

An Investigation of the Risk Factors of Osteoporosis and the Correlation between Opium Consumption and Osteoporosis in Adults

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Original Article

Abstract

Background: Osteoporosis and osteopenia are the most common metabolic bone diseases making the patients vulnerable to bone fragility and fracture. In this study, the association of opium consumption and osteoporosis adjusted for other risk factors was studied.

Methods: In this cross-sectional study, 619 cases including 73 men and 546 women referred to densitometry center in Kerman, Iran, were studied. Demographic information, history of opium consumption, medications, and other risk factors were collected using a structured questionnaire.

Findings: In a univariate analysis, opium consumption, aging, and having a body mass index (BMI) lower than 24 accompanied an increased chance of osteoporosis, while taking physical exercises on a daily basis reduces the chance of osteoporosis. Through multivariable analysis, the two variables of age group and BMI group turned out to be of significance; that is, the chance of osteoporosis or osteopenia in the age group of higher than 60 years and 45-60 years being placed in one of the levels of osteoporosis or osteopenia was 4.9 and 3.1 times higher than the age groups lower than 45 years, respectively, after being adjusted to the other variables.

Conclusion: Considering the results of this study, though the risk of bone density reduction in the individuals consuming opium was higher, due to the disparity between opium consumption in the two sexes, the difference was not significant between the two groups, and it is proposed that studies on larger samples and in the both sexes be conducted to determine the impacts of opium on the bone density.

Keywords: Opium; Osteoporosis; Osteopenia

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Introduction

Osteoporosis and osteopenia are the most common metabolic bone diseases which can be characterized by low bone density. Osteoporosis is an asymptomatic disease causing the patients to be vulnerable to bone fragility and fracture even following the mild blows and falls.¹ The majority of fractures in individuals over 50 years of age are due to osteoporosis. In addition to increasing pain and mortality, the fractures caused by osteoporosis increase the length of hospitalization.² Osteoporosis is a prevalent issue and, in other words, a hidden epidemic which is currently turning into a major healthcare concern worldwide. The statistics indicate that 200 million adults are suffering from it, and the prevalence of osteoporosis varies from 4% to 40% globally.³ It has been estimated that one out of 2 women and one out of 8 men are exposed to fractures caused by osteoporosis in the course of their lives. In European nations, every 30 minutes, one individual experiences fracture caused by osteoporosis.⁴ By 2050, approximately 44 million people will have been suffering from varied degrees of osteopenia and 5 million more will have suffered from osteoporosis. In Iran, the prevalence of osteopenia and osteoporosis in women older than 50 years is 22.2% and 59.9% respectively, and among the men of the same age is 11.0% and 50.1%, respectively.³ A study on the burden of osteoporosis conducted in 2004 indicated that disability-adjusted life years (DALYs) related to osteoporosis in the Iranian population was 36026.⁵

The major risk factors of bone mineral density (BMD) reduction include age, sex, lifestyle, nutrition, hormonal changes,⁶ personal history of fractures in adulthood, background of fracture in a first-degree relative, low body weight (< 58 kg), smoking, and consumption of oral glucocorticosteroids for three months or longer.^{7,8} Furthermore, it has been reported that 20%-50% of bone mass changes are associated with lifestyle. Lack of physical activities, smoking, alcohol consumption, and low calcium and vitamin D intake are the major lifestyle factors contributing to low bone density and the increasing risk of osteoporosis and the related fractures.^{1,9} Moreover, some evidence suggest that bone fractures including pelvic fractures are higher in

the individuals using opioids chronically.¹⁰ Epidemiologic studies have reported the risk of fracture to be 1.4 to 5 times more among the drug users. A study conducted by Li et al.¹¹ indicated a dose-response relationship between opioid consumption and risk of fracture. The findings of a study by Gozashti et al.¹ indicated that opium addicts are more vulnerable to the occurrence of BMD loss comparing with non-addicts. Pedrazzoni et al.¹² conducted a study regarding the effect of chronic consumption of heroin on mineral and bone metabolism and indicated that the trabecular bone mass and the density of bone minerals in vertebrae was significantly lower among heroin consumers compared to control group. Most of these studies suffer from ignoring the role of potential confounders such as physical activity and dietary factors in their analysis.

