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SNAKE VENOM POISONING IN KINGDOM OF SAUDI ARABIA

(With 3 Tables)

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التسمم بلدغ الثعبان
في المملكة العربية السعودية

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اشتملت هذه الدراسة على عدد ٥٦ حالة من مرضى مصابين بلدغ الثعبان على مدى أربع سنوات بمستشفى الملك خالد بالخرج بالمملكة العربية السعودية. وقد توفي أربعة من المرضى، ثلاثة منهم بسبب الفشل الكلوى والرابع بسبب هبوط حاد في الدورة الدموية، ولقد أثبتت النتائج أن هناك تهتك في الأنسجة وخصوصا الكلوية كما تشير لذلك الزيادة المعنوية في مستويات مصل الدم لكل من البوليا والكرياتينين والبوتاسيوم مصحوبة بنقص معنوى في مستوى الصوديوم ، كما لوحظ إرتفاع جوهرى في مستويات الأنزيمات الناقلة لمجموعة الامين GOT , GPT وأنزيم فوسفوكيناز الكرياتين، ولقد أظهرت نتائج صورة الدم الكاملة وجود أنيميا وزيادة في عدد كرات الدم البيضاء ونشاط في خاصية عدم التجلط كما لوحظ ظهور كل من الدم والهيموجلوبين والألبومين في بول هؤلاء المرضى. ولم يتم عزل أى ميكروبات مرضية من مكان اللدغ.

SUMMARY

A total of fifty six cases, during a four-year period, with various risk factors for a snakebite was clinically screened in King Khalid Hospital, Al-Kharj, Kingdom of Saudi Arabia. Four patients died (8%), three died with renal failure and one died with circulatory collapse. Renal damage as indicated by a significant ($P \leq 0.0001$) increase in serum levels of urea, creatinine and potassium as well as a significant decrease in serum level of sodium were observed. Serum glutamic oxaloacetic transaminase (sGOT), glutamic pyruvic transaminase (sGPT) and creatine phosphokinase were significantly ($P \leq 0.0001$) elevated which are indicative of liver and cardiac damage. Hematological data were indicative of anaemia and leukocytosis and showed anticoagulant activity. Hematuria, hemoglobinuria, myoglobinuria and albuminuria were concurrent in this study. No pathogenic organisms were isolated from fang marks.

INTRODUCTION

Snakebites are serious medical, social and economic problems in many parts of the world, especially in tropical countries. Of the 2500 species of snakes, only onetenth is venomous (STIMSON and ENGEL, 1960). The annual mortality rate from snakebites throughout the world is about 85% in South Asia and less than 1% in Europe (REID, 1961). Echis cartinatus, commonly known as the saw-scaled viper, is the snake of the middle east (MOHAN, 1988). According to WARRELL (1977) this snake probably bites more people than any other species of snakes.

Snake venoms are complex mixture containing peptides or polypeptides, enzymes, glycoproteins, and other substances capable of producing several pharmacologic activities, some of which are deleterious to living organisms (RUSSELL, 1980).

The objective of this study is to report on some effects of snakebites on the biochemical and hematological parameters in serum of 52 patients during a four year period admited to King Khalid Hospital, Al-Kharj, Kingdom of Saudi Arabia.

MATERIAL and METHODS

Fifty six patients who had been bitten by snakes were reported to King Khalid Hospital, Al-Kharj, Kingdom of Saudi Arabia for a four-year period. They were 53 males and 3 females aged from 12 to 75 years (mean 32.9). For each patient, a urine sample was analysed both chemically and microscopically.

Immediately upon arrival, blood samples were taken and sera were separated. Blood cells and platelet were counted for all patients using routine analysis. Fresh plasma samples (within 2 hrs.) were used to determine Prothrombin and partial thromboplastin times using Kits supplied by Dia Med AG CH-3280 Murten, Switzerland. Sera were subjected to the following biochemical analyses using Kits: urea and creatinine (Sclavo Diagnostics, Italy); sGOT and sGPT (Biochemical company, Taiwan) and creatine phosphokinase (Human Gesellschaft fur Biochemica und Diagnostica MbH, Germany). Electrolytes (K^+ and Na^+) were estimated using flame photometer. Twenty normal healthy adults (controls) were subjected to the forementioned tests and compared with the patient's levels using student's t-test.

The fang marks were swabbed for bacteriological examination.

RESULTS

Tables 1,2,3 show the data obtained during this study. Data from patient who had been died were not included in the results.

Table (I): Microscopical and chemical findings in urine of 52 patients.

	Microscopical data									Chemical data								
	Red blood cells			Polymorphs			Granular casts			Hemoglobin			Myoglobin			Albumin		
	+	++	+++	+	++	+++	+	++	+++	+	++	+++	+	+	+++	+	++	+++
No. of patients.	13	16	23	16	5	31	22	13	17	14	8	30	42	6	4	41	8	3
Incidence (%)	25	31	44	31	10	60	42	25	33	27	15	58	81	12	8	79	15	6

Table (2): Effect of snakebite on the hematological parameters in serum of 52 patients.

	Hematological parameters					
	WBCs ($X 10^3$/ ml	RBCs ($X 10^6$/ml	Hb (g %)	Platelet ($X 10^3$/ml	PT (Sec.)	PTT (Sec.)
Control (n=20)	7.2±2.1	4.5±0.5	14.0±1.1	265.5±61.4	12.9±0.9	32.6±2.5
Patients (n=52)	14.6±4.4*	2.9±0.4*	9.4±1.3*	136.2±36.5*	21.98±5.4*	57.7±12.0*

*. Values are mean ± S.D. and compared with values in control using student's t test at $P < 0.0001$.

