

SERUM CALCIUM, INORGANIC PHOSPHATE, URIC ACID, COPPER, ZINC AND MAGNESIUM IN OSTEOARTHRITIS PATIENTS

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Abstract

This study aimed to know the effect of serum calcium(Ca), inorganic phosphate(P), uric acid (UA), copper(Cu), zinc(Zn) and magnesium(Mg) on osteoarthritic (OA) patients who are having pure OA of knee & those having diffuse OA (knee and spine), and to clarify the relationship of those parameters with severity of symptoms and radiological findings.

This is a prospective case control study conducted at Basrah province through of a period of 9 months from October 2001 to June 2002, during which 100 patients with different types of OA were admitted to the Orthopedics Clinic of Basrah General Hospital. Their age ranged from 40 to 68 years olds (24 males and 76 females), were allocated into 3 groups (mild, moderate and sever OA) according to their symptoms and radiological findings. On the other hand 80 apparently health subjects (23 males and 57 females). Their ages ranged from 40-70 years old were participated as a control group.

Venous blood samples were collected from each subjects and patients participated in this study for measurements Ca, P, UA, Cu, Zn and Mg by using standard methods.

Among two age groups and in female patients serum Ca level was highly significantly lowered ($p > 0.01$) in patients with moderate OA of knee as compared with mild OA patients.

Serum uric acid was significantly increased ($p > 0.05$) in patients having mild OA of knee as compared with mild OA of (knee and spine) at age group ≥ 55 years, the same results was observed in male patients as compared to the females group. Serum Cu and P levels were non-significantly altered ($p < 0.05$) in two types of OA among different age and sex groups. Serum Zn levels was significantly lowered ($P < 0.05$) in patients with moderate and mild OA of knee and in sever and moderate OA of knee and combined for serum Mg levels among different age and sex groups.

On the basis of this study, it can be concluded that incidence of moderate OA were high and represent 58% of total numbers of patient studied who were at higher risk of significantly decrease in the concentration of calcium, zinc and magnesium.

Introduction

Osteoarthritis (OA) is a chronic disorder in which there is progressive softening and disintegration of articular cartilage accompanied by new growth of cartilage and bone at the joint margins (osteophytes) and capsular fibrosis^{1,2}.

Osteoarthritis was classify as primary when no cause is obvious and secondary when it is follows a demonstrable abnormality^{1,3}. In general OA was a disease of advancing years but the young

people can develop it, if articular cartilage is damage or subjected to abnormal stress from an early age⁴. OA was more common in joints of hip, knee and spine than elbow and ankle, more over individual joint are affected with differing frequency in men and women (terminal interphalangeal OA chiefly affects postmenopausal women)⁵.

Genetic predisposition, metabolic and hormonal influences cartilage patterns of joint usage, local mechanism stresses or

pre-existing joint disease and specific incident of cartilage damage are some causes to OA⁴.

The most obvious thing about OA is the increases in frequency with age. This does not mean that it is an expression of senescence it simply shows that OA takes many years to develop, cartilage ageing does occur resulting in splitting and flaking of the surface, diminished cellularity, reduction of proteoglycane ground substances and loss of elasticity with decrease in breaking strength¹.

There is no single cause of OA, it result from a disparity between the stress applied to cartilage and ability of cartilage to with stand that stress, this may be due to either increased stress or weak cartilage or on the other hand abnormal support by sub chondral bone⁴. Zinc play a fundamental role in the collagen biosynthetic activity which largely responsible for the development tensile strength in the wound healing⁶. In zinc deficient state, there is a significant reduction in the total collagen⁶. On the other hand the strength of collagen is due to a considerable extent to the formation of covalent cross-links the first reaction in this process was catalyzed by the copper containing enzyme lysyl oxidase which convert lysine residues to aldehyde allysine⁷.

Calcium, phosphate and magnesium were involved in the formation of crystals on the matrix of protein collagen. These crystals called hydroxyl apatite invade the bone mineralization⁸.

Uric acid is the end product of the purine metabolism, and when it precipitated in the joints as mono sodium urate crystals it causes gout, which is the acute inflammatory arthritis and can lead to chronic destructive joint disease⁹.