Based on the latest statistics issued by the United Nations Office on Drugs and Crime (UNODC) in 2016, there are 29 million addicts in the world, 3 million of whom reside in Iran, and approximately 5%-9% of the Iranian population is currently addicted to addictive substances.^{1,13} Considering the high prevalence of addiction in Kerman,^{14,15} and contradictory reports on the association between opium consumption and osteoporosis, and methodological limitations of current literature, and also regarding the healthcare, economic, and social significance of osteoporosis and fractures, the present study was conducted with the purpose of investigating the association of opium consumption and osteoporosis adjusted for potential confounders.

Methods

In this cross-sectional study, individuals above 18 years who referred to a private densitometry center in Kerman, Iran, in 2015, recruited to the study using convenience sampling. The inclusion criteria were: absence of rheumatoid arthritis disease, thyroid, parathyroid, and adrenal diseases, hepatic and renal failure, metabolic bone disease, diabetes mellitus type 1, infertility, malabsorption, immobility longer than 1 week, lactation, and previous history of malignancy. The final sample consisted of 619 cases including 73 men and 546 women.

After obtaining informed consent, independent variables including demographic (age, sex) and anthropometric (height, weight,

waist size) information, past history of medications (cortisone, levothyroxine), risk factors of osteoporosis (past history of fracture, family history of fracture, lactation, taking physical exercises on a daily basis, milk intake, age at menopause), and history of smoking and opium consumption were collected using a structured questionnaire. According to Diagnostic and Statistical Manual of Mental Disorders-5th Edition (DSM-IV) criteria, the individuals who had at least three of the following seven signs during a 12-month period were considered as opium-dependent: 1) tolerance to opium consumption, 2) having withdrawal signs in the case of non-consumption, 3) need for increasing opium consumption with passing of time, 4) persistent desire for decreasing or quitting consumption, 5) spending significant amount of time for preparing opium or freedom from this substance effects, 6) leaving social, professional and recreational activities, 7) persistent opium consumption in spite of knowing the physical or psychological outcomes of opium consumption.

Patients underwent the BMD testing in their lumbar vertebrae (L1-L4), neck of femur, and total of femur using hologic explorer dual X-ray absorptiometry (DXA) system. Based on the definition by World Health Organization (WHO), osteoporosis and osteopenia was defined on the basis of the bone density at the site compared to average of maximum bone density in young, healthy adults of the same race and sex. The T-score of -1 and -2.5 were considered as osteopenia and the T-score of -2.5 or lower considered as osteoporosis. If an individual had osteoporosis or osteopenia in at least one of three evaluated areas, the diagnosis of osteoporosis or osteopenia was assigned to them.

The data analysis was conducted by ordinal regression and chi-square statistical tests using SPSS software (version 20, IBM Corporation, Armonk, NY, USA). The variables with a P value of less than 0.20 in the univariable analysis were

entered to the multivariable ordinal regression model. The P value of less than 0.05 was considered as the level of significance.

Results

Of 619 recruited cases, 73 cases (11.7%) were men and 550 cases (88.3%) were women. The age range of participants was 24 to 83 years with the mean \pm standard deviation (SD) of 56.8 ± 9.7 . Most of the individuals had the body mass index (BMI) of 25-29.99 (38.2%), drunk one-glass of milk daily (50.7%), and took physical exercises for one hour a day (75.0%). Totally, 92 cases (14.7%) used opium, of whom 66.3% were women and 33.7% were men. Only 42 cases (6.7%) were tobacco consumers from whom 21 cases were women and 21 cases were men. Around 39% of cases had osteopenia and 46% had osteoporosis in at least one site, and 15% of cases had normal BMD in all three sites (Table 1).

In univariable analysis, opium consumption, aging, and having a BMI lower than 24 increased the risk of osteoporosis, while daily physical exercise reduced the risk; so that, the risk of osteoporosis or osteopenia in opium consumers was 1.68 times higher than those not consuming opium, and 33% lower in those taking physical exercises for more than 1 hour a day comparing to those with 1-hour daily physical exercise (Table 2).

