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Original Article

Changing of serum metabolic hormone and liver size during acute phase of severe adult burn patients

Lam N Nguyen[1,2*], Khanh Q Phan[3*], An H Nguyen[1,2*]

[1]National Burn Hospital, Hanoi, Viet Nam; [2]Medical Military University, Viet Nam; [3]Region 4 Medical Military Hospital, Viet Nam. [*]Equal contributors.

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Abstract: The aims of this study were to determine characteristics and factors influencing metabolic hormones including serum catecholamines, cortisol level and liver size in severe adult burn patients. A prospective study was conducted on 44 adult burn patients with burn extent from and over 20% TBSA admitted during 72 h after burn to burn intensive care unit, National Burn Hospital, Vietnam. Serum levels of epinephrine, norepinephrine and cortisol were measured on admission and 7th day after burn. Liver size was measured by ultrasound on admission and 21st day after burn. The results indicated that norepinephrine level did not significantly change along the time meanwhile epinephrine concentration significantly increased after 1 week ($P < 0.01$). Serum cortisol level was higher than normal physiological value and then significantly reduced at 7th day post burn ($P < 0.05$). Significantly increased liver size was seen at the 21st day postburn ($P < 0.01$). Age, gender, burn severity, inhalation injury and death did not affect concentration of catecholamines and liver size. Meanwhile, cortisol level was significantly higher in patients with deep burn area ≥ 20% TBSA at 7th day after burn and in non-survivors ($P < 0.05$). Further studies are necessary to understand clearly metabolic state in severe adult burn patients.

Keywords: Metabolic hormones, liver size, adult burn patients

Introduction

Recently, burn outcomes have been significantly improved based on advances in fluid resuscitation, wound care and surgery, infection control and better nutritional support [1]. Hypermetabolic response following burn injury is considered as highest level in compared with any types of trauma and diseases [2-4]. This state is associated with elevations in cardiac output, increased release of metabolic hormone, cytokines and others resulting in increased energy expenditure, muscle wasting and loss of lean body mass, impairing immune function, prolonging wound healing, increased complications and mortality [5, 6].

Mechanism of hypermetabolic response after burn is complicated and not yet fully understood. Studies on mechanisms of metabolic hormones and inflammatory and organ dysregulation are still being conducted [7-10]. The hypermetabolic state was well reported and played a significant role in burn pediatric patient [11, 12].

It is clear that, with mature visceral organs, psychological, physiological, biochemical, endocrine, and immune functions are complete in adults. Due to such characteristics, the metabolic response and organ disorder after burns in adults may be different from that of children, who often have a stronger response to stimuli including burn injuries. To date, limited reports have been mentioned about the characteristics of metabolic state in adult burn patients. Numerous studies have been conducted with inconsistent results. To our best knowledge, the largest study on adult metabolic states after burn was conducted by Stanojcic and colleagues in 2018 focusing on inflammatory markers, glucose and lipid metabolism, organ function, and clinical outcomes but did not determine plasma levels of metabolic hormones [13].

In this study, we determined features and factors which influence serum level of metabolic hormones including catecholamines and cortisol and changes of liver size in severe adult burn patients.

Table 1. Patient characteristics

Criteria	Subgroup	Mean	Min-max
Gender, n (%)	Male	35 (79.5)	
	Female	9 (20.5)	
Age, year	Mean	34.3 ± 9.8	19-53
	16-39	30 (68.2)	
	40-60	14 (31.4)	
Admission time after burn, h		7.4 ± 8.1	1-50
Burn extent, % TBSA	Mean	52.5 ± 17.5	20-95
	20-59	32 (72.7)	
	≥ 60	12 (27.3)	
Full thickness area, % TBSA	Mean	19.3 ± 17.2	0-69
	< 20%	29 (65.9)	
	≥ 20%	15 (34.1)	
Inhalation injury, n (%)	Yes	5 (11.4)	
	No	39 (88.6)	
Death, n (%)	Yes	7 (15.9)	
	No	37 (84.1)	

Patients and methods

A prospective study was conducted on 44 severe adult burn patients admitted to intensive care unit, National Burn Hospital, Vietnam during a period from June 2016 to June 2017.

Inclusive and exclusive criteria

Studied patients were selected with following criteria: admitted during 72 hours after burn, age from 16 to 60 year old, burn extent from and over 20% total body surface are (TBSA). All patients under 16 or over 60 year old and patients with concomitant trauma, comorbidity, pregnancy or admitted later 72 hours after burn or died before 72 hours post burn were excluded from this study.

