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## Zinc, hydrochlorothiazide and sexual dysfunction

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### SUMMARY

This study was designed to test the hypothesis that hydrochlorothiazide a diuretic used to treat hypertension depletes body zinc and thereby cause sexual dysfunction. Serum zinc and sexual dysfunction were measured in 39 middle aged hypertensive men who had been taking hydrochlorothiazide in average daily doses of between 25 and 50 mg daily for at least six months, and a control group of 27 unmedicated middle aged normotensive men. The medicated group had a higher incidence of sexual dysfunction (56 pc) as compared to 11 pc in the control group. The use of hydrochlorothiazide did affect serum zinc levels significantly in 20 patients. Sexual dysfunction occurred more often in older and overweight patients ( $p < 0,004$ ). Three of the normotensive men experienced sexual dysfunction probably related to old age.

Twenty two of the 39 on hydrochlorothiazide and experiencing sexual dysfunction were divided into two groups of 11 patients. Bloods were taken from the 27 normotensive and 22 hypertensive men receiving hydrochlorothiazide for the analyses of zinc. Subsequently one group of the patients were supplemented with zinc 500 mg daily for 30 days while the other group was supplemented with magnesium chloride 1 g daily for 30 days. The normotensive men were not treated. After 30 days, bloods were again taken from the three groups of analyses for zinc and magnesium.

Serum zinc was significantly decreased ( $p < 0,05$ ) by hydrochlorothiazide and a non significant decrease in

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serum magnesium ( $p = ns$ ) was observed. After supplementation with zinc, the serum zinc levels returned to normal only in eight patients. There was improvement in the symptoms of sexual dysfunction in five patients. Two patients gained weight.

Hydrochlorothiazide decreased serum zinc levels ( $p < 0,05$ ) and was unchanged with magnesium supplementation but the serum magnesium returned to normal values. Improvement of symptoms of sexual dysfunction was positive in one patient.

This study shows that low serum zinc levels may be associated with sexual dysfunction but the definitive role of zinc in the pathogenesis of sexual dysfunction will remain controversial.

### INTRODUCTION

Hydrochlorothiazide, a thiazide diuretic, is widely used in the treatment of mild to moderate hypertension. A common side effect experienced by our Black male patients on hydrochlorothiazide treatment for blood pressure control is sexual dysfunction. Hydrochlorothiazide causes increased potassium, magnesium and zinc excretion.<sup>1</sup>

Magnesium is gaining recognition as a clinically important electrolyte in that it helps in the restoration and the movements of ions across membranes. It affects the functioning of pumps,<sup>2</sup> carriers<sup>3</sup> and channels.<sup>4</sup> Based on these diverse functions of magnesium, it was hypothesised that magnesium supplementation might help in the restoration of serum zinc to normal levels.

Zinc is an essential element of more than 200 enzymes and is involved in the metabolism of nucleic acids, protein synthesis and normal functioning of the immune system. Growth retardation, delayed wound healing, glucose intolerance, hyperlipidemia, skin changes, hypogonadism and impotence are the characteristics of zinc deficiency.<sup>5</sup>

A study was conducted to determine whether magnesium or zinc supplementation given to patients on hydrochlorothiazide treatment for blood pressure control would restore their serum zinc to normal levels and subsequently improve symptoms of sexual dysfunction.

### MATERIALS AND METHODS

The protocols were approved by the Ethics Committee, University of Natal Medical School. Informed consent was obtained from all patients. Twenty four normotensive men served as control for both the study groups.

#### Protocol 1.

Eleven Black male patients receiving hydrochlorothiazide ranging from 25 to 50 mg once daily for blood pressure treatment experiencing sexual dysfunction took part in the study. Bloods were collected for serum zinc and magnesium analyses. These patients were supplemented with 1 gm magnesium chloride daily. After 30 days serum zinc and magnesium levels were measured.

#### Protocol 2.

Another 11 Black male patients experiencing sexual dysfunction on hydrochlorothiazide on a dose of 25 to 50 mg once daily for blood pressure treatment were included in the study. Blood was collected for serum zinc analyses. These patients were supplemented with 500 mg zinc sulphate for 30 days and subsequently serum zinc was analysed. Serum zinc and magnesium levels were analysed by Natal Regional Laboratories, King Edward VIII Hospital, Durban.

### RESULTS

The patients in both groups were aged between 52 and 68 years. Their body mass ranged between 76 to 109 kg and height from 162 to 187 cm. Hydrochlorothiazide was effective in controlling blood pressure.

#### Protocol 1.

Serum zinc was significantly decreased ( $p < 0,05$ ; Table I) and a non significant decrease in serum magnesium ( $p = ns$ ; Table I) was observed. After supplementation with magnesium chloride, the serum zinc levels were unchanged but the serum magnesium levels returned to normal values. There was improvement in the symptoms of sexual dysfunction in one of the patients. Serum zinc levels before and after magnesium supplementation are presented in Table I.

#### Protocol 2.

Hydrochlorothiazide decreased serum zinc levels ( $p < 0,05$ ; Table II) and was corrected with zinc supplementation only in eight patients. Improvement of symptoms of sexual dysfunction was positive in four patients. Two patients gained weight. Serum zinc levels before and after zinc supplementation are shown in Table II.