In the multivariable model, age group and BMI significantly have been associated with having osteopenia and osteoporosis. Therefore, the probability of the age group of higher than 60 years and 45-60 years being placed in one of the levels of osteoporosis or osteopenia was 4.9 and 3.1 times higher than the age groups lower than 45 years, respectively, after being adjusted to the other variables. Moreover, the chance of osteoporosis or osteopenia in BMI of 25-29.99 and BMI > 30 was 0.54 and 0.50 times lower than BMI < 24.99, respectively, after being adjusted to the other variables (Table 2).

Table 1. The dispersion of the samples under study in the bone mineral density (BMD) range

BMD	Lumbar [n (%)]	Neck of femur [n (%)]	Total of femur [n (%)]	Total [n (%)]
Normal	114 (18.4)	335 (54.0)	482 (78.2)	94 (15.1)
Osteopenia	228 (36.8)	238 (38.5)	118 (19.1)	240 (38.8)
Osteoporosis	277 (44.8)	46 (7.5)	19 (2.7)	285 (46.1)

BMD: Bone mineral density

Table 2. The ordered logistic regression to investigate the simultaneous effects of the independent variables on osteoporosis or osteopenia

Variable	n	Multivariable analysis		Univariable analysis		
		CI 95%	OR	CI 95%	OR	
Sex	Men	73	-	-	0.73-1.87	1.20
	Women	546				
Age group (year)*	< 45	59	-	1.00	-	1.00
	45-60	359	1.80-5.40	3.10	1.70-4.80	2.90
	> 60	193	2.70-9.10	4.90	3.40-10.60	6.00
Smoking*	No	577	0.58-2.90	1.34	0.99-3.50	1.90
	Yes	42				
Opium*	No	527	0.74-2.00	1.24	1.08-2.70	1.70
	Yes	92				
BMI group (kg/m ²)*	< 24.99	201	-	1.00	-	1.00
	25-29.99	231	0.37-0.81	0.54	0.36-0.75	0.52
	> 30	177	0.30-0.70	0.50	0.30-0.70	0.45
Daily milk intake*	No consumption	303	0.66-1.30	0.91	0.60-1.10	0.81
	one glass and more	312				
Daily exercise*	≤ one hour	148	0.55-1.20	0.82	0.47-0.95	0.67
		444				

OR: Odds ratio; CI: Confidence interval; BMI: Body mass index

*Variables entered to the final adjusted model

Discussion

In the present study, the relationship between opioid and osteoporosis were studied in Iranian population. In the adjusted analysis, having lower BMI and belonging to older sex group have been associated to an increased chance of osteopenia or osteoporosis. However, the significant relationship between opioid and osteoporosis was not found.

The results of this study indicate that the risk of osteoporosis and osteopenia is higher in the cases older than 60 years which is consistent with other studies.^{9,16-20} In a study by Soheyl Azad et al., it was indicated that there is a significant association between the age higher than 50 years and osteoporosis occurrence, with the higher risk of osteoporosis occurrence among the cases higher than 50 years of age comparing to those lower than 50 years.¹⁹ In a study by El-Desouki on the postmenopausal women of Saudi Arabia, it was indicated that 58% of women aging 50-59 years have osteoporosis and osteopenia with the rate increasing to 89% in case of the age group of 60-69 years and to 94% in case of the age group of 70-80 years.²⁰

The results of a number of epidemiologic studies suggest that obesity is a protective factor against osteoporosis.^{4,8,16,18,21-23} The present study also indicated an association between BMI and osteoporosis, with the risk of osteoporosis and

osteopenia being higher among the cases with BMI more than 30. This can probably be attributed to the point that an increase or decrease in BMI changes the amount of estrogen production through affecting the body fat amount resulting in impacts on the extent of bone density.⁸ Moreover, in the present study, BMI was found out to be a strong predictor variable in a way that its correlation with the outcome variable increased through controlling other variables. The mentioned results confirmed the result of a study by Seeman et al., indicating a correlation between BMD and low weight in a way that a 10% increase in the mass of femur neck accompanied a 15% increase in the fat-free mass.²⁴

Though in most studies smoking is an independent risk factor related to osteoporosis,^{1,7,18,22,25} in the present study the association was not significant. Since the majority of the sample cases were women and the number of tobacco consumers is lower in women than men, the varied results of this study compared to other studies might be attributed to the low number of tobacco consumers in the present study.