Treatment standard

All patients in this study received the same management regime. Standard treatment included early excision and grafting with auto and allo-skin grafts. Enteral feeding was applied within 24 h of admission.

Sample collection and processing

In order to determine the serum level of metabolic hormone, blood samples were taken on the day of admission and day 7 after burn. Accordingly, 5 ml of blood was collected from central venous catheters, then transferred to the laboratory for processing: it was centrifuged, aspirated and stored at -70°C. Serum levels of epinephrine, norepinephrine and cortisol were measured using the enzyme linked immunosorbent assay (ELISA) method. Liver size was measured by ultrasound which was conducted on admission and 21st day after burn on 26 patients without deep burn at upper abdominal area.

Statistical analysis

Data were collected, tabulated and analyzed with t test or Chi square to find to find down the influence of age, gender, burn extent and inhalation injury on metabolic hormone and liver size by using Stata software version 14.0, with p value < 0.05 regarded as the significant level. Normal physiological epinephrine, cortisol levels (volunteers without any trauma or disease) reported in Mosby's Diagnostic & Laboratory Test Reference were used as references [14]. This study was approved by the hospital's Committee for human research ethics.

Results

Patient demographic and outcomes

Demographic parameters and outcome of patients are showed in **Table 1**. As can be seen, males were predominance and 68.2% of patients was less than 40 year of age with average burn extent of 52.5 ± 17.5% total body surface area (TBSA) and mean of deep burn of 19.3 ± 17.2% TBSA. Inhalation injury was diagnosed in 5 (11.4%) patients. Overall mortality rate was 15.9%.

Changing of serum metabolic hormone and liver size

On admission, serum levels of catecholamine, liver size were in normal physiological value. Meanwhile, serum cortisol level was higher than normal physiological value. After one week, epinephrine concentration increased significantly from 82.8 ± 71.3 ng/l to 166.5 ± 90.1 pg/ml (P < 0.01) meanwhile, norepinephrine level did not change (P > 0.05). In contrary, cortisol level significantly reduced from 328.4 ± 133.4 to 249.7 ± 100 ng/ml (P < 0.05), but

Table 2. Plasma level of metabolic hormone along the time

Criteria	Admission	7th day after burn	p
Epinephrine, pg/ml	82.8 ± 71.3	166.5 ± 90.1	0.001
Norepinephrine, pg/ml	817.5 ± 1149.8	870.4 ± 721.9	0.69
Cortisol, ng/ml	328.4 ± 133.4	249.7 ± 100	0.001
Right liver, mm	134.9 ± 13.8	144.4 ± 10.9	0.001
Left liver, mm	73.6 ± 7.7	82 ± 6.8	0.001

was still higher than normal physiological value. It is noted that, significant increase of liver size after 21 days post burn ($P < 0.01$) was recorded (**Table 2**).

Factors influencing serum level of metabolic hormone and liver size

Plasma cortisol level was only significantly higher than in patients with deep burn area ≥ 20% TBSA ($P < 0.05$) on admission. Liver size and serum catecholamine were not remarkable difference among subgroups of age, gender and burn severity at difference time points (**Tables 3**-**5**). In addition, catecholamine levels were not difference between survivors and non-survivors. Meanwhile, plasma cortisol level was remarkably higher than in non-survivors (368.2 ± 150.2 vs. 227.3 ± 70.2 ng/ml; $P < 0.05$) at 7th day after burn (**Table 6**).

Discussion

Burn injury is considered as event with the highest metabolic response as compared to any types of trauma and critically ill patients. Hypothalamic function alterations due to burn injury, resulting in increased systemic catecholamine are associated with stress, inflammation, hypermetabolism, and impaired immune function [15, 16].

