in 28-day mortality in NR or responders b/w groups In all pts, time to shock reversal faster in steroid group Higher rates of superinfxn in steroid group	Only 500 pts enrolled Etomidate used in 26% pts Enrollment allowed up to 72 hours from onset of sepsis

Clinical Bottom Line:

While steroids improve the time to reversal of hypotension in septic shock in all patients, the most recent data suggests there is no improvement in overall mortality. Based on updated guidelines, there seems to be agreement among experts that steroids should not be used for patient with sepsis who are not in shock. However, the decision to give steroids in septic shock is one based on clinical judgment, rather than laboratory testing to determine RAI or protocols.

Original Surviving Sepsis Guidelines:

“Administer Low-Dose Steroids as a Standard Policy”

IV corticosteroids (hydrocortisone 200-300mg/day, divided BID or TID x 7 days) are recommended for patients with septic shock who require vasopressor therapy despite adequate fluid resuscitation..

250ug ACTH stimulation test is optional, but steroids should not be withheld to wait for stim test results. Although the steroids may not be helpful in patients without RAI, data has not shown them to be harmful.

Low-dose steroids improve survival in septic shock.

2008 Updates Guidelines, *Critical Care Medicine*:

Consider hydrocortisone in patients with septic shock who are poorly responsive to fluids and pressors (2C)

ACTH stim test is not recommended to ID pts who should get steroids (2B)

Do not use steroids to treat sepsis in the absence of shock unless the patient’s endocrine or corticosteroid history warrants it. (1D)