Corticosteroid after etomidate in critically ill patients: A randomized controlled trial*

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Objective: **To investigate the effects of moderate-dose hydrocortisone on hemodynamic status in critically ill patients throughout the period of etomidate-related adrenal insufficiency.**

Design: **Randomized, controlled, double-blind trial (NCT00862381).**

Setting: **University hospital emergency department and three intensive care units.**

Interventions: **After single-dose etomidate (H0) for facilitating endotracheal intubation, patients without septic shock were randomly allocated at H6 to receive a 42-hr continuous infusion of either hydrocortisone at 200 mg/day (HC group; n = 49) or saline serum (control group; n = 50).**

Measurements and Main Results: **After completion of a corticotrophin stimulation test, serum cortisol and 11β-deoxycortisol concentrations were subsequently assayed at H6, H12, H24, and H48. Forty-eight patients were analyzed in the HC group and 49 patients in the control group. Before treatment, the diagnostic criteria for etomidate-related adrenal insufficiency were fulfilled in 41 of 45 (91%) and 38 of 45 (84%) patients in the HC and control groups, respectively. The proportion of patients with a cardiovascular Sequential Organ Failure Assessment score of 3 or 4 declined comparably over time in both HC and control groups: 65% vs. 67% at H6, 65% vs. 69% at H12, 44% vs. 54% at H24, and 34% vs. 45% at H48, respectively. Required doses of norepinephrine decreased at a significantly higher rate in the HC group compared with the control group in patients treated with norepinephrine at H6. No intergroup differences were found regarding the duration of mechanical ventilation, intensive care unit length of stay, or 28-day mortality.**

Conclusion: **These findings suggest that critically ill patients without septic shock do not benefit from moderate-dose hydrocortisone administered to overcome etomidate-related adrenal insufficiency. (Crit Care Med 2012; 40:29–35)**

KEY WORDS: adrenal insufficiency; critical care; etomidate; outcome

The issue over etomidate use in critically ill patients is generating considerable debate (1–9). As a result of its excellent hemodynamic tolerance, etomidate is a first-line anesthetic agent used to facilitate endotracheal intubation in hemodynamically unstable patients (10, 11) and has emerged as an agent of choice for rapid-sequence intubation (RSI) in critically ill patients. However, single-dose etomidate blocks cortisol synthesis by specifically inhibiting the activity of 11β-hydroxylase that converts 11β-deoxycortisol into cortisol in the adrenal gland, resulting in a primary adrenal insufficiency with effects lasting for up to 48 hrs postadministration (12). Such adrenal insufficiency is associated with higher rates of mortality and morbidity in the intensive care unit (ICU) (13), raising concerns over the potential for etomidate to worsen patient outcome as was shown in patients with septic shock or with trauma (14–19). On the other hand, the exposure to episodes of arterial hypotension is also associated with poorer outcome (20, 21) and the hemodynamic profile of etomidate is superior to all available induction agents. Physicians therefore face an awkward dilemma in their choice of agents to facilitate emergency tracheal intubation while minimizing any cardiovascular effects of sedation: to eliminate the use of etomidate or to add concomitant administration of corticosteroids (1, 2, 5).

Moderate-dose hydrocortisone (200–300 mg/day) has been successfully proposed to overcome critical illness-related adrenal insufficiency, particularly in septic patients responding poorly to fluid resuscitation and vasopressor agents. The more rapid resolution of septic shock (22–26) suggested the potential usefulness of moderate-dose hydrocortisone in patients with vasopressor-dependent septic shock (27). A reduction in norepinephrine doses required to maintain hemodynamic stability in brain-dead patients was also found with hydrocortisone supplementation (28). However, the effectiveness of moderate-dose hydrocortisone has never been prospectively tested during the period of etomidate-related

***See also p. 301.**

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adrenal insufficiency. Our aim was therefore to investigate the effectiveness of such supplementation at decreasing the proportion of vasopressor-dependent patients without septic shock after single-dose etomidate.

