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RESEARCH ARTICLE

The effects of snake venom on serum copper, zinc and magnesium levels in patients with snake bite

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ABSTRACT

Objective: Envenoming resulting from snakebites is a common devastating problem that is frequently seen in eastern and southeastern regions of Turkey. This aim of this study is to observe the changes of snake venom on serum copper (Cu), zinc (Zn), and magnesium (Mg) levels in patients with snakebite.

Materials and Methods: Patients with snakebite and healthy individuals as control group were included in the study. Overall 10 ml venous blood sample was taken from each study individuals. Serum trace elements were measured using an atomic absorption spectrophotometer.

Results: Forty patients with snakebite and 80 healthy individuals in the control group were included in the study. The mean age of the patients with snakebite was 40.1 ±12 years; of these, 18 were male (45%). The mean age of the 80 healthy individuals was 40.6 ±10 years; of these, 36 were male (45%). Serum Cu, Zn, and Mg levels of patients with snakebite were 75.8 ±20.9, 86.9 ±25.2, and 1201 ±562 µg/dL, respectively. Serum Cu, Zn, and Mg levels of healthy individuals were 57.6 ±17.2, 55.8 ±12.4, and 1454 ±278 µg/dL, respectively. There were statistically significant increasing in serum Cu and Zn levels ($p<0.001$), and decreasing in serum Mg levels ($p=0.001$) in patients with snakebite when compared to healthy individuals.

Conclusion: Snake venom produces significant alterations on serum Cu, Zn, and Mg levels in patients with snakebite. Investigating of these changes caused by snake venom through further studies may provide novel developments in the treatment of patients with snakebite. *J Microbiol Infect Dis 2013; 3(2): 71-74*

Key words: Snakebite, snake venom, copper, zinc, magnesium

Yılan ısırığı olgularında yılan zehirinin serum bakır, çinko ve magnezyum seviyesi üzerine etkisi

ÖZET

Amaç: Yılan ısırıkları Türkiye'nin doğu ve güneydoğu bölgelerinde sık görülen önemli bir problemdir. Bu çalışmada yılan ısırığı vakalarında serum bakır (Cu), çinko (Zn) ve magnezyum (Mg) düzeylerindeki değişiklikler araştırıldı.

Yöntemler: Çalışmaya 40 yılan ısırıklı hasta ile kontrol amaçlı 80 sağlıklı gönüllü alındı. Yaklaşık 10 ml venöz kan çalışmaya alınan her bir bireyden alındı. Serum eser element düzeyleri Atomik Absorbsiyon Spektormetre cihazı kullanılarak ölçüldü.

Bulgular: Çalışmaya alınan 40 yılan ısırıklı hastanın yaş ortalaması 40,1 ± 12 yıl olup, 18'i (% 45) erkek idi. Sağlıklı 80 bireyin yaş ortalaması 40,6 ± 10 yıl olup, 36'sı (% 45) erkek idi. Yılan ısırıklı hastaların serum Cu, Zn, ve Mg düzeyleri sırasıyla 75,8 ± 20,9; 86,9 ± 25,2 ve 1201 ± 562 µg/dL bulundu. Sağlıklı gönüllülerin serum Cu, Zn, and Mg düzeyleri sırasıyla 57,6 ± 17,2; 55,8 ± 12,4 ve 1454 ± 278 µg/dL bulundu. İstatistiksel olarak sağlıklı gönüllüler ile karşılaştırıldığında, yılan ısırıklı hastaların serum Cu ve Zn düzeylerinde anlamlı bir artış ($p<0.001$) ve serum Mg düzeylerinde anlamlı bir düşüş ($p=0,001$) saptandı.

Sonuç: Yılan zehiri, yılan ısırığı olan hastaların serum Cu, Zn ve Mg düzeyleri üzerinde anlamlı değişimler oluşturmaktadır. Yılan zehrinin serum eser element düzeylerinde oluşturduğu bu değişimlerin ileri düzey çalışmalarla araştırılması yılan ısırığı olan hastaların tedavisinde yeni gelişmeler sağlayabilir.