Table (3): Effect of snakebite on the biochemical parameters in serum of 52 patients.

	Biochemical Parameters						
	Urea (mM/L)	Creatinine (uM/L)	Sodium (mM/L)	Potassium (mM/L)	sGPT (Iu/L)	sGOT (Iu/L)	CPK (Iu/L)
Control (n=20)	4.394±0.67	80.65±18.57	139.30±5.48	4.66±0.6	11.8 ±4.4	14.9±3.2	56.2±23
Patients (n=52)	13.68±6.54*	145.3±67.5*	124.92±11.3*	5.56±0.8*	53.37±14.3*	61.3±17.3*	100.3±80

* Values are mean ± S.D. and compared with values in control using student's t test at $P < 0.0001$.

DISCUSSION

The microscopical results of urine (Table 1), of 52 patients admitted to King Khalid Hospital, Al-Kharj, Saudi Arabia, showed that 44% of the patients had hematuria and 60% had high polymorphonuclear leukocytes. Granular casts, which are indicative of inflammation and degeneration of the renal tubules, were concurrent. On the other hand, the chemical results of the urine showed that 58% of the patients had hemoglobinuria whereas myoglobinuria and albuminuria were common features. HAMAGYL et al. (1965) reported that extensive muscle damage was the cause of myoglobinuria. WARRELL et al. (1989) also reported that both plasma and urine myoglobin concentrations were raised.

Table 2 shows the characteristic features of snakebites on the hematological data of the serum. Although no pathogenic organisms were isolated from fang marks throughout the 52 patients bitten by snakes, leukocytic count was significantly ($P/$ 0.0001) higher in the patients group than in the control group. However, HAMAGYL et al. (1965) reported that some snakes harbour pathogenic organisms in their mouth when kept in captivity that may contaminate the wound. Furthermore, WARRELL et al. (1989) observed that local envenoming (Swelling, blistering and necrosis) was severe in two victims of both cobra and viper snakes. In the present study, leukocytosis may be explained as an inflammatory reaction effect of snake venom. Phospholipase A_2 (PLA_2) is found in the venom of snakes (ROSENBERG, 1979). PLA_2 is an important enzyme in the synthesis of arachidonic acid and its metabolites such as prostaglandins and leukotrienes (HAMMARSTON, 1983 and SAMUELSSON, 1983). CHU et al. (1989) found that PLA_2, purified from Trimeresurus mucrosquamatus snake venom, induced edema formation and mast cell degranulation. The granular components of mast cell include histamine, serotonin, bradykinin, prostaglandin and leukotrienes. Exogenous PLA_2 may cleave the phospholipid on biological membrane (WHELAN, 1978), resulting in the release of arachidonic acid and promoting prostaglandin and leukotriene synthesis which subsequently causes permeability changes, vasodilatation, cell chemotaxis and inflammation reactions (SAMUELSSON, 1983).

The number of red cells and the amount of hemoglobin, table 2, were significantly lower in the patients than in the controls. Moreover, the hematologicl parameters that are important for blood clotting hemostasis, such as platelet count and prothrombin and partial thromboplastin times, were determined. Platelet count was significantly ($P/$ 0.0001) lower in the patient group than in the control group, whereas prothrombin and partial thromboplastin times were significantly ($P/$ 0.0001) longer in the patients than in the controls. Therefore, anemia was the result of both hemolysis and bleeding. WARRELL et al. (1989) also reported evidence of intravascular hemolysis in most ofthe patients, whereas EL-ASMAR et al. (1989) isolated a hemorrhagic fraction with a fibrinogenase activity from cerastes vipera (Known as sahara sand viper venom).

The procoagulant and anticoagulant proteins from snake venous have been isolated and characterized for their mechanisms of action on blood clotting (RUSSELL,

1980 and EL-ASMAR et al., 1989). The same protein may have both coagulant and anticoagulant activities. In this study the anticoagulant activity was a common feature (Table 2), as shown by a significant decrease in platelet count and prolongation of prothrombin and partial thromboplastin times.

Renal damage as determined by a significant ($P/ 0.0001$) increase in serum levels of urea, creatinine and potassium and a significant decrease in the serum level of sodium were noted (Table 3). Serum enzymes sGOT, sGPT and creatine phosphokinase were significanty ($P/ 0.0001$) elevated in all patients when compared with normal levels.

An increase in serum enzymes following snake venom injection has been reported (NAKADA et al., 1980; HASSAN et al., 1986; HODHOD et al., 1989). Direct attack of snake venom on cell membrane is an obvious cause of enzyme release (MOSS et al., 1987). On the other hand, PLA_2, found in the venom of snakes, may affect the biological membranes resulting in changes of membrane structure and function (GOPALAKRISHNAKONE et al., 1984). Serum GOT and GPT increase whenever disease process affects hepatocytes integrity (ELLIS et al., 1978). However, GPT is more specific liver enzyme and used as a test of hepatocellular damage while GOT is a diagnostic parameter of the heart (WHITBY et al., 1984). Therefore the increase in serum enzymes is due to their leakage from damaged tissues i.e. kidney, liver and heart. Furthermore, the significant increase and decrease in serum K^+ and Na^+, respectively, may be explained not only by direct changes of snake venom on the integrity of cell membrane, particularly on $Na^+ - K^+$ ATPase (HODHOD et al., 1989), but also due to hemolysis.

This study shows that of 56 caes ofsnakebites, only four patients died (8%), three died with renal failure and one died with circulatory collapse. Furthermore, the biochemical parameters demonstrate that hematological changes as well as renal liver and cardiac damages were a common clinical feature in aptients who had been bitten by snakes.

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