METHODS

Patient Selection. This prospective, randomized, controlled, double-blind (caregiver, investigator) trial was conducted between July 2008 and July 2010 at the University Hospital of Grenoble and included three ICUs. The local institutional ethics committee approved the design of the study (08-CHUG-4). Written informed consent was obtained from the patients or their relatives before inclusion wherever possible or from a legally authorized representative and subsequently from the patient in accordance with French Ethics Law. Adult patients were prospectively enrolled in the study if they needed sedation to facilitate endotracheal intubation in the field or in the emergency room, through RSI with intravenous single-dose etomidate and suxamethonium. The induction time was considered as the reference time (H0). Sedation was further maintained through the continuous intravenous administration of sedative/analgesic agents, i.e., midazolam, propofol, sufentanil, and fentanyl. The decision to use etomidate was left to the discretion of the in-charge physician whenever RSI was required. Exclusion criteria were: septic shock requiring steroid supplementation; chronic adrenal insufficiency; pituitary disorder; HIV infection; concomitant or prior treatment with steroids, ketoconazole, or fluconazole; previous corticotrophin stimulation test for reasons other than the study protocol; probability of survival $<$48 hrs, etomidate administration $\geq$24 hrs after patient admission to the ICU; or enrollment in the study $\geq$5 hrs after etomidate induction.

Study Protocol. Patients were randomly assigned in a 1:1 ratio to receive either hydrocortisone (HC group) (Hydrocortisone; Upjohn, Serb, Paris, France) or saline (0.9% NaCl) (control group) from 6 hrs (H6) to 48 hrs (H48). Randomization was assured using a computerized random-number generator list provided by a statistician not involved in patient recruitment or outcome assessment and the allocation into groups was achieved using a sequentially numbered grid. ICU physicians and nurses were blinded to the assigned treatments indiscernible in appearance and undisclosed in verbal or written reports.

On completion of clinical data and the blood sampling for the corticotrophin test (see subsequently) at H6 (baseline), patients then received daily intravenous injections of either 50 mL isotonic saline solution (control group) or 200 mg hydrocortisone diluted in 50 mL saline solution (HC group). A bolus of 12.5 mL of the solution, containing 50 mg hydrocortisone in the HC group, was initially injected over 30 mins at a rate of 25 mL/hr. The solution was then continuously infused at a rate of 2.1 mL/hr until H48, unless the patient was discharged beforehand. The HC group therefore received 200 mg/day hydrocortisone over a total of 42 hrs infusion.

Variables were collected on admission and at 6, 12, 24, and 48 hrs (H6, H12, H24, and H48, respectively), especially the cardiovascular Sequential Organ Failure Assessment (SOFA) score (29) (Supplemental Digital Content 1, http://links.lww.com/CCM/A293). Vasopressive support (norepinephrine) was continuously infused to maintain mean arterial pressure between 65 and 90 mm Hg. In the presence of severe brain injury, mean arterial pressure values were maintained at 80–90 mm Hg. Insulin was administered to maintain serum glucose $<$10 mmol/L.

Hormonal Assays. Adrenal function was assessed using the high-dose corticotrophin stimulation test (CST). Serum total cortisol and concomitant 11β-deoxycortisol concentrations were determined at H5 and 60 mins after the intravenous administration of 250 μg of synthetic 1-24 adrenocorticotropic hormone (Synacthen Novartis Pharma, Rueil-Malmaison, France) (H6). Subsequent measurements of serum total cortisol and 11β-deoxycortisol concentrations were performed at H12, H24, and H48 (Supplemental Digital Content 2, http://links.lww.com/CCM/A293). Etomidate-related adrenal insufficiency was defined as δ serum cortisol concentrations $<$250 nmol/L (9 μg/dL) after CST (CST nonresponders) (27) associated with serum 11β-deoxycortisol concentrations $>$8 nmol/L (0.28 μg/dL) (12).

End Points. The primary study outcome was the course of patients with a cardiovascular SOFA score of 3 or 4, i.e., requirement of norepinephrine to treat moderate-to-severe cardiovascular failure at H6, H12, H24, and H48. Secondary study outcomes included the course of norepinephrine dose, maximum serum glucose, the number of patients treated by insulin, maximum SOFA score, and maximum cardiovascular SOFA score during the study period. Other secondary end points were 28-day all-cause mortality, the duration of mechanical ventilation and of ICU stay, and the number of ICU days with norepinephrine support.

