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Efficacy of blood purification therapy for heat stroke presenting rapid progress of multiple organ dysfunction syndrome: a comparison of five cases

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Abstract Five patients were admitted to our hospital because of classical heat stroke during the heat waves which attacked our country in the summers 1994 and 1995. The clinical and laboratory findings of all patients suggested the rapid progress of multiple organ dysfunction syndrome (MODS). Blood purification (BP) therapy, in addition to conventional treatment, was performed in three of the patients. Despite their disastrous general condition, all completely recovered or recovered sufficiently to be transferred to a rehabilitation hospital. Two additional patients were treated with conventional treatment only and both died in 1–3 days after admission.Clinical characteristics and laboratory findings on admission showed no differences between the cases receiving BP therapy and those not receiving BP therapy. These findings suggest that, in heat stroke patients, additional BP therapy may provide a better prognosis than conventional therapy only. These beneficial effects of BP may have been due mainly to the removal of proinflammatory cytokines related to heat stroke.

Key words Heat stroke · Multiple organ dysfunction syndrome · Blood purification therapy · Continuous venovenous hemofiltration · Plasma exchange

Introduction

Heat stroke is a true medical emergency which may result in widespread organ system dysfunction and failure, with a potentially high mortality rate [1]. Environmental factors such as heat and humidity are important causes of heat stroke, and climatic heat waves have increased its incidence [2].

The mortality rate of heat stroke ranges from 17 to 70 % [3]. It has been suggested that prompt recognition and treatment by immediate cooling and supportive measures greatly reduce its high mortality, and more understanding of its causes makes the catastrophe of heat stroke preventable. However, the underlying mechanism(s) of the progression to multiple organ damage and death, the course in some heat stroke cases, has not been fully understood [4]. And there has been no suggestion as to the management of the condition when widespread organ system dysfunction occurs.

We had five heat stroke patients presenting rapid progress of multiple organ dysfunction syndrome (MODS) during intense heat waves in the summers of 1994 and 1995. Blood purification (BP) therapy was performed in three of them. We evaluated the efficacy of additional BP therapy by comparing it with conventional treatment for heat stroke accompanied by MODS.

Case reports

We retrospectively reviewed five patients admitted to our hospital because of classical heat stroke during the heat waves in the summers 1994 and 1995. Heat stroke was diagnosed on the basis of the presence of neurological disturbances, elevated body temperature (usually higher than 40 °C but there is no absolute cut off), and the patient's current history of exposure to heat stress. We record-

Table 1 Clinical caracteristics and laboratory findings on admission, and therapy and outcome in five patients with heat stroke

Case number	1	2	3	4	5
Age (years)	69	45	41	58	72
Sex	Female	Male	Male	Male	Female
Underlying disease	–	Schizophrenia	Deaf and mute	Alcholic liver injury	–
Glasgow Coma Scale	6	4	6	4	10
Axillary temperature (°C)	42.3	39.3	41.3	40.8	38.8
Blood pressure (mm Hg)	80/40	68/40	70/30	60/40	108/70
Respiratory rate (/min)	30	56	32	52	36
Duration of coma (h)	36	3	16	72	0.5
Duration of hyperthermia (h)	7	1.5	7	4	2
Pulse rate (/min)	104	166	120	150	102
Hematology					
WBC (/mm^3)	4,800	16,000	2,100	18,500	6,500
HT (%)	38.9	50.2	38.5	45.1	40.4
PLT ($\times 10^4$/mm^3)	24.1	21.9	14.2	31.9	19.8
Blood chemistry					
GOT (IU/l)	24	73	18	86	49
GPT (IU/l)	22	23	21	24	28
LDH (IU/l)	593	623	483	815	600
CPK (IU/l)	163	1,007	211	619	239
T-Bil (mg/dl)	0.8	0.4	0.3	3.5	1.3
BUN (mg/dl)	33.6	14.4	15.9	9.3	11
Cr (mg/dl)	1.0	2.2	1.4	2.7	1.7
K (mEq/l)	5.3	5.1	4.3	4.2	3.7
Arterial blood gas					
PO_2 (mm Hg)	54.4	142.4	71.1	82.3	63.5
PCO_2 (mm Hg)	26.4	16.4	16.2	49.4	21.5
HCO_3 (mEq/l)	18.8	9.6	11.9	15.5	14.1
PH	7.46	7.38	7.48	7.13	7.43
APACHE II score	25	33	20	38	17
Therapy	Conventional only	Conventional only	Conventional and CHF+PE	Conventional and CHF+PE	Conventional and CHF
Outcome	Death	Death	Survival	Survival	Survival

ed axillary rather than rectal temperature, as is customary for patients on admission to our hospital.

The patients' baseline characteristics, laboratory findings, therapy and outcome are summarized in the Table. All patients were sent to our institute and received emergency treatment within 2 h of the condition's onset. On admission, all patients except case 5 were unconscious, and had Glasgow Coma Scale scores of 4–6. In all cases, examination of vital signs in the emergency room revealed tachypnea, tachycardia and hyperthermia. Four of the five patients underwent intravenous fluid and dopamine administration but remained in shock. Three of five patients had a temperature of above 40 °C by axilla and the remaining two around 39.0 °C. The cooling time required to reduce the axillary temperature to 37.9 °C was 7 h or less in all cases.