**Table I: Serum magnesium and zinc levels before and after magnesium chloride supplementation in patients on hydrochlorothiazide in a range of 25 to 50 mg daily for blood pressure treatment. Results are expressed as mean  $\pm$  SD.**

	Normal range	Control (n = 27)	Experimental (n = 11)	
			before supplementation	after supplementation
Zinc ( $\mu$ mol/l)	11,6 – 19,1	13,67 $\pm$ 2,23	7,8 $\pm$ 1,67*	15,8 $\pm$ 2,3

\* $p < 0,05$ .

**Table II: Serum zinc levels before and after zinc supplementation in patients taking hydrochlorothiazide 25 to 50 mg daily for blood pressure treatment. Results are expressed as mean  $\pm$  SD.**

	Normal range	Control (n = 27)	Experimental (n = 11)	
			before supplementation	after supplementation
Zinc ( $\mu$ mol/l)	11,60 – 19,1	13,67 $\pm$ 2,23	7,3 $\pm$ 1,6*	6,89 $\pm$ 1,35
Magnesium (mmol/l)	0,74 – 0,99	0,95 $\pm$ 0,03	0,90 $\pm$ 0,06	1,09 $\pm$ 1,1

\* $p < 0,05$ .

## DISCUSSION

Although the value of treating hypertension has been well established, a substantial number of patients fail to comply with drug therapy and thus do not receive the benefits of blood pressure reduction because there is growing evidence suggesting an increase in drug induced sexual dysfunction among antihypertensive agents.<sup>6,7</sup> In a study comparing prazosin and hydrochlorothiazide in sexual dysfunction, decrements in buckling pressure and subjective aspects of sexual dysfunction were greater during hydrochlorothiazide treatment than during prazosin treatment.<sup>8</sup>

In a large clinical trial of zinc supplementation, zinc depleted subjects showed a remarkable increase in height, body weight and gonadal development following zinc supplementation.<sup>9</sup> In our study, there was a significant decrease in serum zinc and a non significant decrease in serum magnesium. After supplementation with magnesium chloride, the serum zinc levels showed no change but the serum magnesium levels were corrected. Improvement of sexual dysfunction was observed in one patient.

Zinc supplementation corrected serum zinc levels in 80 pc of patients and improvement of sexual dysfunction was observed in 36 pc of patients.

It is possible that low serum zinc levels may be associated with sexual dysfunction. Until other clinical factors have been studied, the definitive role of zinc in the pathogenesis of sexual dysfunction will remain controversial. It is important to obtain adequate history before and after initiating antihypertensive drug therapy. If sexual dysfunction develops in a patient, a different class of medication can be tried.

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## Neuropsychiatric HIV-1 infection study: in Kenya and Zaire cross-sectional phase I and II

MB SEBIT

### SUMMARY

The objective of the study was to determine the prevalence and natural history of human immunodeficiency virus type 1 (HIV-1) associated psychiatric, neuropsychological and neurological abnormalities. A total of 408 subjects were recruited in Nairobi and Kinshasa. The study consisted of a cross sectional phase and a longitudinal follow up.

Assessment was made by a data collection instrument including six modules. The intercentre and intracentre reliability in the use of the each module have been formally evaluated. The mean global score on the Montgomery-Asberg Depression Rating Scale

was significantly higher in symptomatic seropositive individuals than in matched seronegative controls.

In conclusion, these data suggest that the risk of subtle cognitive deficits may be increased in asymptomatic stages of HIV-1 infection.

### INTRODUCTION

The presence of psychological problems in people with human immunodeficiency virus type one (HIV-1) infection has been the subject of considerable attention recently. According to world wide estimates by the World Health Organization (WHO),<sup>1</sup> 85 pc of adults infected with HIV-1 live outside Western industrialized countries. Over 75 pc of infections in adults are transmitted through heterosexual intercourse and more than 45 pc of infected subjects are women.

Most of the available evidence comes from surveys of well educated, mostly White homosexual men<sup>2,4</sup>, or gays and drug users.<sup>5</sup> A series of studies has shown an increased vulnerability to psychological distress and a significant prevalence of psychiatric disorders associated with HIV-1 infection, ranging from 30 to 63 pc.<sup>6,7</sup> Furthermore, infection with HIV-1 may lead to a number of neurological complications, one of the most important of which is AIDS dementia complex.<sup>8</sup>

The incidence of HIV-1 dementia is approximately seven per 100 patients per year following development of AIDS, with up to 20 pc of HIV-1 infected individuals receiving a diagnosis of HIV-1 dementia before death.<sup>9,10</sup> However, a recent study has found no significant decline in cognitive functions before AIDS, unless overt dementia is present.<sup>11</sup>

Concerns about generalization of the currently available information on the psychiatric, as well as the neuropsychological and neurological complications of HIV-1 infection has prompted the World Health Organization to implement the cross-cultural venture called World Health Organization Neuropsychiatric AIDS Study. The project's objective was to assess the prevalence and the natural history of the above mentioned complications in these two geographic areas, with respect to sex ratio and distribution of HIV-1 in at-risk groups.

### MATERIALS AND METHODS

**Subjects:** A total of 408 subjects (n = 203 in Nairobi, Kenya and n = 205 in Kinshasa, Zaire) was recruited between October 1990 and August 1991, to participate in a cross-section (phase I and II) study. The drop outs

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