ZINC AND OSTEOPOROSIS IN PATIENTS WITH SPINAL CORD INJURY

By A. OHRY, M.D.,¹ Y. SHEMESH, M.D.,¹ R. ZAK, M.Sc.² and M. HERZBERG, Ph.D.²

¹ The Sir Ludwig Guttman Spinal Cord Injury Center, Chaim Sheba Medical Center, Tel Hashomer, Israel; ² The Department of Chemical Pathology, Ichilov Medical Center, Tel Aviv, Sackler School of Medicine, Tel Aviv University, Israel

Abstract. Thirty-eight patients (8 women and 30 men) with spinal cord injury were investigated. All had been immobilised after the traumatic event. The time elapsed since their accidents varied from 2 to 74 weeks. Blood and urine samples were collected to investigate calcium, zinc, magnesium, sodium, alkaline phosphate, phosphore, haemoglobin, creatinine, uric acid and proteins in blood, and the urinary excretion of phosphore, hydroxyproline, creatinine, amino acids, calcium, magnesium and zinc. The methods were estimated by atomic absorption spectrophotometry. The serum zinc levels did not differ statistically from normal and the calcium and magnesium levels in the serum were lower among the patients than in normal controls.

The urinary excretion of zinc, calcium, phosphore and hydroxyproline was higher among the patients without correlation to the patients' age. The zinc excretion is negatively correlated to the time elapsed since the injury, but it is still high 3 months after trauma. The highly significant correlation between urinary zinc and hydroxyproline excretion, together with increased calcium and phosphore excretion, suggests that zinc may be involved in the process of osteoporosis in patients with spinal cord injury.

Key words: Zinc; Calcium; Bone metabolism; Osteoporosis; Spinal cord injury; Immobilisation.

Introduction

THE physiological and biochemical changes due to prolonged immobilisation have been much investigated. Spinal cord injured patients are usually confined to bed for a long period, causing loss of tissue mass in bone, muscle, connective tissues and reduction of the blood volume.

Osteoporosis and rapid mineral loss in bones are the main features of immobilisation (Chantraine, 1971). The progressive but self-limited osteoporotic process leads to increased fracture incidence. The bone loss occurs predominantly because of increased resorption, as in the ageing population. Decreased osteoblastic and increased osteoclastic activity occur as a result of immobilisation, thus causing hypercalcuria with increased incidence of renal stones and ectopic bone formations.

In the literature concerning bone and muscle metabolism of patients with spinal cord injury, much attention has been paid to calcium (Bergman *et al.*, 1978) magnesium, phosphore, hydroxyproline and alkaline phosphatase changes (Claus-Walker *et al.*, 1975), but the zinc ion was overlooked. The only work we could find was by Burr (1973), who found low fasting plasma zinc concentration in paraplegic patients with pressure sores.

The zinc content of bone in man and in animals is higher than in other tissues (Alhava *et al.*, 1977; Calhoun *et al.*, 1974; Richards *et al.*, 1975). The exact role of zinc in bone metabolism is not fully understood. Until now, most of the infor-

mation available came from zinc deficiency states (Hambridge *et al.*, 1972; Solomons *et al.*, 1976; Brown *et al.*, 1978; Flynn *et al.*, 1971) and it was concluded that an adequate zinc supply is necessary for proper growth, as well as for wound healing processes.

The present study was undertaken in order to investigate the status of zinc and other biochemical and hematological values in spinal patients in whom osteoporosis is a constant feature.

Material and Methods

Thirty-eight patients (8 women and 30 men) aged 13–49 years were investigated. All were immobilised after traumatic spinal cord injury. The time elapsed since the accident varied from 2 to 74 weeks. During the study, no patient suffered from pressure sores, urinary infection or any pulmonary or circulatory complications. They were given normal hospital diet without any medication.

Blood was collected by venopuncture and drawn into plastic test tubes in the morning following an overnight fast. Serum was separated after 2 to 3 hours.

A sample of morning urine was taken in a sterile, clean plastic container. All estimations were made in acid prewashed tubes and much care was taken to avoid contamination. In some of the patients the laboratory examinations were repeated several times and the results were averaged. Zinc, calcium and magnesium in serum and urine were estimated by atomic absorption spectrophotometry (Perkin-Elmer, model 290-B).

For the zinc estimation, serum and urine were diluted 1 : 5 with deionised water. For the estimation of magnesium and calcium, a dilution of 1 : 40 with 0.1 per cent lanthanum chloride was used.