Statistical Analysis. The study population size was calculated considering a proportion of 53% of patients with a cardiovascular SOFA score of 3 or 4 at H24 in the control group, as previously reported (12). Assuming a clinically relevant reduction by 50% in the number of patients with such a score at H24 in the HC group, with a two-sided type 1 error of 0.05 and a power of 80%, 50 patients per group were needed to detect this difference. Patients with premature ending of the 42-hr infusion treatment resulting from death or ICU discharge alive were considered in the analysis (intent-to-treat study).

Results are given as the median (25th and 75th percentiles) for continuous variables and frequencies and percentages (95% confidence interval) for categorical variables, unless otherwise stated. The chi-square and nonparametric Mann-Whitney tests were performed for categorical and continuous variables, respectively. Analysis of the statistical significance of temporal changes during the study period was performed using the random effect linear model. Intragroup analysis of any interaction between groups and time ($p \leq .10$) was performed using Bonferroni's correction for multiple comparisons with H6 taken as the reference time. Statistical analysis was performed using Stata version 11.0 (Stata Corp, College Station, TX). Statistical significance was declared when $p \leq .05$.

This study is registered with ClinicalTrials.gov, No. NCT00862381.

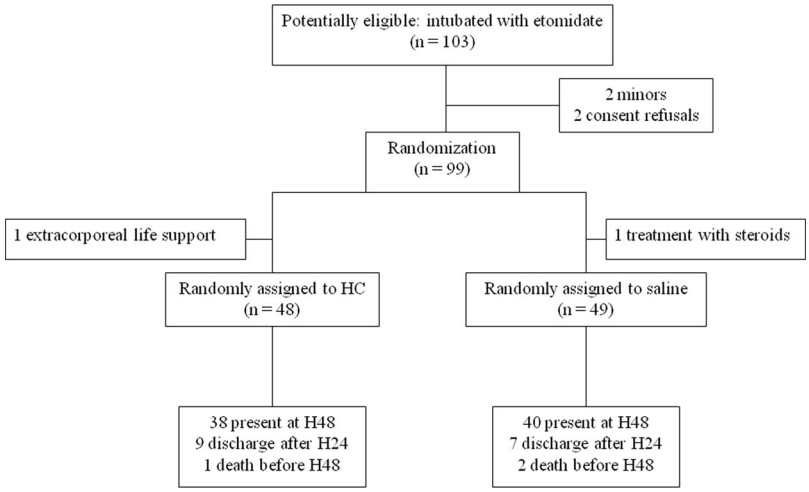

Figure 1. Patient flow diagram showing the number of identified, excluded, and analyzed patients. *HC*, hydrocortisone.

RESULTS

Of the 103 eligible patients, 99 were consecutively and randomly assigned for treatment and 97 were analyzed (Fig. 1). Four patients were excluded before randomization (two minors and two refusing consent) and two after: one treated by extracorporeal life support (HC group) and one receiving concomitant treatment with steroids (control group). Ten patients from the HC group and nine from the control group did not receive the entire 42-hr infusion treatment as a result of discharge alive from the ICU after H24 (9 and 7, respectively) and death (1 and 2, respectively). The 16 patients who were discharged alive from the ICU had a cardiovascular SOFA score of 0.

Baseline characteristics of the 97 included patients are shown in Table 1 (H0, etomidate administration) and Table 2 (H6, before the initiation of treatment). Hormonal assays were performed in 93 patients at H5 (46 HC and 47 control), and CST results were available in 90 patients. Of these, there were 41 of 45 (91%) and 38 of 45 (84%) patients in the HC and control groups, respectively, who fulfilled the diagnostic criteria for etomidate-related adrenal insufficiency at H6. After the CST, the median δ cortisol was comparable between the two groups: 91 nmol/L (46–179) vs. 85 nmol/L (38–175), respectively. A significant interaction between groups and time ($p = .10$) was the result of the higher serum cortisol concentrations at H12, H24, and H48 in the HC group compared with the control group (Table 3). Noteworthy was the gradual decrease in serum cortisol concentrations in the HC group between H6 and H48 ($p < .01$). The accumulation of serum 11β-deoxycortisol progressively declined over time ($p < .01$) with no difference between the two groups (Table 3). The evolution of serum albumin, while declining at H48 vs. H6, was similar between the two groups.

