Alcohol Intake: A Review of Effects and Mechanisms in Bone and Alcoholization Methods

Abstract
Alcohol is widely consumed in the world. Excessive alcohol intake causes alterations in bone tissues. The objective of this paper is to review the effects of chronic alcohol use in bone microarchitecture and the mechanisms by which this abuse may decrease bone mineral density. Furthermore, in the second part of the review, it’s related the different techniques to induce bone loss in rats by alcoholization.

Objectives: The aim of this paper is to review in the recent literature the negative effects of chronic alcohol intake in bone health and the mechanisms responsible for that. It’s also review the different techniques available for experimental alcohol-induced osteopenia in rodents.

Methods: Pubmed database was systematically searched to obtain all the eligible papers, published in English language, covering the period between 1997 and 2014. The literature search combined several key words including: bone, alcoholism, cortical bone, ethanol, bone density, rat and animal models.

Results: A total of thirty-eight articles were selected in Pubmed database, considering the key words aforementioned. In the review, it is included twenty-nine articles published in English, in the period between 1997 and 2014.

Keywords: Bone; Alcoholism; Ethanol; Cortical bone; Bone density; Animal model

Introduction
Alcohol is highly consumed around the world. It is clear that excessive alcohol consumption may be deleterious for bone microarchitecture, depending on the many levels of intake [1].

Akvisa-Negrin et al. [2] showed that chronic alcohol abuse affects negatively bone formation, bone mineral density (BMD) and bone mineral content (BMC), related to the inhibition of the osteoblastic activity and proliferation [2]. Fracture risk and osteoporosis is also associated with chronic alcohol intake due to a modify in the microarchitecture of the trabecular and cortical bone [3,4].

Here, we first review the detrimental effects of alcohol on bone tissues health and the mechanisms responsible for that, according to the amount of ethanol consumed. Therefore, in the second part of this review, it’s analyzed the different techniques already used to study these effects in rats.

Discussion
Although there are not many articles comparing deleterious effects on bone microarchitecture caused by alcohol abuse in each gender [5] according to Turner et al. [3] alcohol consumption decreases BMD in different skeletal sites [3]. It is known that the skeleton is composed of cortical and trabecular bone, in different proportions, and both are affected by chronic alcohol intake [1].

On the other hand, epidemiological study indicated that moderate alcohol consumption higher bone mass in postmenopaused women [6]. However, it is important to classify the quantity of alcohol intake. Ganry et al. [1] suggested that lower than 10g per day of ethanol as light consumption, moderate as 11-30g of ethanol and more than 30g a day as heavy intake [1].

According to this classification, considering the BMD, some papers show benefits for light and moderated consumption including the postmenopaused women. These same doses were pointed as deleterious on prememopausal women [7,8].

For heavy intake, it is unanimous the presence of bone commitment, both in BMD loss, as in microarchitecture and bone remodelling [3]. There are discrete differences in the level of bone commitment among the reviewed papers, perhaps due to the psychosocial character and profile of the sample studied. However, the total of the studies have presented positive results for the deleterious effects of alcohol intake on bone [1,9,10].

The most important determinant of bone strength is the cortical bone microarchitecture [11]. The negative effect of alcohol abuse on cortical thickness and volume, even as the inhibition of bone formation has been reported in male patients with pancreatitis [10,12]. The decrease in cortical thickness is dose-dependent and is related to alcohol metabolism that probably
modifies the nutrients absorption provided by diet [11] besides consequently causes hormonal alterations, reducing the number and the activity of osteoblasts [13]. Maurel et al. [14] classified into direct and indirect the mechanisms of action of chronic heavy consumption on bone [14].

As indirect, mentioned the decrease of fat and muscular mass, inducing the not gain of bone mass. Consequently, alterations on hormone secretions occur, including leptin [15]. Leptin is a bone mass regulator, which is able to stimulate the central nervous system and peripheral tissues to produce osteoblasts [16]. Insufficiency of vitamin D and decrease of sexual steroids like magnesium and phosphate, are also related. These hormones are commonly known to have positive effects on osteoblasts [17,18].

Heavy chronic alcohol consumption also reduces the ability of the stem cells to differentiate into osteogenic lineage cells [19]. Recent studies concluded that heavy alcohol consumption inhibits bone neo-formation in fracture sites [20,21].

In the direct mechanisms of action, alcohol abuse reduces the activity and the level of osteoblastic differentiation and increases the osteoclastogenesis [22]. Therefore, it is suggested that the heavy chronic alcohol abuse intensifies the apoptosis or dying of osteocytes and consequently the osteoclasts activation, correlated to the BMD loss [23].

Moreover, Wnt/B-catenin is a glycoprotein that acts as a potent regulator, directly responsible for stem cells differentiation into osteoblastic lineage cells. Chronic alcohol consumption stimulates its antagonism formation, the DKK1, causing disturbs on bone formation [24]. Alcohol intake causes significant commitment in quality of cortical bone demonstrated through the analysis of the cross-sectional geometry of femur in young rats [4]. In rats, Nishiguchi et al. [25] reported bone loss in different ages and sex [25]. Another two study examined the negative consequences of alcohol intake on cortical bone of mice and presented negative alterations on thickness and porosity of cortical bone, as well as on density of trabecular structure [24,26].

Considering the bone alterations above, the risk of fractures is highly elevated in chronic alcohol users compared to a non-alcoholic group, in addition to the increase of the risk of falls, even without bone affections [3,27]. In animal models, there are different procedures for alcoholization. The most common and less stressful technique is the ethanol dilution in a liquid diet. Thereby, there is easy control of ethanol intake percentage and of the quantification of the nutrients of the diet. Another option is the intraperitoneal and gavage techniques that although efficient, may be classified as indirect, through alterations in corporal composition, hormone secretions and cell functions, and as direct, associated to modifications in the osteocyte functions and glycoprotein secretions. There are many methods used to study the consequences of chronic alcohol intake on bone health in animals. The most advantageous and efficient technique available for experimental alcohol-induced osteopenia in rodents, induces alcoholization by exposure to alcohol vapours, because keep constant blood ethanol levels and induce physical dependence in lower time than the other techniques.

**Conclusion**

Alcohol abuse affects negatively bone formation, BMD and BMC, linked to the inhibition of the osteoblastic activity and proliferation. The mechanisms, by which these losses occur, may be classified as indirect, through alterations in corporal composition, hormone secretions and cell functions, and as direct, associated to modifications in the osteocytes functions and glycoprotein secretions. There are many methods used to study the consequences of chronic alcohol intake on bone health in animals. The most advantageous and efficient technique available for experimental alcohol-induced osteopenia in rodents, induces alcoholization by exposure to alcohol vapours, because keep constant blood ethanol levels and induce physical dependence in lower time than the other techniques.

**References**


