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Association Of The Hipoadiponectinemia With Smoking And Its Effects On The Body: A Systematic Review

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ABSTRACT

Objective: To evaluate the relationship between smoking and hypoadiponectinemia and the effects it causes in humans. **Methods:** A systematic review was conducted in PubMed, Cochrame, EMBASE, Plos, BMC Public Health and American Thoracic Society, 20 studies selected, applying criteria of inclusion and exclusion respectively, according to the interests of the investigation. It was analyzed in a global population of 1'070.425 cases. **Results:** Low levels of adiponectin in people exposed to snuff were associated with increased risk of diabetes, nonalcoholic hepatic steatosis (NASH), early atherosclerosis, renal cell carcinoma and asthma (95% CI P = 0.04). It was determined that hypoadiponectinemia during pregnancy was associated with intrauterine disorders in newborn baby (95% CI P = 0.057). The findings suggest that exposure to snuff dipping has a stronger association with low levels of adiponectin, high glucose and triglycerides (95% CI P = 0.001); and that adiponectin is considered a predictive factor in the activity and prognosis of chronic diseases such as rheumatoid arthritis. **Conclusion:** The findings of this study suggest that decreased serum adiponectin levels represent a significant relevant factor in humans, mainly in which they are immersed or exposed to smoking; causing such effects that lead people to be susceptible to cardiometabolic diseases, cancer or other comorbidities.

Keywords: hypoadiponectinemia, adiponectinemia, adiponectin, Tobacco, smoking.

Introduction

Adiponectin is a plasma protein that regulates adipocyte energy metabolism of the organism, as it stimulates fatty acid oxidation, reduced plasma triglycerides and improves glucose metabolism by increasing sensitivity insulin. This is also called ARCP30 adipocytokine, ADIPOQ, apM1 or GBP28, is a peptide of 247 amino acids corresponding approximately 0.05% of total serum proteins, whose normal plasma concentration ranges from 5 to 30µg / ml in males, while that in women are found in higher concentrations. (Ahmad, 2015).

The clinical and biochemical conditions associated with hypoadiponectinemia are: obesity, male sex, diabetes mellitus type 2, inflammation, insulin resistance, lipodystrophy, hypertension and cardiovascular disease, in the latter highlights the artery disease coronary, myocardial infarction, atherosclerosis, sclerosis, restenosis after percutaneous coronary intervention; while factors that cause hiperadiponectinemia include: normal weight, female gender, diabetes mellitus type 1 agonists peroxisome proliferator activator receptors (PPARa), insulin sensitivity and elevation of HDL-cholesterol (Fan, 2015).

Recent studies suggest that adiponectin has anti-atherogenic and anti-inflammatory properties, it reduces cytokines such as C-reactive protein, tumor necrosis factor α and interleukin-6. Furthermore, adiponectin inhibits the early stages of atherosclerosis, as it reduces the expression of adhesion molecules in endothelial cells, the transformation of macrophages into foam cells, the expression of tumor necrosis factor and cell proliferation of smooth muscle tissue. Adiponectin can also counteract the proinflammatory effects of TNF-α in vascular cells; therefore, the insulin resistance induced by TNF-α could be partially explained by the inhibition of secretion of adiponectin; also suppresses secretion and TNF-α signaling in cell cultures of macrophages and endothelial cells, and inhibits the process of cell adhesion (D. Moreno, 2012).

TNF-α increases the while adiponectin reduces the expression of these proteins on endothelial cells. In cultures of these cells, it has also been shown that administration of adiponectin stimulates the formation of nitric oxide. C-reactive protein (CRP), a marker of coronary artery disease, is considered an independent risk factor for cardiovascular disease, and shows a negative correlation with adiponectin in adipose tissue. IL-6, which is a regulator of hepatic production of CRP, also negatively correlated with adiponectin. Adiponectin also suppresses proliferation and migration of smooth muscle to the arterial wall cells and the proliferation and monocyte phagocytic ability, key cells in the development and training of vascular injury.

Snuff consumption either passive or active is an important risk factor that contributes to heart disease and metabolic especially noncommunicable diseases, leading to approximately six million deaths worldwide each year. The trend towards increased consumption of snuff in developing countries is alarming, where it is expected that 80% of deaths

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that occur in coming decades are due to the use of snuff (Hui, 2014).

There are two ways to consume snuff, smoke (non-immersion) and smoke (immersion). The snuff smokeless has not gained the attention of the scientific research community compared to smoking, although its use is common throughout the world but in less proportion, therefore there is misinformation on consumers of snuff dipping, as they cause less damage compared to those who do not produce smoke. This type of snuff is consumed ground, wet leaves, which is positioned between the lower lip and gum, discarding it after about 15-30 minutes. In the local language (Pashto), it is called naswar referred to moist snuff (Ahmad, 2015).