The clinical course of patients with cardiovascular SOFA scores of 3 or 4 is shown in Figure 2. All of these patients received norepinephrine, and dobutamine was additionally administered at similar frequencies in the HC and control groups: eight vs. six patients at H6, 14 vs. 12 at H12, 12 vs. 12 at H24, and eight vs. 11 at H48, respectively. No patient was given epinephrine. Reasons for administering norepinephrine at H6 were the presence of multiple trauma and/or isolated brain injury ($p < .01$ vs. no norepinephrine). In the HC and control groups, the proportion of patients with cardiovascular SOFA scores of 3 or 4 declined comparably over time between H6 and H48 ($p < .01$): 31 of 48 (65%) vs. 33 of 49 (67%) patients at H6, 31 of 48 (65%) vs. 33 of 48 (69%) at H12, 21 of 48 (44%) vs. 26 of 48 (54%) at H24, and 16 of 47 (34%) vs. 21 of 47 (45%) at H48 in the HC and control groups, respectively. The mean

Table 1. Characteristics and physiological data collected at the time of etomidate administration (H0) from 97 patients according to their subsequent allocation into treatment groups receiving saline solution (control) vs. hydrocortisone

	Control (n = 49)	Hydrocortisone (n = 48)
Age, yrs	45 (33–59)	52 (34–63)
Male sex, no.	32 (65%)	31 (65%)
Weight, kg	75 (65–80)	70 (65–79)
Patients with body mass index >30, kg/m^2	9 (18%)	8 (17%)
Patient history, no.		
Hypertension	10 (20%)	13 (27%)
Coronary artery disease	5 (10%)	6 (13%)
Congestive heart failure	2 (4%)	2 (4%)
Diabetes	6 (12%)	8 (17%)
Reasons for endotracheal intubation, no.		
Isolated severe traumatic brain injury	7 (14%)	11 (23%)
Subarachnoid hemorrhage	5 (10%)	5 (10%)
Multiple trauma	24 (49%)	18 (37%)
Acute poisoning	5 (10%)	7 (15%)
Sepsis with no shock	1 (2%)	2 (4%)
Others	7 (14%)	5 (10%)
Disease severity before intubation, no.		
Glasgow Coma Scale score	12 (7–15)	9 (6–14)
Heart rate, beats/min	89 (74–103)	89 (75–110)
Systolic blood pressure, mm Hg	120 (105–136)	114 (101–130)
Temperature, °C[a]	36.5 (35.7–36.9)	36.5 (35.5–37.0)
Cardiovascular Sequential Organ Failure Assessment	0 (0–1)	0 (0–1)
Etomidate dose, mg/kg	0.33 (0.25–0.46)	0.32 (0.29–0.43)
Simplified Acute Physiology Score II	42 (32–51)	45 (34–54)
Injury Severity Score[b]	27 (21–34)	25 (16–29)

[a]Forty-one missing values; [b]injury Severity Score was not calculated for the 37 nontrauma patients.

Data are median (25th–75th interquartile range) or number (%), unless otherwise specified.

Table 2. Baseline clinical and biological characteristics from 97 study patients collected at H6, before the initiation of treatment, i.e., saline solution (control) vs. hydrocortisone

