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## OKING : TOXIC EFFECTS 1N OSTEOARTHRITIS

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# SMOKING : TOXIC EFFECTS 1N OSTEOARTHRITIS

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## ABSTRACT

The material for the present study included 24 patients (18males & 6femals) with osteoarthritis (OA) selected from Rheumatology and rehabilitation out patients clinic Mansoura University Hospital with age range from (45-67 years). 16 patients were heavy smokers consuming > 20 cigarette /day for long duration > 15 years while 8 patients were non smokers. 8 normal (non smokers) healthy volunteers with matched age and sex served as control. All patients were subjected to radiologic assessment of (OA) using Kellgren Lawrence grading scal, and clinical assessment including body mass index (BMI) and WOMAC (Western Ontario and McMaster universities) index of osteoarthritis. Using Perkins

Elmer atomic absorption spectrophotometry , both plasma cadmium (Cd) and lead (Pb) levels were found to be significantly increased among patients with OA exposed to intoxication through heavy cigarette smoking for long duration. A+ve correlation was found between plasma Cd & Pb levels and severity of OA. Also plasma Cd & Pb levels were found to be significantly increased among, middle aged , slim (non obese) smokers with OA compared with elderly obese patients. In light of previous findings we can conclude that exposure to toxic effect of smoking for long duration may contribute to pathogenesis of OA even in absence of some other risk factors such as older age and obesity

**Introduction and Aim of work**

Tobacco plant naturally absorbs, accumulate and concentrate toxic elements as cadmium (Cd) and lead (Pb). Most probably from soil fertilizers or pesticides (Wagner: 1993) other environmental factors that may influence the uptake of toxic elements by tobacco plant include pH of soil, contaminated irrigated water and sewage sludge used as fertilizers. Cd and Pb readily pass from inhaled smoke to the blood stream (Csalari.; and Szantai. 2002). These heavy metals are known to have toxic effects not only to bones but also to cartilage (Milachowski, 1988). Osteoarthritis is the most common form of arthritis (Lawrence et. al 2008) while some risk factors for osteoarthritis (OA) are known such as older age and obesity (Zhang, and Jordan 2008). The disease process remains poorly understood and no effective disease modifying treatments are currently available. Regional difference in arthritis prevalence are suggestive of possible contribution of other factors. Haemochromatosis a genetic disorder of heavy metal (iron) metabolism is frequently associated with arthropathy with features similar to those with (OA), Sokoloff (1985) and Jordan (2004). Putting

these observations in consideration, we considered the possibility of heavy exposure to toxic effects of smoking for long duration as novel risk factor for (OA).

**MATERIAL AND METHODS**

The material for the present study included 24 patients with osteoarthritis (OA) selected from rheumatology and rehabilitation outpatients clinic of Mansoura University Hospital, including 18 males and 6 females with age ranged from 45 – 67 years. Eight normal (non smokers) healthy volunteers with matched age and sex served as control group. All patients and volunteers were subjected to the following investigations.

**1) Radiological assessment of osteo-arthritis**

Using Kellgren Lawrence grading scale (Kellgren and Lawrence; 1957).

*Grade I* : Doubtful narrowing of joint space and possible osteophytic lipping.

*Grade II* : Definite osteophytes and definite narrowing of joint space.

*Grade III* : Moderate multiple osteophytes , definite narrowing of joint space, some sclerosis and possible deformity

of bone contour.

*Grade IV* : Large osteophytes , marked narrowing of joint space, severe sclerosis and definite deformity of bone contour.

## 2) Clinical data

Including age, sex , personal habits (smoking), body mass index (BMI) and clinical assessment of osteoarthritis (OA) using WOMAC (Western Ontario and McMaster university index) (Bellamy 1989).

Total score : (Minimum score = 0 maximum score = 96).