Sustaining an active lifestyle in the last decades of life can potentially decrease the risk of osteoporosis,²⁶ and a number of studies confirm this point;^{17-19,26,27} however, no association was detected between osteoporosis and daily physical exercise in this study. Although a number of

studies confirmed a direct association between dairy intake and osteoporosis,^{19,28} the present study did not detect such association. In a study by Stracke et al., it was maintained that sufficient calcium intake by consuming milk and dairy products in childhood and adolescence leads to obtaining the maximum bone mass and prevention of osteoporosis; nevertheless, an increase in dairy products intake in years afterwards might not reduce the risk of osteoporosis caused by insufficient calcium intake in childhood and adolescence.²⁹ As we asked about the current milk intake of participants (and not their intake during their childhood or adolescence), obtaining a non-significant association may be plausible. On the other hand, in a study by Sowers et al., it was pointed out that there is no considerable association between the estimated amount of calcium intake and the bone density; however, in the individuals receiving more than 800 mg of calcium per day alongside with 400 IU of vitamin D, the average bone density had been considerably higher.³⁰

The majority of studies have indicated a correlation between opioids and osteoporosis;^{1,5,7,11} however, in the present study we have not captured any significant association between opium and osteoporosis, which is in line with a number of other studies.^{10,31,32} This may be because of the fact that most studies have not adjusted the association of opium and BMD based on potential confounders, while we, in our adjusted analysis, considered the role of smoking, dietary factors, BMI, and physical exercise simultaneously which may provide a more valid results. On the other side, we chose the normal group from referees to densitometry clinic. It is possible that these individuals do not represent the healthy individuals in the population which resembles then in some risk factors to the patient with osteopenia and osteoporosis, and consequently causes dilution in odds ratio.

Although discrepancy between the results of related researches may limit our understanding of the role of opium consumption on bone density, some studies have suggested the following mechanisms in opium related osteoporosis: First is the increased risk of fall due to opioid influences on the central nervous system (CNS), and the second mechanism may be alteration of bone metabolism through hypogonadism caused

by opioids. Hypogonadism is a potential side-effect of opioids which can be a secondary cause of osteoporosis. Some studies suggested that opium influences μ receptors in hypothalamus, inhibiting Gonadotropin-releasing hormone (GnRH), and causes central hypogonadism. Therefore, hypogonadism in both men and women may be associated with increased risk of osteoporosis.^{10,17,33} Moreover, opioids have been associated with reduction in dehydroepiandrosterone (DHEA) release from adrenal glands which in turn may be contributed to reduction in bone mass.³⁴ In a study by Grey et al., the intake of intrathecal drugs has been related to reduction in bone density among 50% of the patients and osteoporosis in 20% of them.³⁴ Differences in route of opium administration and design of study (interventional vs. observational) may explain this difference of our result with that study. An additional pathway that may be contributing to opium-related osteoporosis is inhibition of osteoblasts which is theoretically brought about by opium being attached to osteoblasts' μ receptors causing the inhibition of osteoblasts.¹⁷

Sex is a major factor contributing to the occurrence of osteopenia and osteoporosis in those consuming opium. In one study, the men and women with substance addiction had early osteoporosis and women had a bone density within the range of osteoporosis before the age of 40 years. The male cases of the mentioned study had testosterone levels lower than 50 ng/dl, and their bone density was within the range of osteopenia.¹⁰ However, in a study conducted on individuals receiving methadone maintenance doses, only male cases had lower bone density. In a study by Grey et al., men's bone density was 10% lower than the control group, while the female cases had a similar bone density as the control group of their age group.³⁴ The mentioned 10% lower bone density can increase the risk of future fractures by 2 times. Since the majority of the cases participating in the present study were women, no bone mass reduction was probably detected; although the risk of bone mass reduction was higher than other cases. Further studies are required to determine the effect of sex on the bone mass in individuals with substance addiction.

Limitations: The cross-sectional nature of data limits our understanding regarding the causal

role of opium consumption and other risk factors in bone density reduction. Furthermore, most of the recruited participants were women and recruited from a private clinic which limits the generalizability of our findings. Moreover, these people do not represent the general public because they came to themselves.

Conclusion

Considering the results of this study, though the risk of bone density reduction in the individuals consuming opium was higher, due to the disparity between opium consumption in the two sexes the difference was not significant between the two groups, and it is proposed that studies on larger samples and in both sexes be conducted to determine the impacts of opium on the bone

density. Moreover, other studies conducted in different countries have generally been on methadone and morphine in the individuals consuming opium as a pain reliever for other diseases, and their underlying diseases might be of impact on their bone density, while the cases investigated by the present study had no underlying diseases.