	Control (n = 49)	Hydrocortisone (n = 48)
Systolic blood pressure, mm Hg	119 (103–131)	120 (101–137)
Diastolic blood pressure, mm Hg	65 (57–72)	61 (56–70)
Mean arterial pressure, mm Hg	85 (73–90)	83 (71–89)
Heart rate, beats/min	75 (65–90)	79 (66–103)
Temperature, °C	36.5 (35.0–37.3)	36.4 (35.4–37.1)
Cardiovascular Sequential Organ Failure Assessment	3 (1–4)	4 (1–4)
Laboratory values		
White blood cells, Giga/L	11.0 (8.6–14.7)	12.1 (9.7–15.3)
Hemoglobin, g/L	114 (103–128)	113 (98–133)
Platelets, Giga/L	178 (125–225)	191 (153–228)
Plasma sodium, mmol/L	141 (139–144)	141 (138–143)
Plasma glucose, mmol/L	7.5 (5.8–9.0)	7.4 (5.9–9.8)
Plasma protein, g/L	50 (44–58)	58 (46–62)
Serum albumin, g/L	28 (24–33)	31 (25–35)
Plasma creatinine, μmol/L	67 (50–89)	71 (52–84)
PaO_2, mm Hg[a]	147 (114–179)	151 (110–198)
$Paco_2$, mm Hg[a]	38 (33–45)	35 (32–40)
Arterial pH[a]	7.36 (7.29–7.40)	7.36 (7.29–7.44)
Arterial lactate, mmol/L	1.8 (1.8–3.1)	1.9 (1.5–3.1)

[a]Eight missing values.

Data are median (25th–75th interquartile range) or number (%), unless otherwise specified.

Table 3. Time course of adrenal function assessment according to treatment, saline solution (control) vs. hydrocortisone[a]

	Before Treatment	During Treatment			
	H5	H6	H12	H24	H48
HC/control, no.	(46/47)	(45/46)	(39/45)	(41/43)	(35/35)
Cortisol, nmol/L					
HC	279 (174–457)	425 (289–579)	1383 (1062–2195)[b,c]	1105 (956–1415)[b,c]	1009 (819–1191)[b,c]
Control	317 (187–466)	422 (287–540)	447 (274–651)	368 (196–549)	334 (239–579)
11β-deoxycortisol, nmol/L					
HC	121 (36–190)	165 (112–291)	62 (31–161)[c]	20 (15–61)[c]	10 (8–19)[c]
Control	81 (26–149)	147 (104–275)	115 (58–172)[c]	32 (21–66)[c]	11 (8–34)[c]
Serum albumin, g/L					
HC	30 (24–36)	31 (25–35)	33 (25–36)	32 (26–35)	28 (24–32)[c]
Control	31 (26–33)	28 (24–33)	29 (26–31)	27 (24–32)	26 (22–31)[c]

HC, hydrocortisone.

[a]Treatment was initiated after the completion of a corticotrophin stimulation test (H6). Serum cortisol and 11[βετα]-deoxycortisol concentrations (nmol/L) were determined at H5, H6 (baseline), H12, H24, and H48 after single-dose etomidate (H0); [b]$p < .01$ vs. control; [c]$p < .01$ vs. H6. Data are median (25th–75th interquartile range).