Anahtar kelimeler: Yılan ısırığı, yılan zehiri, bakır, çinko, magnezyum

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INTRODUCTION

Envenoming due to snakebites is a common devastating environmental and occupational problem, particularly in rural areas of tropical and subtropical developing countries. It constitutes a medical emergency requiring immediate evaluation and intervention, but its importance in view of the public health has been generally ignored in medical practice. In addition, snakebites cause increasing morbidity and mortality worldwide.[1,2] According to World Health Organization (WHO) statistics, almost 2.500.000 poisonous snakebites are reported annually worldwide; of these, 125.000 are fatal.[3]

The scientific study of snakebites is a part of clinical toxicology. Snake venoms are the most complex of all natural venoms and poisons; the venom of any species might contain more than 100 different toxic and non-toxic proteins and peptides, as well as non-protein toxins, carbohydrates, lipids, amines, and other small molecules. The most significant toxins in human envenoming include those that affect the nervous, cardiovascular, and haemostatic systems, as well as those that cause tissue necrosis.[1,2]

Serum trace elements, especially Cu, Zn, and Mg, are of critical importance in the human body,[4-7] and their serum levels may change over the course of many diseases.[8,9] Although Mg technically is not a trace element, it is considered a trace element in literature.[4] In the human body, these elements are important components of various proteins, enzymes, complex carbohydrates, and biological processes [4-7,10] and deficient or excessive serum levels of these elements may result in numerous disorders.[4]

In this study, we aimed to examine the changes of snake venom on serum Cu, Zn, and Mg levels in patients with snakebite, and to compare the serum levels of these elements between patients with snakebite and healthy individuals.

METHODS

Setting

This prospective study was performed at Dicle University Hospital, an 1150-bed tertiary referral center, and at Elazig Teaching Hospital, a 650-bed secondary referral center, in southeastern and eastern Turkey between April 2008 and October 2010. Patients with snakebite were treated at the Departments of Infectious Diseases and Clinic Microbiology of both hospitals. A total of 40 patients with snakebite and 80 healthy individuals as a control group were included in this study. All of the 120 study individuals were selected from the same geographic region. Nonpoisonous snakebite cases were not included in the study. The history of all study individuals were taken in detail, and individuals having any chronic disease and/or nutritional disorder, which could affect serum trace element levels, were not included in the study. Serum samples of patients with snakebite were taken 48-72 hours after the snakebite event. By this time, three or five standard doses of snake anti-venom had been given to each patient with snakebite. Tetanus prophylaxis and two grams of cephazolin prophylaxis had been administered to all patients with snakebite during admission in the emergency room.

The Local Ethic Committee of Dicle University Medical Faculty approved this study. The study protocol conforms to the ethical guidelines of the 2008 declaration of Helsinki.

Measurement of serum trace elements

After the required information was obtained and the 120 study individuals had fasted overnight for 10 hours, a total of 10 ml of venous blood was taken from the median cubital vein of each study individual. The blood samples were immediately decomposed centrifuging at 5200 turns for 5 minutes at room temperature. Serum samples were stored in a deep freeze at -80°C. When working with the samples, all serum samples were dissolved and diluted with deionized water at room temperature. Serum Cu, Zn, and Mg levels were measured in all serum samples using a Unicam 929 atomic absorption spectrophotometer (U929-AAS). The U929-AAS was calibrated using standards of known concentrations (Beers' Law) before working time. The lower limits for detection of Cu, Zn, and Mg levels of U929-AAS were 2 µg/dL, 1 µg/dL, and 5 µg/dL, respectively.

This study protocol was approved by Local Ethic Committee of Dicle University Medical Faculty, Ref 334.

Statistical analysis

All the data collected from the 120 study individuals were recorded and analyzed using SPSS for Windows 15.0 software. The Student's t-test was used to compare the data between patients with snakebite and the healthy individuals, and p values lower than 0.05 were accepted as significant.

RESULTS

Forty patients with snakebite and 80 healthy individuals in the control group were included in the study. The mean age of the 40 patients with snakebites was 40.1 ± 12 years; 18 were males (45%) and 22 were females (55%). The mean age of the 80 healthy individuals in the control group was 40.6 ±10 years; 36 were males (45%). There were no statistically significant differences in terms of gender between the groups. In addition, there were no nutritional disorders or chronic diseases affecting the serum trace element levels in any of the 120 study individuals. Serum Cu, Zn, and Mg levels of patients with snakebite and the control group are shown in the Table. Statistically significant increases in serum Cu and Zn levels, and decreases in serum Mg levels were detected in patients with snakebite when compared with the control group (Table 1).