It is noted that hypermetabolic state in pediatric burns is well recognized by many reports [17-19]. Jeschke et al., showed that morbidity and mortality in childhood patients was burn size dependent, starts at a 60% TBSA burn and is due to an increased hypermetabolic and inflammatory reaction, along with impaired cardiac function and serum cortisol significantly increased immediately postburn and remained elevated for 3 weeks before returning to normal levels [20]. Reports from other studies indicated that urinary levels of cortisol, epinephrine, and norepinephrine were significantly increased after a major burn. Urine cortisol increased 5-7 fold during the critical phase, then decreased along the time. In addition, the urine cortisol level was the highest in patients with burn extent ≥ 60% TBSA, and associated with significant myocardial depression and increased change in liver size [21]. Kulp and coworkers studied on 413 pediatric burn patients and compared with healthy normal volunteer found that catecholamine levels were consistently and significantly changed postburn. Catecholamine levels were significantly higher in boys and non-survivor, correlated with burn size greater than 40% TBSA, and were increased in older children [22]. In addition, Norbury and colleagues studied on 212 children with burns greater than 40% TBSA found that urinary cortisol level were significantly increased (3 to 5 folds) up to 100 days after burn. The urine cortisol concentration was significantly higher in male than female patients. Significantly increased urinary catecholamines levels were determined at 11-20 days after the burn. Meanwhile urinary norepinephrine levels were significantly increased up to 20 days [23]. In another study by Jeschke and coworkers on 230 children with burns exceeding 30% TBSA, requiring at least 1 surgical procedure showed that non-survivors experienced more severe hypermetabolic response as compared with that in survivors [24].

In adult burn patients, Hanz and coworkers, determined concentration of blood catecholamine in 30 severe burn patients with mean burn area of 58.6% TBSA found that catecholamine release was persistent in severe burn patients showing two peaks in shock period and infection period. The quantity of epinephrine was normal, while norepinephrine was persistently high and it was over two fold of the normal value [25]. In other study conducted by Stanojcic and colleagues on 1288 adult burn patients, significantly increased inflammatory cytokines, chemokines, and metabolic hormones were observed with time and burn size dependent. It is also noted that patients with medium burn (20% to 40% TBSA) revealed a very strong response similar to large burns [13]. Our results show that on the 7th day after burn, serum epinephrine concentration was significantly higher than normal physiological value

Table 3. Influence of age, gender on metabolic hormone and liver size

Criteria	Time point	Age		p	Gender		p
		16-39	40-60		Male	Female	
Epinephrine, pg/ml	Admission	84.7 ± 76.4	78.6 ± 61.6	0.79	81.2 ± 74.2	88.8 ± 62.7	0.78
	7th day	172.7 ± 97.7	153.3 ± 74.7	0.51	161.6 ± 92.6	185.5 ± 84.6	0.48
Norepinephrine, pg/ml	Admission	856.5 ± 1292.4	733.9 ± 797.4	0.74	824.8 ± 1230.2	789.4 ± 820.5	0.93
	7th day	980.6 ± 794.3	634.3 ± 478.1	0.14	854 ± 718.8	934.3 ± 774.4	0.77
Cortisol, ng/ml	Admission	326 ± 133.7	333.5 ± 137.7	0.86	315.3 ± 140.4	379.5 ± 90.7	0.20
	7th day	252.9 ± 157.3	242.8 ± 45.4	0.75	253.3 ± 102.1	235.6 ± 95.7	0.64
Right liver, mm	Admission	136.5 ± 10.8	134 ± 15.5	0.54	137.1 ± 13.7	129.6 ± 13	0.17
	21st day	144.5 ± 11.7	144.2 ± 10.7	0.93	146.3 ± 11.4	139.6 ± 8.1	0.14
Left liver, mm	Admission	73.6 ± 7.3	72.4 ± 8.4	0.51	73.6 ± 7.3	73.4 ± 9	0.62
	21st day	83.3 ± 6.8	82.1 ± 7	0.75	83.3 ± 6.8	79.1 ± 6.2	0.09

Table 4. Influence of burn extent and deep burn area on metabolic hormone and liver size

Criteria	Time point	Burn extent		p	Deep burn area		p
		20-59%	≥ 60%		< 20%	≥ 20%	
Epinephrine, pg/ml	Admission	819 ± 680.1	1007.5 ± 840.1	0.61	85 ± 83.7	78.4 ± 39.8	0.77
	7th day	791 ± 1169.2	888.2 ± 1143.9	0.43	160.1 ± 95.5	179 ± 81.8	0.51
Norepinephrine, pg/ml	Admission	77.9 ± 64.3	95.6 ± 89.5	0.34	851.4 ± 1359.9	752 ± 595.8	0.78
	7th day	163.2 ± 93.6	175.3 ± 85.3	0.88	827.8 ± 720.5	952.8 ± 742.7	0.59
Cortisol, ng/ml	Admission	333.2 ± 120.7	324.1 ± 146.6	0.82	295.1 ± 130.5	392.7 ± 117.8	0.02
	7th day	222.4 ± 87	274.6 ± 106.3	0.08	232.8 ± 74.8	282.3 ± 133.3	0.12
Right liver, mm	Admission	136.8 ± 14.7	133 ± 7.9	0.97	134.4 ± 12.9	135.1 ± 14.3	0.49
	21st day	145.6 ± 10.6	142 ± 13.8	0.50	141 ± 8.7	145.6 ± 11.5	0.50
Left liver, mm	Admission	73.5 ± 7.5	76.3 ± 10.5	0.73	74.2 ± 10	73.3 ± 6.9	0.28
	21st day	81.5 ± 7.6	80.3 ± 5.9	0.20	81.6 ± 5.1	82.2 ± 7.4	0.95