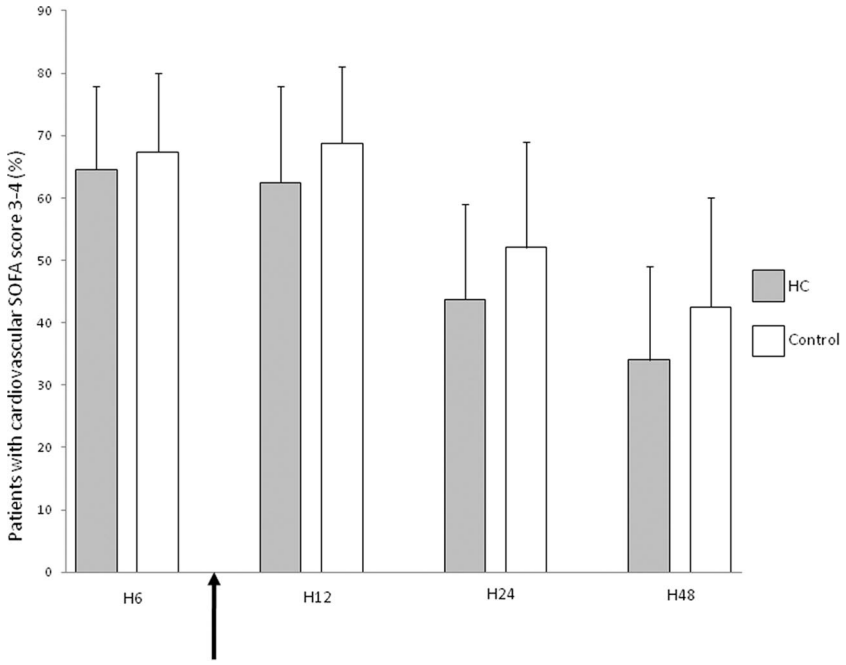

Figure 2. Clinical course of patients with a cardiovascular Sequential Organ Failure Assessment (*SOFA*) score of 3 or 4, i.e., moderate-to-severe cardiovascular failure at H6 (baseline), H12, H24, and H48 according to their allocated treatment, hydrocortisone (*HC*) vs. saline (control). Treatment was initiated once the data completed at H6 (*arrow*). Data are expressed as median and 95% confidence interval.

arterial pressure values were comparable between the two groups with higher values at H48 vs. H6 ($p < .05$) (Fig. 3). For patients treated with norepinephrine at H6, a significant interaction was found between temporal evolution of drug dose and group ($p < .01$). This was the result of higher doses of norepinephrine in the HC group compared with the control group at H6 (intergroup analysis; $p < .05$) and lower doses required at H24 and H48 vs. H6 in the HC group only (intragroup analysis) ($p < .01$) (Fig. 4). The norepinephrine dose decreased over time in this group, whereas the mean arterial pressure values remained stable and comparable to the control group. No differences existed regarding the doses of dobutamine between the two groups. Finally, except for the higher maximum plasma glucose in the HC group, no significant differences were found between groups considering the other secondary outcomes (Table 4).

DISCUSSION

Moderate-dose hydrocortisone used to overcome etomidate-related adrenal insufficiency was not associated with changes in the proportion of patients with cardiovascular SOFA scores of 3 or 4. Nor did it affect the ICU length of stay, the number of ventilator days, or the 28-day mortality. The treatment was, however, associated with a significant decrease in norepinephrine dose at H24 and H48.

According to the etomidate-induced blockade of cortisol synthesis, a serum accumulation of 11β-deoxycortisol and a low response of serum cortisol to the CST are two diagnostic criteria indicating drug-induced adrenal impairment. Surprisingly, these criteria have been rarely exploited in studies exploring the contribution of etomidate to adrenal insufficiency. Because there are numerous other causes of adrenal derangement in critically ill patients (30–33), it is essential to concomitantly assess levels of serum cortisol and 11β-deoxycortisol in the search for etomidate-related adrenal insufficiency. In the present study, 88% of patients fulfilled these diagnostic criteria at H6, in line with the 80% of patients previously reported at H12 after single-dose etomidate (12). The progressive decline in serum 11β-deoxycortisol by 48 hrs confirms the transient blockade of cortisol synthesis, as described elsewhere (12, 34, 35).

Even with a large proportion of patients presenting etomidate-related adrenal insufficiency at the time of allocated treatment, we failed to find any impact of moderate-dose hydrocortisone according to our primary outcome. This suggests that etomidate and its resulting transient adrenal derangement play no major role in the evolution of cardiovascular status. It should be noted that according to their