Therefore, we suggested this study and our aims were to measure serum levels of calcium, inorganic phosphate, magnesium zinc and copper and uric acid in osteoarthritic patients and non osteoarthritic subjects and to find out

the effect of age sex and severity of the daises on the above parameter studied and to know under limit extent whether these parameters can or cannot affect the progressive and disintegration of articular cartilage.

Materials and methods

A prospective case control study conducted at Basrah province through a period of 9 months from the first of October 2001 till the end of July 2002 through which 100 patients with different types of osteoarthritis, whom were admitted to the Orthopedic Clinic of Basrah General Hospital were included. There age range from 40 to 68 years (24 males and 76 females) and were allocated into three groups according to their symptoms and radiological finding.

Group 1: Those were 22 patients with mild OA, figure1.

Group2: Those were 58 patients with moderate OA, figure2.

Group3: Include 20 patients with severe OA, figure 3. The above three groups are 100 patients with osteoarthritis of knee included 19 patients were associated with degenerative changes of spin.

The other 80 asymptomatic patients were (23 males and 57 females), their ages range from 35 to 68 years were participated as a control group from each patients and subjects full information were obtained by using questionnaire that include name, ages, sex, occupation as well as the following questions about the medical history. Physical and radiological examination was done including X-rays to exclude secondary osteoarthritis & laboratory investigation for erythrocyte sedimentation rate (ESR), white blood cell count, blood sugar and latex fixation were also done for all subjects and patients participated in this study.

Blood samples were collected and serum was separated and tested for calcium, inorganic phosphate, uric acid,

copper, zinc and magnesium by using standard methods and kits from Biomerix.

Statistical analysis with each group of subjects was performed by analysis of variance (ANOVA) and the results were expressed as mean \pm SD. A P value less than (0.05) was considered as statistically significant.

Results

The basic clinical characteristic for all subjects (patients and non-patients) participated in this prospective study regarding to age, sex, type of OA and severity of disease are presented in table I.

Table II shows the mean \pm SD of serum calcium, inorganic phosphate uric acid copper, zinc and magnesium in different types of OA and severity of disease at different age groups. Among two age groups serum Ca and Zn levels were significantly lowered ($p > 0.05$) in patients having moderate OA of knee as compared with mild OA. However serum uric acid was significantly increased ($p > 0.05$) in patients having mild OA of knee as compared with mild OA of knee and spine.

Serum Cu and P levels were non significantly altered ($p < 0.05$) in two types of OA among two different age groups and as compared with control subjects.

The only significance reduction in serum Mg level was in severe and moderate OA of knee and combined among two age groups.

The effect of type of sex on the mean \pm SD of serum Ca, P, UA, Cu, Zn and Mg levels in two different types and severity of OA was presented in Table III.

High significant decrease ($p > 0.01$) in serum Ca and Zn was observed in the female patients having moderate OA of knee compared with mild females and with moderate of OA of knee and spine and on the other hand in the total Ca and Zn levels in the female patients having

OA of knee compared with control subject.

Significant increase ($p > 0.05$) in serum UA levels in the male patients having moderate OA of knee compared with female patients and also in the total groups when compared to control subject.

Serum Mg level was highly significantly decrease ($p > 0.01$) in male patients, who have sever OA of knee compared with diffused patients or on the other hand in the male patients with mild OA of knee and female group ($p > 0.05$).

Non-significant alteration ($p < 0.05$) was observed in serum inorganic phosphate and copper among different sex groups.

Discussion

This study revealed the high percentage of OA at age range from 40-55 years and at the same time high percentage confined to the females rather than males or on the other hand the moderate OA of knee represent the higher proportion which is nearly compatible with other studies¹⁰⁻¹².

Many different factors and possibilities cause the significant decreases in the serum calcium levels. One of the possibilities was due to the high phosphate: calcium ratio which leads to the excessive loss of calcium in the urine or might be the low intake of vitamin D which was associated with the increased the risk for progression of OA of knee^{13,14} or on the other hand to increase the stress or excretion of calcium¹⁵.

The significant increase in serum uric acid level in the present study was almost as the same finding that was observed by other study¹⁶. This observation was found in respect to age, sex and to the type of OA. The possible explanation for these results could be attributed to increase turnover of nucleic acids in tissue break down after tissue damage or due to the sex hormonal

effect leads to increase urate excretion as in female¹⁷.

and spin, such results was matching with other study¹⁴. The responsible causes of such finding might be due to either the interruption of intake for prolong periods, or due renal wastage either due to the effect of drugs or chemicals or on the other hand due to renal pathology¹⁴.