The initial laboratory findings were as follows: complete blood cell count showed leukocytosis in cases 2 and 4, and leukocytopenia in case 3. C-reactive protein (CRP) was not increased in any cases. Serum enzymes at the time of admission were not unusual in any of the cases. Increased serum creatinine concentrations ranging from 1.4 to 2.7 mg/dl (normal range, 0.45–0.95 mg/dl) were present in four patients. Bililubin concentration was increased only in case 4. Arterial blood gas analysis showed low bicarbonate levels in all cases.

In this hospital, as a rule, a substantial number of patients to receive blood purification (BP) therapy are referred to our section of nephrology, where this therapy is provided. The progress of MODS, indicated in all cases, is commonly estimated as follows: neurological failure GCS of 6 or less. The presence of respiratory failure is indicated by the requirement for ventilation, and hepatic and renal failure are assumed based on the elevation of serum bilirubin and creatinine concentration, respectively. An approximate estimate of the occurrence and degree of cardiovascular and hematological failure are made based on the need for inotropes to support arterial pressure and the decreasing platelet count, respectively. With regard to subsequent laboratory findings, platelet count showed a decreasing tendency (3.3–4.1 $\times 10^4$/mm^3) in all cases; serum creatinine concentration was markedly increased in cases 2 and 5 (4.7 and 4.3 mg/dl, respectively); and bilirubin concentration

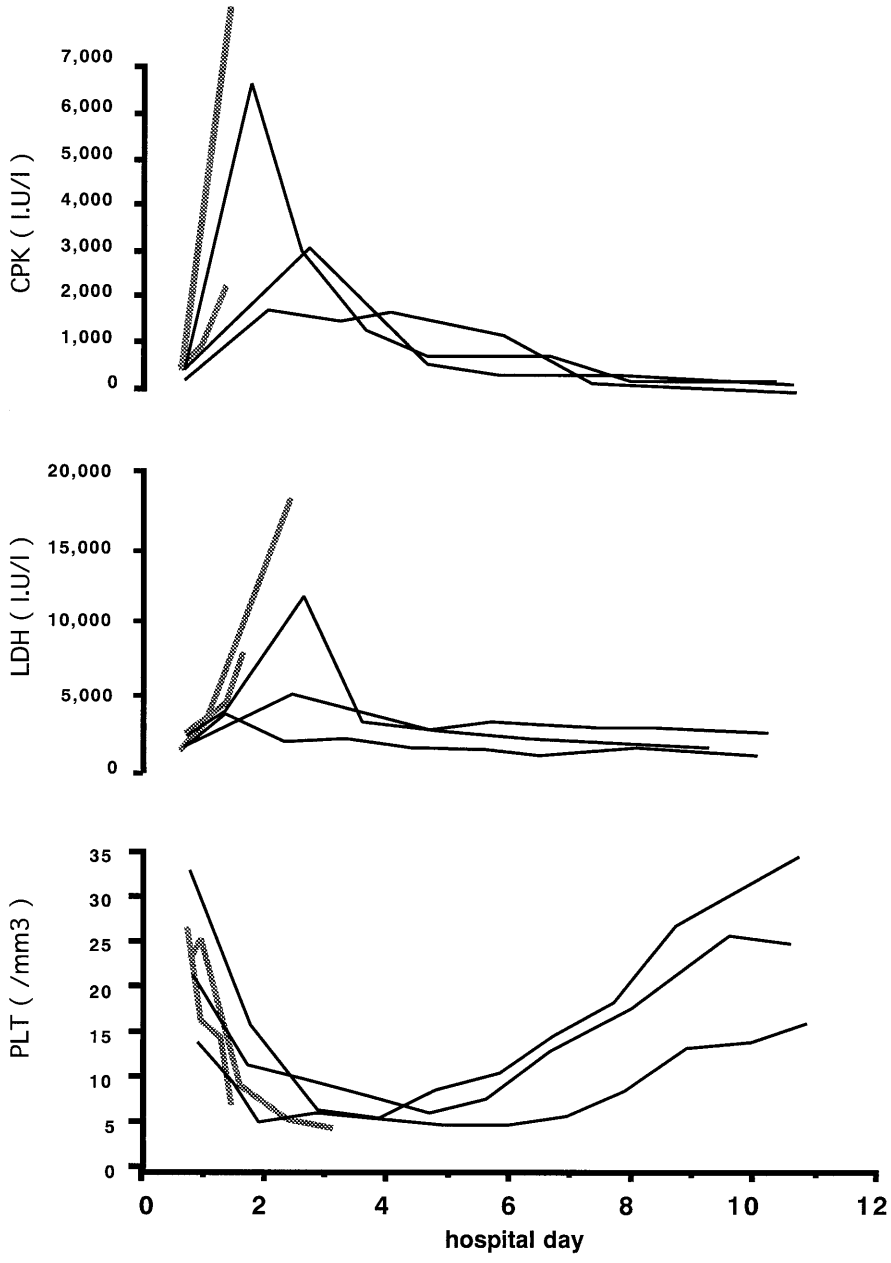

Fig. 1 Changes in blood level of LDH, CPK and PLT in each patient; *black lines* show changes in three patients receiving BP therapy and *gray lines* show those in two patients not receiving BP therapy

was increased to over 5.0 mg/dl in cases 2, 3, and 4. Cases 1 and 3 were each placed on a ventilator because of the progression of hypoxia. Thus, all patients satisfied at least two of the above-mentioned criteria within 12 h of admission.