Serum phosphore and alkaline phosphatase were estimated by standard Technicon SMA 12/60 methods. Creatinine in urine was determined with alkaline picrate (Jaffe reaction), and phosphore was determined by the Fiske-Subbarow methods. Hydroxyproline was determined according to Firshein and Shill (acid method B). The concentrations of the various substances in urine were expressed per gram creatinine. Statistical analysis was done by students' *t*-test and linear regression analysis. The other biochemical and hematological variables investigated in blood were: haemoglobin, leukocytes, glucose, urea, chloride, potassium, sodium, CO₂CP, uric acid, cholesterol, creatinine and proteins. The urinary excretion of amino acids was also determined.

Results

Table I shows the serum concentration of four elements and alkaline phosphatase in spinal patients and in healthy controls. It can be seen there are no statistical differences in serum zinc levels between patients and healthy controls. There is marked reduction of serum magnesium and calcium in the patients in comparison to controls. The serum phosphore and alkaline phosphates were significantly higher in the patient group, although they are still within normal limits.

Table II shows the urinary excretion of these four elements in these groups. The excretion of zinc and hydroxyproline was nearly three-fold higher in the patients than in the control group.

The range of zinc excretion in spinal patients was wide, and in the majority of the patients the zinc concentration was in excess of the highest value found in

TABLE I

Serum concentration of four elements and alkaline phosphatase in spinal patients and healthy controls

Patients	Controls		
	Mean $\pm$ SE	Mean $\pm$ SE	
Zinc μ g/dl	125.3 $\pm$ 3.9	124.2 $\pm$ 2.2	n.s.
Calcium mg/dl	9.17 $\pm$ 0.08	9.7 $\pm$ 0.02	p < 0.001
Magnesium mg/dl	1.72 $\pm$ 0.05	1.96 $\pm$ 0.02	p < 0.001
Phosphore mg/dl	4.1 $\pm$ 0.08	3.25 $\pm$ 0.05	p < 0.001
Alkaline Ph-ase U/l	74.2 $\pm$ 4.9	60.0 $\pm$ 0.8	p < 0.001

TABLE II

Urinary excretion of four elements and hydroxyproline in spinal patients and healthy controls

Patients	Controls		
	Mean $\pm$ SE	Mean $\pm$ SE	
Zinc μ g creatinine	1699 $\pm$ 150.8	584.1 $\pm$ 40.3	p < 0.001
Calcium mg/g creatinine	309.3 $\pm$ 32	109.7 $\pm$ 9.5	p < 0.001
Magnesium mg/g creatinine	118.3 $\pm$ 7.6	95.1 $\pm$ 11.0	n.s.
Phosphor mg/g creatinine	699.6 $\pm$ 59.2	563.3 $\pm$ 51.1	n.s.
Hydroxyproline (mg/g creatinine)	98.9 $\pm$ 7.5	35.5 $\pm$ 1.7	p < 0.001

normal controls (Fig. 1). The excretion of the calcium ion was also high, but not that of magnesium and phosphore.

Table III shows the relation between zinc excretion and other variables in the patient group.

Linear regression analysis shows there is no correlation between serum and urinary zinc, whereas urinary zinc is positively correlated with serum alkaline phosphatase, and with magnesium, phosphore and hydroxyproline excretion. Figure 2 shows the linear correlation between zinc and hydroxyproline excretion. Despite the increase of calcium excretion, no correlation was found with zinc excretion. We found that there is negative correlation between zinc excretion and the time (in weeks) elapsed since the accident.

As for the other laboratory findings, there are no statistical changes between the spinal patients and the controls in blood values, glucose, chloride, creatinine, uric acid and CO₂CP. The creatinine clearance tests in the patient group were within normal limits. The mean haemoglobin concentration and total leukocytes count were lower than in normal, but within normal limits. The serum sodium concentration was statistically (P < 0.005) higher in the patient group and the potassium ion lower (P < 0.01), but within normal range. The mean cholesterol levels were significantly lower than in normals (P < 0.001). There was no significant finding of urinary amino acids in the patient or normal groups. The total mean serum protein level was lower in the patient group, but within normal limits.

