



SEPTIC SHOCK AND ROLE OF LOW DOSE CORTICOSTEROIDS IN REFRACTORY SEPTIC SHOCK

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ABSTRACT **OBJECTIVE:** Whether low dose hydrocortisone therapy decreased the duration of vasopressor therapy and decrease the mortality in patients with refractory septic shock. **MATERIAL AND METHODS:** A prospective observational study was conducted over a period of 15 months in tertiary care Hospital enrolling 104 patients as per the inclusion criteria They were started on Inj. Hydrocortisone 50 mg IV 6 hourly. **RESULTS:** Out of the total 104 patients 43.27% of patients have shown recovery as compared to 33.65% patients who expired. Survivors have significantly less time of shock reversal as compared to non-survivors (30 hours vs 80 hours). APACHE-II score in survivors at 48 hr is 19.40±5.28 SD in comparison to non-survivors i.e. 37.00±5.35 SD indicating APACHE – II score as an important predictor for outcome in severe sepsis. **CONCLUSION:** It was concluded that low dose hydrocortisone therapy decreased the duration of vasopressor therapy by decreasing the time of shock hours and it decreased the mortality in patients with refractory septic shock.

KEYWORDS : Hydrocortisone , Multiorgan failure , Shock , Vasopressor therapy

INTRODUCTION-

Despite recent advancement in the management of sepsis, the mortality associated with severe sepsis remains high. Role of steroids in septic shock remains always a controversial issue. This issue has come to the forefront again with two recent major trials, the French study by Annane et al. [1] and the CORTICUS study [2, 3, 4] reporting conflicting results. In keeping with the recent developments, we aimed to assess the current situation related to the role of steroids in refractory septic shock.

MATERIALS AND METHODS

DURATION OF STUDY:

The study was conducted over a period of 15 months

Source of Data: A prospective observational study was conducted over a period of 15 months in Tertiary care Hospital in Punjab state where patients admitted to MEDICINE wards/ICU's were studied. Total number of patients included in the study is 104.

For selection process criterias are as defined below:

INCLUSION CRITERIA:

1. Within 24 hrs of diagnosis of septic shock as evidenced by
 - A. systemic inflammatory response syndrome criteria
 - B. Evidence for nidus of infection (Proven or suspected infectious etiology)
 - C. Arterial blood pressure <90 mm Hg systolic or 40 mm Hg less than patient's normal blood pressure after fluid resuscitation for at least for 1 hour or need for vasopressors to maintain systolic blood pressure >90 mm Hg.
2. Patients age >18 years with diagnosis of refractory septic shock (septic shock that lasts for than one hour and does not respond to fluid and pressor administration.)

EXCLUSION CRITERIA

1. Age < 18 years,
2. Patients on exogenous steroids for more than 3 weeks,
3. Patients on chemotherapeutic agents, Immune compromised patients – Malignancy, HIV, Rheumatological diseases, Organ transplant recipients,
4. Patients who refuse to participate in the study,
5. Pregnant patients.

Study drug

Drug: Inj. Hydrocortisone (50 mg) IV 6 hourly

All patients were evaluated in detail. At the time of enrollment, the data regarding general characteristics and severity of illness [assessed by acute physiology and chronic health evaluation II (APACHE II)] were assessed. Fluid status (CVP) and total amount of fluid received was also recorded. BP and CVP monitoring was done regularly. Duration of vasopressor requirement was noted. All patients were evaluated for 5 days after inclusion in the study.

Statistical Analysis done using P value.

OBSERVATIONS & RESULTS

The baseline demographic characteristics and various parameters of recovery of patients were evaluated. All patients included in the study were in the age group from 18-85 years. Maximum number of patients, 29 (27.88%) were in the age group of 56-65 years followed by age group 46-55 years (22.12%). Mean age of the patients in the study was 55.3 years ± 16.81 years. It has been observed that out of total 104 patients, 60 patients (57.69%) were males and 44 patients (42.31%) were females. Outcome of patients according to gender can be seen in table 1

TABLE 1 OUTCOME OF PATIENTS ACCORDING TO GENDER

Outcome	Males(n=60)	Females(n=44)
Recovered	24(40.00%)	21(47.73%)
Expired	22(36.67%)	13(29.54%)
DAMA	14(23.33%)	10(22.73%)

Urinary tract was the major source of infection in 63 patients (60.58%) followed by respiratory tract in 43 patients (41.35% of total infection sources), follow by GIT in 11 (10.57%) patients, then Soft tissue in 10 (9.62%) of patients and 1 patient (0.96%) each had CNS and CRBSI. Blood culture was positive in 32 patients. Out of these 32 patients, 10 patients (31.25%) had S. Aureus growth in blood culture (9.61% of total 104 patients). 8 patients (25%) each showed growth of E. Coli and Klebsiella in blood culture (it is 7.69% of total 104 patients). 3 patients (9.3%) had A. Baumannii growth in blood culture (2.88% of total patients), 1 patient (3.13%) each had Enterococcus, Pseudomonas and Candida growth in blood culture respectively (0.96% of total 104 patients). Blood culture was negative in 72 patients (69.23%).

Organisms found in blood culture can be seen in table 2

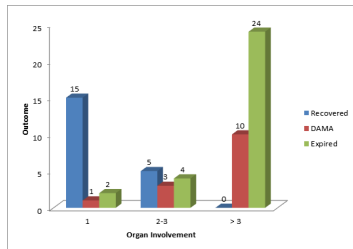
Sr. No.	Number(N=32)	Culture positive %age(N=32)	TOTAL (N=104)
1.	3	9.3	2.88
2.	1	3.13	0.96
3.	8	25	7.69
4.	1	3.13	0.96
5.	8	25	7.69
6.	10	31.25	9.61
7.	1	3.13	0.96

Out of the total 104 patients, 64 (61.54%) patients were having multiorgan failure. 40 patients [38.46%] didn't have multiorgan involvement.