The possible causes of the significant decrease in serum zinc levels in moderate OA of knee at different age and sex groups could be attributed to low dietary intake of food having zinc¹⁸ or on the other hand due to the effect of stress on those patients¹⁵. These results was nearly compatible with other studies^{19,20}. The comparison between variable groups of patients showed high significant decrease in serum magnesium levels in patients with severe OA of knee and those having sever diffuse OA of knee

Serum copper and phosphate showed no significant alteration among different age sex or type of OA groups.

There for the present study has been constructed to throw a light on the levels of those elements in osteoarthritis patients and to show or to know whether these element can promote or suppress the incidence of this disease.

Table II: Serum levels of calcium, inorganic phosphate, uric acid and control subjects, copper, zinc and magnesium in different types of OA and severity of disease at different age groups.

Values are expressed as mean \pm SD. N= no of patients and subjects. *P > 0.05, **P > 0.01, ***P > 0.001

	≤ 55						>55					
	Ca	P	UA	Cu	Zn	Mg	Ca	P	UA	Cu	Zn	Mg
	Mg/dl	Mg/dl	Mg/dl	Ug/dl	Ug/dl	Ug/dl	Mg/dl	Mg/dl	Mg/dl	Ug/dl	Ug/dl	Ug/dl
Mild	9.3 \pm 9 N=7	3.6 \pm 1 N=7	7.9 \pm 0.7* N=7	126 \pm 46 N=7	132 \pm 46 N=7	1.9 \pm 0.5 N=7	10 \pm 0.6 N=2	5 \pm 0 N=2	8.2 \pm 0.4 N=2	66 \pm 31 N=2	10 N=2	2.6 \pm 0.5 N=2
Moderate	7.6 \pm 1 ** N=26	3.3 \pm 1 N=26	7.7 \pm 1 N=26	126 \pm 45 N=26	108 \pm 39 *N=26	2 \pm 0.4 N=26	7.7 \pm 1 *** N=21	3.1 \pm 1.1 N=21	7.6 \pm 0.7 N=21	129 \pm 46 N=21	95 \pm 38 N=21	1.9 \pm 0.4 * N=21
Severe	7.4 \pm 1 N=5	3.9 \pm 1 N=5	8.2 \pm 0.6 N=5	101 \pm 31 N=5	110 \pm 22 N=5	1.7 \pm 0.2 N=5	9.2 \pm 1.9 N=10	3.9 \pm 1.1 N=10	7.9 \pm 0.7 N=10	123 \pm 44 N=10	129 \pm 54 N=10	1.8 \pm 0.2 *** N=10
Total	8.2 \pm 1 N=48	3.4 \pm 1 N=48	7.9 \pm 0.9 *** N=48	116 \pm 44 N=48	116 \pm 37 N=48	1.9 \pm 0.4 N=48	8.3 \pm 1.6 * N=23	3.4 \pm 1.2 N=23	7.7 \pm 0.8 *** N=23	123 \pm 46 N=23	104 \pm 43 N=23	1.9 \pm 0.4 N=23
Mild	8 \pm 2.2 N=3	3.2 \pm 1 N=3	6.6 \pm 1.9 N=3	108 \pm 63 N=3	70 \pm 17 *N=3	1.8 \pm 0.2 N=3						
Moderate	8.8 \pm 1 N=9	3.1 \pm 1 N=9	8 \pm 0.6 N=9	141 \pm 59 N=9	115 \pm 47 N=9	1.8 \pm 0.3 N=9	79 \pm 1.2 N=2	2.6 \pm 1.4 N=2	7.9 \pm 0.1 N=2	110 \pm 32 N=2	98 \pm 3.5 N=2	1.7 \pm 0.1 N=2
Severe	8 \pm 0 N=1	3.3 N=1	8 N=1	55 N=1	110 N=1	2.3 N=1	11 \pm 2 N=4	4.4 \pm 0.6 N=4	7.7 \pm 0.5 N=4	99 \pm 59 N=4	110 \pm 39 N=4	2.4 \pm 0.4 N=4
Total	8.6 \pm 1 N=13	3.1 \pm 1 N=13	7.7 \pm 1.1 *** N=13	126 \pm 60 N=13	104 \pm 43 N=13	1.8 \pm 0.3 N=13	9.9 \pm 2 N=6	3.8 \pm 1 N=6	7.8 \pm 0.4 *** N=6	103 \pm 48 N=6	106 \pm 31 N=6	2.1 \pm 0.4 N=6
Control	8.7 \pm 1	3.6 \pm 1 N=68	4.8 \pm 1 N=68	129 \pm 38 N=68	118 \pm 34 N=68	1.9 \pm 0.4 N=68	8.9 \pm 1 N=12	4 \pm 0.9 N=12	4.8 \pm 0.9 N=12	122 \pm 41 N=12	107 \pm 28 N=12	1.9 \pm 0.6 N=12