Table 1. Serum trace element levels in patients with snakebite and control group (mean ± standard deviation)

Trace elements	Snakebites (n=40)	Control group (n=80)	p-value
Cu (µg/dL)	75.8 ± 20.9	57.6 ± 17.2	<0.001
Zn (µg/dL)	86.9 ± 25.2	55.8 ± 12.4	<0.001
Mg (µg/dL)	1201 ± 562	1454 ± 278	0.001

DISCUSSION

To our knowledge, the effects of snake venom on serum trace elements in patients with snakebite have not been adequately investigated yet. This is the first study to examine the effects of snake venom on serum Cu, Zn, and Mg levels in patients with snakebite. Snake venoms include a number of proteolytic or hydrolytic enzymes, which produce numerous effects ranging from local tissue damage to severe life-threatening systemic anaphylactic reactions that result in generalized edema in the human body. Nephrotoxicity, neurotoxicity, and hematotoxicity are the main problems in the clinical management of envenoming cases.[1,11-13] This study reveals the significant alterations in serum Cu, Zn, and Mg levels among patients with snakebite due to snake venoms. These observations need further studies that may provide the novel developments in the treatment of patients with snakebite.

In healthy populations, nutritional behaviors, geographic location, gender, age, physiological conditions, social and environmental conditions, and lifestyle may affect the serum levels of trace elements.[14] The normal serum levels of Cu, Zn, and Mg among healthy adults have been reported to be 70-140 µg/dL, 70-120 µg/dL, and 1,600-2,600 µg/dL, respectively.[15,16] In the present study, we found the mean serum levels in the healthy individuals to be 57.6±17.2 µg/dL, 55.8±12.4 µg/dL, and 1454 ± 278µg/dL, respectively, which was lower than those reported in the studies. These variations may result from the factors mentioned above, or a deficiency of these trace elements may be present among healthy individuals in the control group in our study.

We observed statistically significant increases of serum Cu and Zn levels in patients with snakebites compared to the control group. The increased serum Cu levels may have resulted from damaged Cu-containing proteins such as ceruloplasmin, metallothionein, albumin, transcuperin, and others, due to the snake venom.[4,7] Similarly, an increasing level of serum Zn may be due to the proteolytic activities of snake venom [11] on the various enzymes and Zn-containing structural proteins, because Zn has a functional role as a co-factor of more than 200 enzymes and has a structural role in a number of Zn finger proteins in the human body.[4,5] In addition, it is well known that erythrocytes contain high concentrations of Zn, and snake venom causes marked hemolysis. We considered that once the various Cu and Zn-containing structural proteins were damaged due to snake venom, the Cu and Zn elements remained free and consequently their concentrations increased in the serum samples. On the other hand, the reason for the decrease in serum Mg levels in patients with snakebite compared to the control group can be explained by the particular renal tissue injury caused by snake venom. In the human organism, about 75% of total plasma Mg is filtrated through the glomerular membrane and a large amount of filtrated Mg is reabsorbed by tubular function. Approximately 3-5% of the filtrated Mg is excreted into the urine under normal conditions.[6,17] It is well known that snake venoms have nephrotoxic activity. Tubular Mg cannot be reabsorbed when the renal tubules are damaged by snake venom, and thus renal Mg loss may increase in patients with snakebites. In result, the urine Mg levels are expected to increase in these patients. In addition, it has been reported that hypoxia and/or anoxia resulting from the snake venom lead to the increasing intracellular Mg concentration as a result of its transition from the extracellular areas to intracellular areas.[6] It was concluded in the present study that serum Mg level decrease due to the reasons mentioned above, especially renal impairment in the snakebite patients.

There are two limitations of this study. First, the urine Mg levels could not be measured due to laboratory restrictions. Increased urine Mg levels could be a good indicator of decreasing serum Mg levels in patients with snakebite. Second, we could not investigate the further metabolic effects of the alterations of the serum Cu, Zn, and Mg levels due to snake venom because of limited clinical and laboratory options.

In conclusion, this study revealed the variations in serum Cu, Zn, and Mg levels in patients with snakebite. Snake venom produces critical changes in serum Cu, Zn, and Mg levels, and detailed investigations are required to elucidate the effects of these alterations on human body in further studies.

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