Cigarette compounds have negative effects against the organism, mainly nicotine which is the major constituent of snuff. This triggers the release of catecholamines that cause damage to the intima of the arteries, increases coronary spasm tone produces coagulation disorders, increased levels of LDL and lowers HDL. However, the blood nicotine concentration depends more on the degree of inhalation of cigarette nicotine content itself.

Smoking is responsible mainly for preterm birth, low birth weight in children and congenital malformations, not only because of its components, but by the effect of lower serum adiponectin levels, that reduces the normal function in the body of the mother and placental step that benefits the fetus, for it is intended to validate the literature with reference articles found (Elkholi, 2013).

Methods

A systematic review was conducted in PubMed, Cochrame, EMBASE, Plos, BMC Public Health and American Thoracic Society.

Study Design

Systematic review where case-control studies, clinical trials, cohort studies, cross-sectional, prospective and observational included.

The study population was 1'070.425 cases distributed in 20 studies involving this review.

Inclusion criteria

All patients who consumed snuff active or passive manner and showed changes in levels of circulating adiponectin independent of age and gender were included.

Only studies journals Q1 and Q2, the same that were published between the years 2012-2016 included.

Exclusion criteria

All studies in which there was no smoking history in which there was no conclusive results and previous publications to 2012, likewise discarded letters to the editor and case reports were discarded.

Results

A systematic search where 20 selected studies described above was performed. Among the results obtained three studies assessed adiponectin levels after stopping the consumption of snuff, where it was determined that levels of adiponectin and leptin rose in the first quarter of abstinence (95% CI P. 0.008) remaining constant the adiponectin and leptin decreased from the third month (95% CI P: 0.05) (Kryfti *et al*., 2015) (Kotani *et al*., 2012) (Won *et al*., 2014); Graph 1.

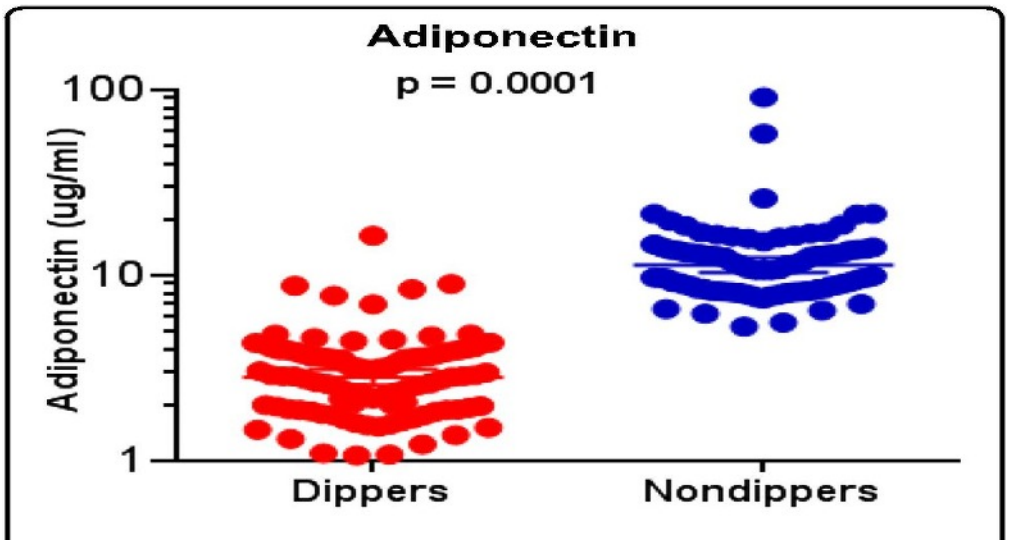

Table 1: Serum concentrations of adiponectin in young men. . (Ahmad, Shah, & Ahmed, 2015)

In graph 1 study of young men with an age range of 20 to 35 years. A statistically significant difference in the average level of adiponectin between Dipper (Immersion) groups and Non Dipper (Non-immersion) (p = 0.0001) was observed. In graph 1, a significant difference between the two groups was also observed in the basal parameters including triglycerides levels and blood sugar random (p <0.05) (Ahmad, Shah, & Ahmed, 2015).

The studies evaluated the relationship of adiponectin with risk and deterioration in COPD, where increased adiponectin, decreased TNF?, Selectin and Cystatin C were associated with

future impairment of forced expiratory volume (FEV) after control of BMI, age and sex. A adiponectin / leptin low ratio was also associated with impaired FEV (P = 0.001) (Yuan *et al.*, 2012) Suzuki *et al*., 2014). Another study of 43 cases found that levels high serum adiponectin treatment with glucocorticoid (fluticasone) in COPD were associated with greater relief of symptoms and hyperinflation (95% CI P: 0.001), however glucocorticoids associated with decreased serum adiponectin (Leivo-Korpela *et al.*, 2014).