FIG. 1

TABLE III

Relation between zinc excretion and other variables in spinal patients

	r-value	significance
Zinc in urine versus		
Serum zinc	0.2606	n.s.
Serum alkaline phosphatase	0.3495	p < 0.05
Zinc in urine versus		
Urinary		
Magnesium	0.4463	p < 0.01
Calcium	0.1599	n.s.
Phosphore	0.3767	p < 0.05
Hydroxyproline	0.5162	p < 0.01
Time since the accident	-0.4191	p < 0.05

Discussion

Patients with spinal cord injury are exposed to various changes in protein and mineral metabolism, as well as in the endocrinological, cardiovascular and respiratory systems (Cooper *et al.*, 1950; Chantraine, 1978-79). Many of the changes occur because of prolonged immobilisation, and one of the consequences is rapid mineral loss from bones and muscle waste. Bergman *et al.* (1977-78), Chantraine (1978-79) and Claus Walker (1975) had found high urinary excretion of calcium

FIG. 2

and hydroxyproline in spinal patients, and our data confirms their findings. We have found marked increase of zinc excretion in these patients in spite of normal serum zinc. Burr (1973) found low values of serum zinc in spinal patients with pressure sores. In normal subjects zinc excretion is independent of intake, and shows little variation (Burch *et al.*, 1975; Halstead *et al.*, 1974). The urinary zinc excretion increases significantly after surgery in cirrhosis of the liver, and after certain diuretics (Walker *et al.*, 1973; Lindeman *et al.*, 1972; Hallbook *et al.*, 1971). Increased zinc excretion was found in patients with thyrotoxicosis and hyperparathyroidism (Bremner & Fell, 1977; Melette & Henkin, 1976). The exact zinc metabolism is not clear. Thirty to forty per cent of serum zinc is firmly bound to alpha 2 macroglobulin (Parisi & Vallee, 1970). The remainder is bound to albumin and a small fraction to amino acids like histidine and cysteine (Freeman & Taylor, 1977). It is quite possible that only the smallest zinc fraction (the one bound to amino acids) can filtrate to the urine. The source of the hyperexcreted zinc is not clear. Fell *et al.* (1973) postulated that after surgery, it originates from muscles. We have found a consistently increased excretion of hydroxyproline and zinc probably only due to marked osteoporosis. The highly significant correlation between these two substances, together with increased excretion of calcium and phosphorus, suggest that the zinc is also involved in osteoporosis process. The zinc, calcium, phosphorus and hydroxyproline are hyperexcreted from the osteoporotic and immobilised limbs. Our findings were similar to those of Alhava *et al.* (1977), who found a decrease in the zinc content of cancellous bone with age in both sexes. It may be that the filtrable fraction of serum zinc rises.

It can be assumed that enhanced catabolic processes of muscle and other tissues after immobilisation, supply amino acids and small polypeptides which bind zinc forming micromolecular ligands, which can be filtered in the kidneys. The other haematological and biochemical findings are compatible with previous reports, namely the relative anaemia and hypoproteinaemia.

RÉSUMÉ

Le zinc et l'ostéoporose chez les patients atteints à l'épine dorsale.

Cette étude porte sur 38 patients atteints à l'épine dorsale depuis 2 à 74 semaines et qui avaient tous été immobilisés après leur accident. La présence de zinc, de calcium ainsi que d'autres matières dans le sang et l'urine fut examinée. Les niveaux de zinc dans le sérum ne différaient pas statistiquement de la norme; les niveaux de calcium et de magnésium dans le sérum étaient plus bas chez les malades que chez des personnes saines examinées pour contrôle. La corrélation très significative entre le zinc dans l'urine et l'excrétion d'hydroxyproline ainsi que l'excrétion accrue de calcium et de phosphore suggèrent que le zinc pourrait jouer un rôle dans l'ostéoporose des patients atteints à l'épine dorsale.

ZUSAMMENFASSUNG

Zink und Osteoporosis bei Rückenmarkverletzten Patienten.

38 Patienten mit Rückenmarkverletzung seit 2 bis 74 Wochen, die alle nach ihrem Unfall bewegungslos lagen, wurden untersucht. Zink, Calcium und andere Stoffe im Blut und im Harn wurden analysiert. Der Zinkbestand im Serum war statistisch nicht von dem Normalbestand verschieden. Die Calcium- und Magnesiumbestände im Serum waren geringer bei den Kranken als bei Gesunden die zur Kontrolle untersucht wurden. Die sehr bedeutsame Beziehung zwischen dem Harnzink und der Hydroxyprolinausscheidung sowie die vergrößerte Calcium- und Phosphorausscheidung deuten an, dass der Zink in der Osteoporosis bei Rückenmarkverletzten Patienten aktiv sein könnte.

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