All patients received conventional treatments (cooling, protection of the airway or intubation, and intravenous fluids) immediately after admission. Following conventional treatment, however, two of these patients (cases 1 and 2) were not referred to our section. These patients were treated with conventional therapy only, whereas the remaining patients (cases 3, 4, and 5), who were referred to our section, received BP therapy in addition to conventional treatment.

BP therapy included continuous venovenous hemofiltration (CHF) and plasma exchange (PE). CHF with polyacrylonitrile hemofilter (APF-06S; Asahi Medical, Japan) and bicarbonate dialysate (Sublood-B, Fuso, Japan) at a flow rate of 500 ml/h was started in these three cases within 12 h of admission, and was performed continuously for 3 (case 5) to 7 (cases 3 and 4) days. Cases 3 and 4 additionally received PE with 40 units of fresh frozen plasma for each exchange of 3 hours three times on the 2nd, 3rd, and 4th hospital days.

Despite vigorous therapy, both of the two patients not receiving BP remained in shock and died on the 2nd and 4th hospital days, respectively. In contrast, vital signs and laboratory findings of all of the three patients receiving BP gradually improved, and eventually they recovered completely or recovered sufficiently to be transferred to a rehabilitation hospital. The complications of heat stroke were found in only one of the patients who survived; that is

secondary dementia due to hypoxic encephalopathy (case 3). No complications of BP therapy were found in any of the cases.

Discussion

In patients with heat stroke, the duration of coma, duration of high temperature, rapidity of cooling, preexisting disease and predisposing factors provide a guide to prognosis [1]. Several biochemical changes in the first 24 h, including concentrations of serum transaminases, lactate dehydrogenase (LDH) and creatine phosphokinase (CPK), are also useful in determining the prognosis [5].

In our cases, the clinical characteristics and laboratory findings on admission were comparable between the cases receiving BP therapy and those not receiving it, although case 5 appeared to be less severely ill than the other patients. The severity of illness indices calculated by APACHE II score [6] varied among the cases from 17 to 38. But differences in APACHE II score were not reflected between these two groups in regard to the efficacy of therapy. Changes in blood levels of LDH, CPK and platelet (PLT) are shown in the Figure. These changes also did not differ between the two groups within at least 24 h of admission.

Thus clinical and laboratory findings were similar in our two groups of heat stroke patients. In each case, BP therapy was selected according not to the case's severity but according to recognition of the indications for BP by the patient's physician. All three patients receiving BP survived and both the two patients who had not received BP died. These findings suggest that, in heat stroke patients, additional BP therapy may provide better prognoses than conventional therapy.

In heat stroke, immediate cooling is reported to reduce the mortality rate. However, the extracorporeal cooling accompanied by BP therapy in our patients may not contribute to a better prognosis, because body temperatures were similarly decreased to less than 38.0 °C within 7 h of admission in both groups, irrespective of receiving BP therapy. These findings suggest that mechanisms other than the cooling produced by BP therapy may be involved in exerting a beneficial effect on patients receiving this therapy.

In sepsis, many patients develop MODS. Increased circulating concentrations of proinflammatory cytokines, such as tumor necrosis factor-alpha and interleukin-1, have been correlated with a poor outcome in these cases [4]. Current studies have demonstrated that the removal of these cytokines by (continuous) hemodiafiltration has a potential to improve the patient's clinical course [7, 8]. PE has also been studied in a smaller series of patients with such a condition, and its beneficial effect was reported [9].

Heat stroke resembles sepsis in many aspects, and there is some evidence that endotoxemia and cytokines may be implicated in its pathogenesis [4]. On the basis of these reports, the improvement of the clinical conditions of our patients receiving BP may have been mainly due to removal of the proinflammatory cytokines related to heat stroke. Unfortunately, we could not investigate the removal of proinflammatory cytokines by BP before and after the therapy because none of the blood samples were recovered to make such a comparison. However, the increase of enzymes (i.e., LDH or CPK) offering an approximation of organ damage and the decrease of PLT suggesting coagulopathy gradually improved 24 h after admission in the BP group (Fig. 1). These findings indicate the probability of the effective removal of proinflammatory cytokines by CHF or PE. Our cases are too few in number for BP therapy to be generally accepted as the most beneficial therapy for heat stroke, but may invite further investigation of the use of BP therapy in such cases.

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