Out of 64 patients with MOFS, 18 patients had single organ

involvement, 12 patients had 2-3 organs involvement, 34 patients were having more than 3 organs involvement. None of these patients recovered. 24 patients expired (70.58%). It can be seen figure 1

FIGURE –1 OUTCOME IN RELATION TO ORGAN INVOLVEMENT IN PATIENTS WITH MOFS (n=64)



Out of the total 104 patients, 45 (43.27%) patients recovered (23.08%), 24 patients took DAMA and 35 patients (33.65%) expired.

Out of the total 45 recovered patients, 16 (35.56%) patients recovered within 24 hours followed by 20 (44.44%) patients at 36 hours and 5 (11.11%) at 48 hours.

Total 41 (91.11%) patients recovered within 48 hours and 4 (8.89%) patients took >48 hours for recovery from shock.

Mean APACHE score in recovered patients at 0, 24 and 48 hours was 27.13 ± 5.61 , 22.78 ± 5.83 and 19.40 ± 5.28 respectively with a p-value of 0.007 (0hrs vs 24hrs), 0.001 (0hrs vs 48 hrs) and 0.009 (24hrs vs 48hrs) which is statistically significant.

Mean APACHE score in expired patients at 0, 24 and 48 hours was 30.37 ± 5.51 , 33.69 ± 6.04 and 37.00 ± 5.35 respectively with a p-value of 0.041 (0hrs vs 24hrs), 0.005 (0hrs vs 48 hrs) and 0.040 (24hrs vs 48hrs) which is statistically significant.

DISCUSSION

Sepsis and septic shock continues to be major cause of morbidity and mortality. Possible therapeutic role of corticosteroids in severe infections have existed for at least 50 years [5-6]. The major theoretical purpose of corticosteroids in sepsis is to restore balance to the altered HPA axis with the goal of improved outcomes such as mortality.

In view of limited data we studied the effect of low dose hydrocortisone on survival and mortality in patients with refractory septic shock.

All patients included in the study were in the age group from 18-85 years. Maximum number of patients, 29 (27.88%) were in the age group of 56-65 years followed by age group 46-55 years (22.12%). The age distribution is comparable to the previous study done by Briegel J et al. [7]

Out of the total 104 patients, 60 patients (57.69%) were males and 44 patients (42.31%) were females. In male patients out of 60 patients 24 recovered (40%), 22 expired (36.66%) and 14 were DAMA (23.33%). In females out of total 44 patients, 21 recovered (47.72%), 13 expired (29.54%) and 10 were DAMA (22.72%). So in our study it has been observed that male patients have higher mortality as compared to female patients.

In total 104 patients, there were total 129 sources of infection identified with some patients having multiple sources of infection.

Urinary tract was the major source of infection in 63 patients (60.58%) followed by respiratory tract in 43 patients (41.35%). GIT in 11 (10.57%) patients then Soft tissue in 10 (9.62%) of patients. 1 patient (0.96%) each had CNS and CRBSI as source of infection

This is comparable to the previous studies by various authors which concluded that the lung is the primary source of infection both in severe sepsis and in septic shock, followed by the abdomen, the urinary tract, soft tissues and primary blood stream infection (Annane et al, 2003) [8]

In our study, blood culture was positive in 32 (30.76%) patients. Out of these 32 patients 31.25% had S. Aureus growth, 25% each showed

growth of E. Coli and Klebsiella. 9.3% had Acinetobacter Baumannii growth in blood culture (2.88% of total patients). 3.13% each had Enterococcus, Pseudomonas and Candida growth in blood culture respectively. Blood culture was negative in 72 patients (69.23%). However, Gram-positive microorganisms have become the most common microorganisms isolated in the more recent studies (Bloch KC et al) [9]. This data is being reflected in the present study.

In our study, out of 104 patients, 64 (61.54%) patients had MOFS and 40 (38.46%) patients were without MOFS. Among 64 patients with MOFS, 30 patients (46.87%) got expired as compared to 40 patients without MOFS where number of patients expired was 5 (12.5%).

MOFS became the main cause of death in ICUs, and, since the first studies which described this entity during the 1970s, mortality remains almost the same, in spite of all the research in laboratories and ICUs. The mortality of ICU septic patients ranges from 20% to 60%.

- In our study, on comparing the time of shock reversal in survivors have significantly less time (30 hours vs 80 hours) of shock reversal indicating increased severity of septic shock in non-survivors.

Out of the total 45 recovered patients, 41 (91.11%) patients showed recovery within 48 hours as compared to only 11 (31.43%) patients out of the total 35 expired patients with a p-value of 0.001 which is statistically significant.

This is in consistency with Corticus study, in which shock reverted in hydrocortisone group in 3.3 days vs 5.8 days in placebo group indicating early shock reversal in hydrocortisone group.

In the present study, it was found that low dose hydrocortisone therapy decreased the duration of vasopressor therapy by decreasing the time of shock hours and decreasing the mortality.

According to French trial, which is a multicentre, double-blind trial conducted in France including 300 patients, hydrocortisone administration leads to faster shock reversal (57% vs 40%) and decreased 28 day mortality (55% vs 61%) in patients with severe sepsis & shock.

The difference in survival benefit in our study could be due to difference in inclusion criteria and patient profile in the above studies and due to different severity of septic shock.

CONCLUSIONS

In the present study, it was concluded that low dose hydrocortisone therapy decreased the duration of vasopressor therapy by decreasing the time of shock hours and it decreased the mortality in patients with refractory septic shock.

Conflicts of interest - None

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