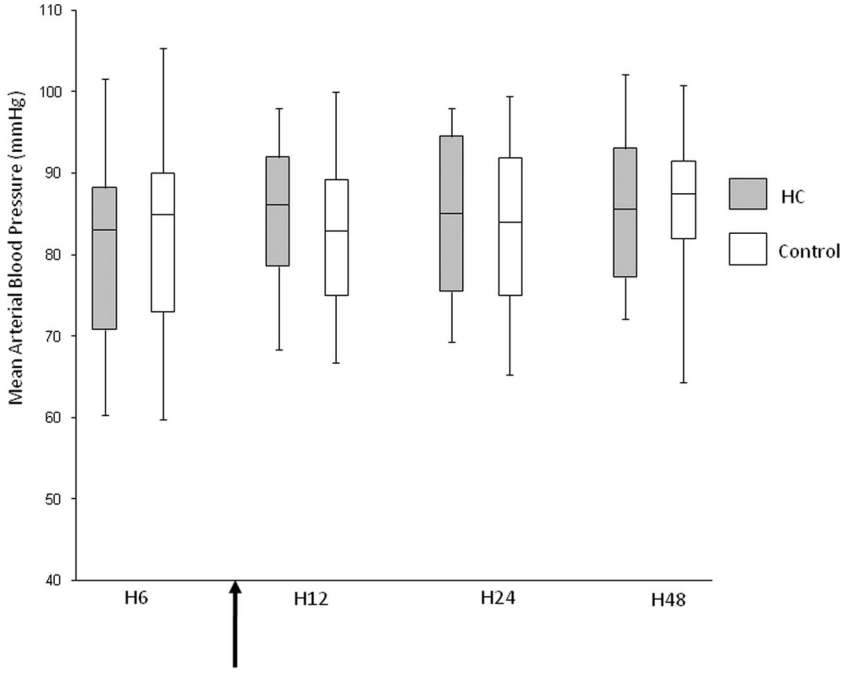

Figure 3. Box (median, 25th and 75th percentiles) and whisker (5th and 95th percentiles) plots of mean arterial blood pressure (in mm Hg) at H6 (baseline), H12, H24, and H48 according to the allocated treatment, hydrocortisone (*HC*) vs. saline (control). Treatment was initiated once the data completed at H6 (*arrow*).

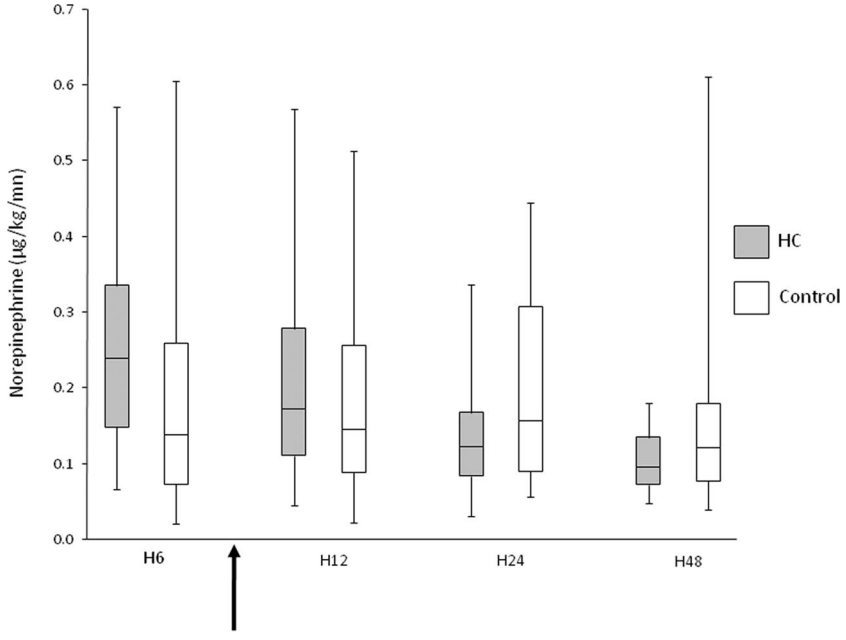

Figure 4. Box (median, 25th and 75th percentiles) and whisker (5th and 95th percentiles) plots of doses of norepinephrine (µg/kg/min) among norepinephrine-treated patients. Doses are recorded at H6 (baseline), H12, H24, and H48 according to the allocated treatment, hydrocortisone (*HC*) vs. saline (control). Treatment was initiated once the data completed at H6 (*arrow*).

stabilized hemodynamic status before randomization, our enrolled patients showed no likely risk of cardiovascular collapse after sedation for tracheal intubation (Table 1). In addition, many had confirmed or suspected brain injury, thus explaining the choice of etomidate to prevent one major predictor of poor outcome, arterial hypotension (36). Our population likely differs therefore from others in terms of baseline hemodynamic status (18, 24).

We found steroid supplementation associated with a significant decrease in required levels of norepinephrine at H24 and H48, in agreement with other studies (22–26, 28). Hydrocortisone treatment can also decrease the cardiovascular SOFA score during the first week of treatment in nonseptic hypotensive patients (37). Schematically, low-dose hydrocortisone acts by increasing the sensitivity to vasopressor agents (38) and/or by replenishing cortisol levels depleted after the overstimulation of the hypothalamic–pituitary–adrenal axis induced by brain death, septic shock, and other situations involving the downregulation of β-adrenergic receptors (39). Concordantly, our findings suggest that the administration of moderate-dose hydrocortisone for <48 hrs might have enhanced the sensitivity to norepinephrine, independent of the etomidate-related adrenal insufficiency.

