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Acute Kidney Injury and Mortality in Patients with Rhabdomyolysis Due to Heat Stroke

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ABSTRACT

Introduction: Heat stroke is a well-known condition among people who live in high climate temperatures. In the city of Mexicali, temperatures above 40° C (104° F) are common during summer time, with constant admissions to the emergency room due to classic heat stroke. Hypotension, polypnea, anuria, coma, respiratory failure and kidney failure, were related to a higher mortality rate.

Methods: This is a prospective observational cohort study of patients during the period of June to August 2018, with heat stroke defined as a central body temperature of 40°c or higher, cognitive impairment and recent exposure to high temperatures, admitted to the Emergency Room of the General Hospital of Mexicali. At arrival, a full medical history was taken and laboratory tests were obtained.

Results: twenty-eight patients were admitted with the confirmed diagnosis of classical heat stroke, with a rectal temperature between 40 to 42.2°C. Of these patients, 13 developed rhabdomyolysis, with CPK levels ranging from 1030 U/l to 18977 U/l. From these 13 patients with rhabdomyolysis, 12 developed AKI (p=0.003). Mortality in the group of patients who developed rhabdomyolysis was greater than those who did not develop rhabdomyolysis.

Conclusion: The development of Rhabdomyolysis is a high-risk factor for acute kidney injury and death.

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INTRODUCTION

Heat stroke is a well-known condition among people who live in communities under extreme climate temperatures, defined as hyperthermia above 40° C (104° F) and an altered neurological state. [1]

When heat stroke occurs during exhausting physical activity or strenuous exercise, it is known as “exertional heat stroke”; while cases of people who develop heat stroke but were not involved in strenuous physical activity are classified as “Classic heat stroke” where impaired thermoregulation and extreme heat are frequently to blame. [1]

Based on a previous study done in Mexicali’s General Hospital, where 78 cases were included, an overall mortality of 34% was observed, demonstrating how serious of a condition this disease can be. In the previously mentioned study, 32 cases were registered during the month of July 2006, when the average temperature was 41.6° C (107° F) with an average humidity of 54.2%[2]. There were three outcomes of these patients according to the Glasgow

Outcome Scale, from the total sample, 44.8% of patients died, 17.2% ended in a vegetative stage or disability and 37.9% had a good recovery[3]. In the city of Mexicali, a northwestern Mexican city that borders the United States' state of California, temperatures can reach up to 49° C or higher in summer, reporting a maximum figure of 52°C in 1995. These extreme temperatures are common during summer time, with constant admissions to the emergency room due to classic heat stroke.[4]

Argaud et al. observed that hypotension, polypnea, anuria, coma, respiratory failure and kidney failure, increased the mortality rate [5]. Being exposed to high climate temperatures can develop physiological adaptations that enhance the loss of endogenous and exogenous body heat in subjects, this is usually observed among construction workers, field workers and homeless people, who commonly live or work in extreme heat conditions without developing heat related diseases[6].

Rhabdomyolysis is a syndrome characterized by the efflux of content from muscle cells to the circulation. Although direct muscle damage persists as the most common cause of rhabdomyolysis, other causes exist such as drugs, toxins, hormonal alterations, malignant hyperthermia, malignant neuroleptic syndrome and of course, heat stroke[7]. In every case, the muscle cell is affected by direct damage to the cell membrane or due to energy depletion, the free ionized calcium then enters the intracellular space, activating proteases and stimulating apoptosis. A production of reactive oxygen species (ROS) is followed by mitochondrial dysfunction and finally, cell death. Edema, ischemia and cellular necrosis cause additional metabolic acidosis, while electrolyte disturbances perpetuate the vicious cycle of cell death. [8]

Acute kidney injury tends to be the most common complication in rhabdomyolysis. It occurs in a wide incidence range of 10 to 55% of cases and is associated with worse outcomes, particularly multiorgan failure. Although, acute kidney injury (AKI) can be present with levels of CPK (Creatine phosphokinase) of 5000U/L when concomitant conditions occur, like sepsis, severe dehydration and acidosis. [9]

In summary, it is important to establish the risk of rhabdomyolysis in patients with heat stroke, as this condition leads to AKI and the mortality rate increases dramatically.