Conflict of Interests

The Authors have no conflict of interest.

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بررسی عوامل خطر پوکی استخوان و رابطه بین مصرف تریاک و پوکی استخوان در افراد بالغ

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مقاله پژوهشی

چکیده

مقدمه: پوکی استخوان و کاهش تراکم استخوان، شایع‌ترین بیماری‌های متابولیک استخوان می‌باشد که بیماران را به شکنندگی استخوان و شکستگی پس از حداقل ضربه یا سقوط مستعد می‌کند. شواهد نشان می‌دهد که شکنندگی استخوان در مصرف‌کنندگان مزمن انواع مخدر بیشتر است. با توجه به شیوع بالای اعتیاد در کرمان و این که پوکی استخوان نیز یک معضل بهداشت عمومی شناخته می‌شود، مطالعه حاضر با هدف بررسی ارتباط بین مصرف تریاک و پوکی استخوان انجام شد. همچنین، سایر عوامل خطر پوکی استخوان مورد بررسی قرار گرفت.

روش‌ها: در این پژوهش مقطعی، از بین مراجعه‌کنندگان به مرکز دانسیتومتری شهر کرمان، ۶۱۹ نفر شامل ۷۳ مرد و ۵۴۶ زن انتخاب شدند. سپس فرم مربوط شامل اطلاعات دموگرافیک و آنتروپومتریک، سابقه مصرف مواد مخدر و داروها و عوامل خطر پوکی استخوان برای آنان تکمیل گردید و سنجش تراکم استخوان (Bone mineral densitometry یا BMD) در مهره‌های کمری (L۱-L۴) و گردن فمور انجام شد.

یافته‌ها: در آنالیز تک متغیره، ارتباط تمام متغیرها با پوکی استخوان با استفاده از آزمون χ^2 مورد بررسی قرار گرفت. بر این اساس، مصرف مواد مخدر، افزایش سن و داشتن شاخص توده بدنی (Body mass index یا BMI) کمتر از ۲۴ کیلوگرم بر مترمربع با افزایش شانس پوکی استخوان و ورزش روزانه با کاهش شانس پوکی استخوان همراه بود، اما ارتباط معنی‌داری بین جنسیت، مصرف سیگار و مصرف شیر با پوکی استخوان مشاهده نشد. در آنالیز چند متغیره، تنها دو متغیر گروه سنی و گروه‌های مختلف BMI معنی‌دار بود؛ بدین صورت که شانس پوکی استخوان یا کاهش تراکم استخوان در گروه سنی بیشتر از ۶۰ سال و ۶۰-۴۵ سال با تعدیل سایر متغیرها به ترتیب ۴/۹ و ۳/۱ برابر گروه سنی کمتر از ۴۵ سال بود. همچنین، شانس ابتلا به پوکی استخوان یا کاهش تراکم استخوان در افراد دارای BMI بین ۲۵ تا ۲۹/۹۹ و بیشتر از ۳۰ کیلوگرم بر مترمربع با تعدیل سایر متغیرها به ترتیب ۰/۵۴ و ۰/۵۰ برابر افراد دارای BMI کمتر از ۲۴/۹۹ کیلوگرم بر مترمربع بود.

نتیجه‌گیری: با این که خطر کاهش تراکم استخوان در افراد مصرف‌کننده مواد مخدر بیشتر است، اما شاید به دلیل عدم تناسب مصرف مواد مخدر بین دو جنس، ارتباط معنی‌داری بین دو گروه مشاهده نشد. توصیه به انجام مطالعات با حجم نمونه بیشتر و در دو جنس، می‌تواند در تعیین تأثیرات مواد مخدر بر تراکم استخوانی کمک کننده باشد.

واژگان کلیدی: اپیوم، پوکی استخوان، کاهش تراکم استخوان

ارجاع: حیدری زینب، شاه‌اسماعیلی آرمیتا، خواجه بهرامی محمدرضا، رضازاده مهریزی ماندانا، گذشتی محمد حسین، معاضد وحید. **بررسی عوامل خطر پوکی**

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