Table 5. Influence of inhalation injury on plasma metabolic hormone levels

Criteria	Time point	Inhalation injury	Non-inhalation injury	p
Epinephrine, pg/ml	Admission	51.7 ± 5.4	86.7 ± 74.9	0.31
	7th day	149.8 ± 63.4	168.7 ± 93.9	0.67
Norepinephrine, pg/ml	Admission	240.8 ± 74.2	891.5 ± 1202.6	0.23
	7th day	691 ± 462.1	893.4 ± 750	0.56
Cortisol, ng/ml	Admission	379.2 ± 143.1	321.9 ± 132.7	0.37
	7th day	373.9 ± 149.7	333,75 ± 81,60	0.11

Table 6. Relationship between death and level of metabolic hormones

Criteria	Time point	Survivor	Non-survivor	p
Epinephrine, pg/ml	Admission	86.3 ± 77.2	64.2 ± 15.2	0.45
	7th day	168.1 ± 94.6	158.2 ± 70.8	0.79
Norepinephrine, pg/ml	Admission	876.7 ± 240.4	504.3 ± 327.7	0.43
	7th day	854.5 ± 687.5	954.4 ± 943.2	0.54
Cortisol, ng/ml	Admission	319.1 ± 132.2	377.7 ± 139	0.24
	7th day	227.3 ± 70.2	368.2 ± 150.2	0.01

and doubled as compared to that at the time of admission. Meanwhile serum level of norepinephrine at both times (on admission and on the 7th day after burns) were within the limits of normal physiological values. In addition, the serum cortisol concentration at the time of admission was higher than the limit of normal physiological values and notably higher than that on the 7th day post burn. Burn extent and deep burn area significantly affected cortisol level but inhalation injury, age and gender did not. In other words, the increase is not as obvious as other studies in pediatric burn and we believe that

the age difference has affected hormone secretion, children are more sensitive than adults in response to stimuli.

Severe burns cause disorders of many organs including the liver. Some studies suggested that an increase in liver size after a severe burn is due to an increase in the amount of triglycerides in the liver and due to post-burn liver edema. Works of Jeschke and coworkers showed that liver size increased, peaked at 2 weeks after burn (220%) and remained at high levels until discharge. Immediately after burn, the liver length increased by about 1 cm, the liver weight increased from 800 g to 1800 g compared to the estimate. Liver size and weight increased by 126% ± 19% at the second week after burns and prolong to 12 months after burns with increased from 40% to 50% compared with estimated weight [26] Barret et al. studied on 37 patients with fatal burns found 81% of patients who suffered fatty liver. The ratio of liver weight/body weight was 2.1 times higher than that in the control group [27]. Report of Barow and colleagues on 38 patients with severe burn indicated that patients who die after 7 days of burns had an increase in liver size from 142 to 406% and most of the liver gained weight due to fat accumulation [28]. Our results are basically similar to the above studies, the significantly increased liver size was seen at the time of 3rd week after burns in compared with that at admission and the change in liver size after burns did not depend on the burn size, gender and age of the patients.

To date, our study is one of the investigations on factors influencing metabolic state in adult burn patients with uncertain results. However, this study had some limitations. First, our sample size was small with variety of burn extent and deep burn area. In addition, the studied patients were admitted to our hospital at different times and they had been previously managed by other health care facilities with different regimes, which can lead to a different state of the patient at admission. It is necessary to conduct further studies with a greater number of patients to clarify the factors influencing hypermetabolic parameters in adult burn patients.

Conclusion

We have showed that in adult burn patients, apart from norepinephrine, serum epinephrine, cortisol level and liver size significantly increased after burn. Deep burn area significantly affects cortisol level meanwhile age, gender and burn severity do not influence metabolic hormone and liver size. It is necessary to conduct further study on metabolic response in severe adult burn patients.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Nguyen N Lam, National Burn Hospital, 263 Phung Hung, Ha Dong, Ha Noi, Viet Nam. Tel: +84-948-316-869; E-mail: lamnguyenau@yahoo.com

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