Clinician preferences for prescription of corticosteroids in patients with septic shock: an international survey

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In 2010, following the publication of two large trials of corticosteroids in septic shock, an international survey[1] of corticosteroid use in the management of septic shock reported marked variability in practice.[1,2,3] Two large randomised controlled trials of corticosteroids in septic shock (ie, the ADRENAL trial comparing hydrocortisone v placebo[4] and the APROCCHSS trial comparing hydrocortisone plus fludrocortisone v placebo[5]) published in 2018 reported divergent effects of steroids on mortality at day 90, although important secondary outcomes such as duration of shock and mechanical ventilation were improved in both trials.[4,5]

Whether the results of these two trials have subsequently influenced clinician preferences for corticosteroid prescription in septic shock remains unclear.

The primary objective of this international survey was to determine the preferred prescription practices of clinicians for the administration of hydrocortisone and fludrocortisone for septic shock management following the publication of the ADRENAL and APROCCHSS trials. In addition, we captured actual steroid use in patients who were in Australian and New Zealand intensive care units (ICUs) with a diagnosis of sepsis via the 2019 Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group (CTG) Point Prevalence Program (PPP).[6]

Methods

Ethics approval was obtained from the Royal Prince Alfred Hospital Human Research Ethics Committee (HREC-X19-0347). An email invitation was distributed via a country coordinator to their respective intensive care networks between August and November 2019 (accommodating local logistics). Intensive care clinicians were the main target sample, as they are the primary decision makers for use and prescription of steroids in sepsis. Each country had the survey open for one month.

The survey questions (Supporting Information) consisted of demographic data of the respondents and specific information around the choice, triggers for prescription, and modes of weaning of steroids in septic shock.

Data on steroid use in patients with sepsis were collected via the 2019 PPP (held in June) coordinated by the George Institute for Global Health and the ANZICS CTG.[6] Ethics approval for a waiver of individual patient consent was obtained. The data collected included sepsis on the study day (using Sepsis-2 definitions),[7] administration of oral or intravenous steroids for sepsis and/or septic shock (combined), and type of steroid administered.

Descriptive statistics are reported. Survey data are grouped by Australian and New Zealand respondents compared with other country respondents to assess PPP steroid use and Australian and New Zealand survey responses. All analyses were performed using Stata 16 (StataCorp, College Station, TX, USA).

Results

A total of 520 clinicians responded to the survey. The respondents' characteristics and prescription practices are shown in Table 1.

Most respondents stated they sometimes prescribe steroids in septic shock (87.7% in Australia and New Zealand v 78.9% in other countries; P = 0.124). Around a third (33.4%) of Australian and New Zealand respondents and more than half (64.8%) from other countries would wait for a minimum duration of vasopressor therapy before initiating hydrocortisone (P < 0.001), with a mean duration in Australia and New Zealand of 5.82 hours (standard deviation [SD], 2.70) and of 11.22 hours (SD, 9.91) in other countries (−5.4 hours in Australia and New Zealand v other countries; 95% CI, −10.16 to −0.64; P = 0.026). Most physicians (78.5% in Australia and New Zealand v 78.4% in other countries; P = 0.988) would wait for a minimum dose of vasopressor therapy, with the dose level varying between 0.1 μg/kg/min and 0.25 μg/kg/min. Around a third of respondents did not use other criteria to initiate hydrocortisone therapy, and one-fifth to one-third of participants used more than one inotrope or vasopressor therapy as criteria. Most respondents would not use fludrocortisone (96.9% in Australia and New Zealand v 86.0% in other countries; P = 0.048) in patients receiving

Table 1. Respondent characteristics and steroid prescribing practices

Characteristic	N (%)	Australia and New Zealand (N = 66)	Other countries (N = 449)	P
Clinical position				
Specialist/consultant	464 (89.23%)			
Resident or fellow trainee	41 (7.88%)			
Non trainee house officer	2 (0.38%)			
Other	13 (2.5%)			
Country				
Australia	55 (10.68%)			
New Zealand	11 (2.14%)			
Denmark	64 (12.43%)			
Brazil	35 (6.80%)			
United Kingdom	118 (22.91%)			
India	64 (12.43%)			
Israel	21 (4.08%)			
Saudi Arabia	91 (17.67%)			
Taiwan	11 (2.14%)			
Hospital type				0.005
Tertiary		36 (54.55%)	186 (42.56%)	
Public teaching		14 (21.21%)	136 (31.12%)	
Public non-teaching		0 (0%)	31 (7.09%)	
Private teaching		1 (1.52%)	27 (6.18%)	
Private non-teaching		1 (1.52%)	15 (3.43%)	
Metropolitan		9 (13.64%)	21 (4.81%)	
Rural		2 (3.03%)	10 (2.29%)	
Not-for-profit		1 (1.52%)	5 (1.14%)	
Other		2 (3.03%)	6 (1.37%)	
Prescription of steroids in septic shock				0.124
Always		8 (12.31%)	72 (16.55%)	
Sometimes		57 (87.69%)	343 (78.85%)	
Never		0 (0.0%)	20 (4.60%)	
Do you wait for a minimum duration of vasopressor therapy before administering hydrocortisone therapy?				
Yes		22 (33.85%)	267 (64.81%)	< 0.001
No		43 (66.15%)	145 (35.19%)	
What is the duration?				0.227
4 hours		5 (20.83%)	58 (21.17%)	
6 hours		8 (33.33%)	62 (22.63%)	
12 hours		2 (8.33%)	31 (11.31%)	
18 hours		0 (0.00%)	6 (2.19%)	
24 hours		0 (0.00%)	46 (16.79%)	
Other		71 (25.91%)	9 (37.50%)	
Duration as continuous variable				
Mean (SD)		5.82 (2.70)	11.22 (9.91)	
Linear regression (t test) of continuous data*, hours		−5.4[†]		0.026