- 3) Determination of plasma Cd and Pb concentrations using Perkins Elmer atomic absorption spectrophotometry (Stockwell and Corns. 1993) were done for all patients and volunteers.
- 4) Patients with osteoarthritis included 8 non smokers (6femals and 2males) while 16males were heavy smokers consuming > 20 cigarettes /day for long duration > 15 years.
- 5) Among heavy smokers 7 patients were elderly > 60 years and obese with body mass index (BMI) > 30 while 9 patients were middle aged (45-56) years , slim (non obese) with BMI (23-26).
- 6) Assessment of osteoarthritis

among heavy smokers according to WOMAC index score and Kellgren Lawrence radiologic grading scale revealed.

- i. Mild OA in 8 patients with radiologic scale (Grade I & II) and WOMAC index total score <30.
- ii. Moderate and severe disease in 8 patients with radiologic scale (Grade III & IV) and WOMAC index total score (>60)

\* Statistical analysis was done using Student T test and pearson correlation test Rifenburgh (1999).

## RESULTS

1. Plasma Cd & Pb concentrations were significantly increased ( $P=<0.001$ ) among heavy smokers patients with osteoarthritis compared with healthy volunteers (Table I).
2. plasma Cd and Pb level were insignificantly increased among non smokers OA patients compared with control group (table II).
3. plasma Cd and Pb levels in patients with (OA) were significantly increased ( $P=<0.001$ ) among heavy smokers compared with non smokers (table III).
4. plasma Cd and Pb levels were significantly increased among

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middle aged – non-obese smokers OA patients compared with elderly obese smokers (table IV).

5. A+ve correlation was observed between plasma Cd and Pb con-

centrations and severity of osteoarthritis in patients heavily exposed to toxic effects of smoking for long duration (Table V).

**Table (I):** Plasma Cd and Pb levels in patients with OA (smokers) compared with control group

Plasma Cd & Pb concentration	(OA) patients (smokers)	Control group	P value
	M ± SD	M ± SD	
Cd µgm/dL	8.6 ± 1.3	0.23± 0.02	< 0.001
Pb µg/dL	32 ± 1.2	12 ± 3.6	< .001

**(Table II):** Plasma Cd and Pb levels in patients with OA (non smokers) compared with control group

Plasma Cd & Pb concentration	(OA) patients (Non smokers)	Control group	P value
	M ± SD	M ± SD	
Cd µgm/dL	0.28 ± 0.6	0.23± 0.02	> 0.005
Pb µgm/dL	13.2 ± 0.4	12 ± 3.6	> .005

**(Table III):** Plasma Cd and Pb levels in patients wit OA (smokers versus non smokers)

Plasma Cd & Pb concentration	patients with (OA) smokers	patients with (OA) Non smokers	P value
	M ± SD	M ± SD	
Cd µgm/dL	8.6± 1.3	0.28 ± 0.6	<0.001
Pb µgm/dL	32 ± 1.2	13.2 ± 0.4	<0.001

**(Table IV):** Plasma Cd and Pb levels in patients wit OA (smokers) elderly obese versus middle aged slim (non obese) patients

Patients with OA (smokers)	Middle aged non-obese patients	Elderly obese patients	P value
Cd & Pb plasma concentration	M ± SD	M ± SD	
Cd µg/dL	9.8 ± 0.41	7.4 ± 0.32	< 0.05
Pb µg/dL	36 ± 0.6	28 ± 0.23	< 0.05

**(Table V):** Cd & Pb plasma levels in correlation with severity of (OA) in patients exposed to toxic effects of smoking for long duration

Patients with OA (smokers)	Patients Grade I & II (radiologic scale) & WOMAC index score <30 (Mild Disease)	Patients Grade III & IV (radiologic scale) & WOMAC index score >60 (Moderate and severe Disease)	P value
Cd & Pb plasma concentration	M ± SD	M ± SD	
Cd µg/dL	7.6 ± 0.21	9.9 ± 0.3	<0.05
Pb µg/dL	27.3 ± 2.8	37.2 ± 2.4	<0.05