MATERIAL AND METHODS

This is a prospective, observational cohort study of patients during a 3 month period between June and August 2018 *(Table 1)* including patients with confirmed heat stroke diagnosis, defined by a central body temperature above 40°c, altered mental state, and recent exposure to high temperatures admitted to the Emergency Room of the General Hospital of Mexicali. Upon arrival, rectal temperature was registered with a Welch Allyn © Suretemp Plus© electronic thermometer. A full medical history was obtained where possible, and blood tests including complete blood count (CBC), serum electrolytes, Creatinine, Glucose, Urea, liver function test, CPK and coagulation profile were taken. All patients were followed during hospitalization, verifying the maximum levels of CPK and serum creatinine, until discharge or death. Also, ambient temperature and humidity percentage was measured at the time of the admission for each patient. For the purposes of this study, we defined rhabdomyolysis as CPK levels >1000U/L, equivalent to 5 times the highest normal level, and AKI as serum creatinine above 1.5mg/Dl. The computer software Epi Info 7 was used for statistical analysis.

RESULTS

In the 3 months comprising June to August 2018, ambient temperature oscillated between 33 to 46°C, with a mean of 40.6°C, and a mean humidity of 21%. 28 patients were admitted with the diagnosis of heat stroke, with a rectal temperature between 40 to 42.2°C. Of these patients, 13 (46%) developed rhabdomyolysis, in them, CPK levels ranged from 1030 U/l to 18977 U/l, with a mean of 5090 U/l. From these 13 patients with rhabdomyolysis, 12 developed AKI (92%) (OR= 18)(CI 95%; 1.8-177, p=0.003). Mortality in the group of patients who developed rhabdomyolysis was greater than those who did not develop rhabdomyolysis with 11 (90.1%) patients in the first group compared to only 1 patient in the second group (9.09%)(OR= 46)(CI 95% 4.2-526; p<0.001). With these results *(Table 2)* we observed that in patients with heat stroke who developed rhabdomyolysis, the risk of AKI is greater than the risk of those who did not develop rhabdomyolysis, with a higher risk of death as well.

DISCUSSION

Although recent scientific reviews have established a strong correlation between exertional heat stroke and rhabdomyolysis[10], our study in classic heat stroke patients found that almost half of our population developed rhabdomyolysis. The previously mentioned results show a high incidence of rhabdomyolysis in patients with classic heat stroke. Although classic heat stroke is a rare condition in most communities, in our study taking place in a local hospital, 28 patients were admitted with the confirmed diagnosis of heat stroke, in whom almost half developed rhabdomyolysis which proved to be a high risk factor for AKI and death. Because of this, we consider it a matter of the greatest importance to implement measurements to avoid the development of rhabdomyolysis, hopefully limiting the risk of AKI. We expect this work to be a precedent for future studies looking to diminish these conditions.

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Table 1. General characteristics of patients with heat stroke.

Number of patient	Sex	Env temp (°C)	Temp (°C)	GCS	CPK	Creatinine (mg/dL)	AKI	Die
1	M	39	40	5	1161	4.48	YES	YES
2	M	41	40.7	5	10	1.52	NO	NO
3	M	40	40	14	191	1.32	NO	NO
4	M	38	40	3	1030	2.16	YES	YES
5	M	39	40	3	7364	1.98	YES	YES
6	M	40	41	15	2406	1.19	NO	NO
7	M	38	42.2	3	78	1.07	NO	NO
8	M	41	42.2	3	716	1.53	YES	NO
9	F	36	42	3	678	1.36	NO	NO
10	M	38	42	3	625	2.57	YES	NO
11	M	33	40	3	5698	4.38	YES	YES
12	M	42	42.2	8	18977	2.86	YES	YES
13	M	43	40	11	2853	5.86	YES	YES
14	M	46	41	6	690	2.46	YES	NO
15	M	44	42	3	718	1.28	NO	NO
16	M	39	42.2	4	456	1.87	YES	NO
17	M	46	40	9	1724	1.56	YES	NO
18	M	40	40	10	229	1.27	NO	NO
19	M	40	42	13	191	1.57	YES	NO
20	M	37	41	11	7787	1.53	YES	NO
21	M	43	42	7	2982	1.82	YES	YES
22	M	41	42	8	5017	2.11	YES	YES
23	M	41	42	7	782	0.95	NO	NO
24	M	44	42	8	111	1.27	NO	NO
25	M	42	41.7	3	673	1.01	NO	NO
26	M	42	41	3	7031	1.99	YES	YES
27	M	42	42.2	3	311	1.19	NO	YES
28	M	42	41.3	3	2149	5.04	YES	YES

*** Env temp = Enviromental temperature, Temp = temperature, GCS = Glasgow coma scale, CPK = Creatine phosphokinase, AKI = acute kidney injury.**

Table 2. Outcomes

	with rhabdomyolysis	without rhabdomyolysis	OR
	13 (46%)	**15 (54%)**	
AKI	12 (92%)	1 (8%)	18 (p 0.0003)
Deceased	11 (90.1%)	1 (9.09%)	46 (p<0.001)
	***AKI = Acute kidney injury, OR = odds ratio**		