(Continues)

Table 1. Respondent characteristics and steroid prescribing practices (*continued*)

Characteristic	N (%)	Australia and New Zealand (N = 66)	Other countries (N = 449)	P
Do you wait for a minimum dose of vasopressor therapy before administering hydrocortisone therapy?				
Yes		51 (78.46%)	319 (78.38%)	0.988
No		14 (21.54%)	88 (21.62%)	
What is the minimum dose?				
Noradrenaline				0.204
▸ 0.05 µg/kg/min		4 (8.33%)	21 (6.80%)	
▸ 0.1 µg/kg/min		6 (12.50%)	62 (20.06%)	
▸ 0.15 µg/kg/min		6 (12.50%)	20 (6.47%)	
▸ 0.2 µg/kg/min		17 (35.42%)	78 (25.24%)	
▸ 0.25 µg/kg/min		11 (22.92%)	74 (23.95%)	
▸ Other		4 (8.33%)	54 (17.48%)	
Dopamine				1.000
▸ 2.5 µg/kg/min		0 (0.00%)	3 (13.64%)	
▸ 5 µg/kg/min		1 (33.33%)	5 (22.73%)	
▸ 7.5 µg/kg/min		0 (0.00%)	1 (4.55%)	
▸ 10 µg/kg/min		0 (0.00%)	4 (18.18%)	
▸ Other		2 (66.67%)	9 (40.91%)	
Do you use other criteria to initiate hydrocortisone therapy?				0.445
Need for vasopressin therapy		13 (20.63%)	64 (16.04%)	
Need for more than one inotrope or vasopressor therapy		15 (23.81%)	122 (30.58%)	
Vasopressor therapy plus lactacte > 2 mmol/L		4 (6.35%)	47 (11.78%)	
No		22 (34.92%)	117 (29.32%)	
Other		9 (14.29%)	49 (12.28%)	
In patients to whom you prescribe hydrocortisone, do you also prescribe fludrocortisone?				0.048
Yes, always		0 (0.0%)	7 (1.75%)	
Yes, sometimes		2 (3.13%)	49 (12.28%)	
No		62 (96.88%)	343 (85.96%)	
When do you discontinue hydrocortisone and/or fludrocortisone therapy?				0.831
When patients are weaned off inotropes/vasopressors for 24hours		43 (67.19%)	267 (67.25%)	
Regardless of inotrope/vasopressor for a maximum of 7 days or until discharge from ICU (whichever is earlier)		9 (14.06%)	65 (16.37%)	
Other		12 (18.75%)	65 (16.37%)	

ICU = intensive care unit; SD = standard deviation. * The survey question about the duration of vasopressor use was analysed as a continuous measure and analysed with a linear regression model. † 95%CI, −10.16 to −0.64.

hydrocortisone. Steroid therapy was mostly discontinued when patients had been weaned off inotropes/vasopressor therapy for 24 hours (67.2% in Australia and New Zealand v 67.3% in other countries; P = 0.831).

From the 44 Australian and New Zealand adult ICUs participating in the 2019 PPP study, a total of 191/627 patients (30.5%) had sepsis on the study day. Of these, 32 patients (16.8%) received steroids, with hydrocortisone

used most often (24/32, 75.0%), followed by prednisolone (6/32, 18.6%) and dexamethasone (2/32, 6.3%).

Discussion

In this international survey, most clinicians would sometimes or always prescribe steroids for septic shock. Significant practice variation remains, with triggers for initiation of steroid therapy reflecting uncertainty on the optimal time to commencement. Fludrocortisone was not commonly used in conjunction with hydrocortisone, with no patients receiving fludrocortisone in the PPP data.

The strengths of this survey included a broad international representation from specialist doctors and reporting of actual practice from Australian and New Zealand ICUs. The limitations include a small sample size, no denominator limiting the ability to provide a response rate, and no data on the proportion of patients with septic shock in the PPP study.

Conclusions

Almost 2 years after the publication of two large randomised controlled trials of steroids in septic shock, most clinicians would prescribe corticosteroids for septic shock, although substantial variability exists in vasopressor dose and duration triggers for commencement. The low preference for fludrocortisone prescription suggests that more definitive data are required to guide the use in the management of patients with septic shock.

Competing interests

No relevant disclosures.

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