## DISCUSSION

Tobacco leaves naturally accumulate and concentrate relatively high levels of Cd and Pb and therefore smoking of tobacco is an important source for these toxic metals exposure (Kazi et al 2009). In the present study both plasma Cd and Pb concentrations were found to be significantly increased in OA patients exposed to intoxication through heavy cigarette smoking for long duration of time > 15 years. Several studies showed a direct connection between Cd intoxication and bone damage even minimal exposure is supposed to cause skeletal demineralization (Nordberg 2004 and Jarup et al. 1998) cadmium is heavy metal poison with severe risk to human health (Johannes et al. 2006). Cadmium is widely used in industrial processes phosphate fertilizers also show big Cd load (Jarup L 2003). The major source of Cd intoxication is cigarette smoke, the human lung absorbs 40-60% of Cd in tobacco smoke. Smokers generally have cadmium blood level 4-5 times those of non smokers (Goyer 1996). Cadmium alters calcium and phosphorous metabolism thus contributing to arthritis, osteoporosis and neuromuscular disease (Tandon et al. 2001). Cd can

deposit in bone from respiratory exposure, it may deplete glutathione resulting in the production of injurious reactive oxygen species such as super oxide, hydrogen peroxide and hydroxyl radicals (Nordberg 2004). Recent study suggest that even low level of Cd exposure will decrease the viability of osteoblast meanwhile Cd significantly stimulate the formation of osteoclasts (Chen et al. 2011). Approximately 95% of total body (Pb) burden in adults is stored in bone and has half life of decades (Barry, Mossman 1970) which contributes as much as 65 % to measured blood level (Holz et al. 2007). Pb deposition has been observed in both cartilage and bone in human OA (Wittmers et al 1998). The toxic element (Pb) and polycyclic aromatic hydrocarbons in cigarette smoke interact with cells of Skeletal system adversely affecting bone and cartilage (Barry et al. 2008). Recent study reported arthropathy caused by lead bullet causing multiple metallic fragments in and around joint space as well as signs of OA. Physical examination findings were consistent with moderate osteoarthritis removal of (Pb) intra articular foreign body is indicated even if the material is not believed to mechanically interfere with

joint motion. (Barry et al 2008).

In the present study a +ve correlation was found between plasma Cd & Pb levels and severity of OA (assessed according to Kellgren Lawrence grading scale and WOMAC index) in patients heavily exposed to toxic effects of smoking. Also plasma Cd & Pb levels were found to be significantly increased among heavy smokers, middle aged slim, (non obese) patients with OA compared with elderly obese patients. In light of previous findings we can conclude that exposure to toxic effects of smoking for long duration may contribute to pathogenesis of OA even in absence of some other risk factors such as older age and obesity.

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## الملخص العربى

### التدخين وآثاره السامة فى مرضى

### التهاب وخشونة المفاصل

اجرى هذا البحث على ٢٤ مريضا (١٦ من الذكور و٨ من الإناث) يعانون من مرض التهاب وخشونة المفاصل تم اختيارهم من العيادة الخارجية لمرضى الروماتيزم والتأهيل بمستشفى المنصورة الجامعى تراوحت أعمارهم ما بين (٤٥ - ٦٧ عاماً) وكان منهم ١٦ مريضاً يمارسون عادة التدخين بشراهة (يستهلكون أكثر من ٢٠ سيجارة يوميا ولمدة تزيد على ١٥ عاماً) وتم اختيار ثمانية من الأصحاء المتطوعين الذين لا يمارسون عادة التدخين كمجموعة ضابطة متماثلة مع المرضى فى السن والجنس - وتم تقييم الحالة الإكلينيكية للمرضى وتقدير نسبة عنصرى الرصاص والكادميوم بالدم باستخدام تقنية (الامتصاص الذرى) وقد لوحظ من نتائج هذا البحث ان عادة التدخين تؤدي إلى زيادة عنصرى الرصاص والكادميوم بالدم وزيادة ترسيب هذه العناصر السامة بالمفاصل وتبين من نتائج البحث أن الآثار السامة الناتجة عن عادة التدخين من الممكن أن تكون أحد العوامل الهامة المؤدية إلى حدوث التهاب وخشونة المفاصل حتى فى المرضى صغار السن واللذين لا يعانون من السمنة وزيادة الوزن .