In this context, it is intriguing as to why some studies have identified etomidate as one factor independently associated with poorer outcome in critically ill patients (14–18). One explanation is its preferable use in inherently sicker patients, especially in patients with adrenal insufficiency resulting from severe sepsis. However, etomidate was not related to patient outcome in other studies, including patients with septic shock (40–42). A large retrospective study on patients in severe sepsis found no association between etomidate and changes in vasopressor use, ICU length of stay and ventilator days, or hospital mortality (43). Two randomized controlled trials exploring the impact of etomidate on patient outcome found no differences compared with either ketamine or midazolam (44, 45). Interestingly, half of the patients given ketamine in the Jabre study were nonresponders to the CST, thereby underscoring the wide range of causes of adrenal disturbance among critically ill patients. Added to the present results showing the failure of steroid supplementation to overcome etomidate-related adrenal insufficiency, there is reason to consider this drug-induced transient hormonal derangement as a minor contributor, if any, to the worsened outcome in critically ill patients.

There are several limitations with this study. First, the decision to perform RSI in the field or in the emergency room using etomidate was left at the discretion of the in-charge physicians who were then not involved in the subsequent care of the patient once admitted to the ICU. We did not explore the impact of steroid supplementation in patients still present

Table 4. Secondary patient outcomes according to their treatment, saline solution (control) vs. hydrocortisone

	Control (n = 49	Hydrocortisone (n = 48)
During the 48-hr study period		
Maximum Sequential Organ Failure Assessment score	7 (5–9)	7 (5–9)
Maximum cardiovascular Sequential Organ Failure Assessment score	4 (2–4)	4 (0–4)
Cumulative fluid loading, mL/kg	39 (25–62)	35 (14–53)
Cumulative blood cell transfusion, no.	0 (0–3)	0 (0–2)
Urine output, mL/hr[a]	94 (75–122)	93 (79–123)
Maximum plasma glucose, mmol/L	8.3 (7.1–9.6)	9.0 (7.8–10.9)[b]
Patients with insulin, no.	15 (31%)	17 (35%)
During the 28-day follow-up		
Intensive care unit duration of stay, days	8 (4–17)	4 (1–10)
Duration of mechanical ventilation, days	4 (1–10)	2 (1–10)
Duration of norepinephrine support, days	2 (1–4)	2 (1–3)
28-day mortality, no.	6 (12%)	6 (13%)

[a]Eighteen missing values; [b]$p < .05$ vs. control.

Data are median (25th–75th interquartile range) or number (%), unless otherwise specified.

in the ICU and requiring RSI with etomidate. Therefore, this study cannot be considered representative of all clinical situations potentially requiring etomidate, in particular septic shock poorly responsive to fluid and vasopressor resuscitation. Second, hydrocortisone supplementation started at H6 to allow time for hormonal tests, i.e., random cortisol and CST at H5. Whether supplementation given together with etomidate, i.e., at H0, would affect the present results warrants further investigation. However, considering the short duration of the hormonal blockade, any benefit of an immediate substitution seems unlikely. Third, although we administered moderate-dose hydrocortisone at currently recommended doses (200–240 mg/day) (27), we found a progressive decline in serum cortisol in the treated group between H12 and H48. This is partly explained by the bolus effect of hydrocortisone given at H6 followed by smaller infused doses over the following hours. A progressive inhibition of the adrenocorticotropic hormone synthesis secondary to hydrocortisone infusion might be also possible.

In conclusion, critically ill patients without septic shock did not benefit from hydrocortisone administered to overcome etomidate-related adrenal insufficiency. No major effects on hemodynamic status were found in the treated group. These findings suggest that single-dose etomidate could be considered in critically ill patients undergoing RSI in the field or in the emergency room without major concerns about its drug-induced hormonal derangement.

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