Table III: Serum levels of calcium, inorganic phosphate, uric acid, copper, zinc and magnesium in different types of OA and severity disease and control subjects among different sex groups. Values are expressed as mean \pm SD. N= no of patients and subjects. *P > 0.05, **P > 0.01, ***P > 0.001.

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	Male						Female					
	Ca	P	UA	Cu	Zn	Mg	Ca	P	UA	Cu	Zn	Mg
	Mg/dl	Mg/dl	Mg/dl	Ug/dl	Ug/dl	Ug/dl	Mg/dl	Mg/dl	Mg/dl	Ug/dl	Ug/dl	Ug/dl
Mild	9±2 N=5	3.3±1 N=5	8.2±0.2 N=5	121±51 N=5	142±57 N=5	1.7±0.1 N=5	9.5±2 N=14	3.9±1 N=14	7.8±0.7 N=14	129±47 N=14	125±41 N=14	2±0.6 N=14
Mod.	8.2±1 N=10	3.3±1 N=10	8.2±0.69 * N=10	112±49 N=10	104±31 N=10	2±0.5 N=10	7.5±1 ** N=37	3.2±1 N=37	7.5±0.9 N=37	122±46 N=37	102±35 * N=37	1.9±0.3 N=37
Severe	9.5±1 N=6	4.4±0.9 N=6	8.1±0.7 N=6	120±35 N=6	113±65 N=6	1.8±0.2 ** * N=6	8.1±2 N=9	3.6±1 N=9	8±0.7 N=9	118±46 N=9	121±30 N=9	1.7±0.2 *** N=9
Total	8.8±1 N=21	3.6±1 N=21	8.2±0.6 ** N=21	116±44 N=21	116±49 N=21	1.9±0.4 N=21	8.1±1 ** N=60	3.4±1 N=60	7.7±0.8 *** N=60	124±45 N=60	110±37 N=60	1.9±0.4 N=60
Mild	-	-	-	-	-	-	8±2 N=3	3.2±1 N=3	6.6±1 N=3	108±62 N=3	71±17 * N=3	1.8±0.1 N=3
Mod.	8.5 N=1	2.3 N=1	8.5 N=1	111 N=1	81 N=1	2.1 N=1	8.7±1 N=10	3.1±1 N=10	7.9±0.6 N=10	138±58 N=10	115±44 N=10	1.7±0.3 * N=10
Severe	9.1±0.07 N=2	5±0.0 N=2	8±0.7 N=2	94±8.4 N=2	110±57 N=2	2.6±0.4 N=2	11±2.7 N=3	3.7±0.4 N=3	7.6±0.3 N=3	88±78 N=3	110±25 N=3	2.2±0.1 N=3
Total	8.9±0.3 N=3	4.1±1.5 N=3	8.1±0.5 *** N=3	99±11 N=3	100±43 N=3	2.4±0.4 N=3	9±2 N=16	3.2±1.2 N=16	7.6±1*** N=16	123±61 N=16	106±40 N=16	1.8±0.2 N=16
Contr.	8.7±1.2 N=23	4±1.3 N=23	4.9±1 N=23	115.6±26 N=23	116±33 N=23	2±0.4 N=23	8.8±1.3 N=57	3.5±1.2 N=57	4.8±1 N=57	133±42 N=57	116±33 N=57	1.9±0.5 N=57

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