The studies analyzed adiponectin genes involved in smokers and their relationship with COPD finding a higher ratio of rsl561299 gene with the risk of COPD (P.0.04) and KARE koreanos study that included 1570 men who liken the risk of hypoadiponectinemia in obese and non-obese smokers it found that smokers with the TT genotype of CDH13 (rs3865188) who were obese had a higher risk of hypoadiponectinemia (OR: 9.4 P: 0.01) compared to smokers with a circumference of normal waist (OR: 5.1 P: 0.01) (Jo, Sull, Park, & Jee, 2011). However the combined effect of smoking and obesity; individuals with the TT genotype and obesity were significantly associated with a 6.2-fold increased risk of hypoadiponectinemia compared to non-smokers with the same genotype and normal waist circumference (OR: 3.9; 95% CI P: 0.001). In a study gene expression of adiponectin expressed in smokers and their relationship with nonalcoholic fatty liver disease (NASH) where the expression of the promoter-11377 gene was associated with increased risk (: P 0.01) was evaluated) (Zhang, Guo, Qin, & Li, 2016).

In another study of cases and controls in women it was determined that 15 years after control low adiponectin was associated with a significantly increased risk of incident asthma (95% CI P: 0.04) for all women regardless of menopausal status, without embrago BMI did not predict the incidence of asthma in all women a year before the exam (Sood et al., 2012). In 2 cohort studies in pregnant women analyzed adiponectin levels and in utero effects and the newborn was found a positive correlation between the number of cigarettes smoked and the proportion of insulin, proinsulin, and insulin A, but similar levels of adiponectin and leptin both smokers as nonsmokers; the child's weight at birth was in significant limits (P.0.057) (Sood *et al*., 2012). In 2 studies they evaluated the risk of early atherosclerosis and its relation to hypoadiponectinemia smokers determined a negative correlation with intima-media (P: 0.001) and positively correlated with the elasticity of the large arteries (P: 0.001) as a partnership between the serum adiponectin levels and early atherosclerosis (Hui *et al*., 2014) (Hui *et al*., 2014).

In a meta-analysis of observational studies involving 154,406 cases it was found that environmental exposure to snuff smoke (passive smoking) may be associated with risk of diabetes, in passive smokers compared to nonsmokers; it was concluded that the longer snuff smoke exposure is associated with an increase of 21% risk of developing diabetes (95% CI P = 0.090). In this meta-analysis a dose-response relationship between duration of smoke exposure and the risk of diabetes with a stronger long-term relationship (Sun *et al*., 2014), and another cohort study between 2002 and 2011 with a population of 3338 Japanese found, determined the risk of diabetes in smokers and former smokers is significantly higher (risk ratio 1.75, 95% CI 1.25-2,46) and (risk ratio 1.54, 95% CI: 1.07 to 2, 22) compared with nonsmokers. In addition adiponectin levels was associated with the indirect effects of smoking on the risk of diabetes (95%). By contrast, the indirect effects of smoking on diabetes through levels of leptin and CRP were not significant (95%) (Hilawe *et al*., 2015).

Table 1: Baseline Characteristics of young men with immersion snuff consumers without immersion. Bold letters show the significant difference between the two study groups. (Ahmad, Shah, & Ahmed,2015).

Characteristics	Saucepans Dipper (N = 96)		Non-Dippers (N = 90)		Value Of P
Age (years) Mean ± DE	28.84	± 4.77	28.41	± 4.99	0.547
BMI, average ± DE, in kg / m^2	23.07	± 2.68	23.67	± 1.46	0·060
Systolic blood pressure, mean ± DE, mmHg	119.8	± 9.67	118.61	± 8.51	0.379
Diastolic blood pressure, average ± DE, mmHg	80.36	± 9,60	79.5	± 8.74	0.523
Blood sugar at random, average ± DE, mg / dl	101.79	± 15.46	96.54	± 10.06	0·013
Serum creatinine, average ± DE, mg / dl	0·78	± 0.09	0·78	± 0.08	0.941
The total average ± SD cholesterol, mg / dl	161.38	± 19.53	161.16	± 25.22	0.947
TG, average ± DE, mg / dl	127.39	± 33.43	113.81	± 28.57	0·003
HDL cholesterol, average ± DE, mg / dl	48.28	± 3.74	47.22	± 6.48	0·171
LDL cholesterol, average ± DE, mg / dl	113.1	± 18.14	108.7	± 23.11	0.149
Serum adiponectin, average ± DE,µg / ml	3.23	± 2.07	12.94	± 10.50	0.0001

In another study the relationship adiponectin levels and risk of renal cell carcinoma was found that high levels of adiponectin were significantly associated with reduced risk of renal cell carcinoma (: 0.01; 95% CI P) was evaluated (Liao *et al*., 2013).

A cohort study assessed the relationship of the Mediterranean diet and adiponectin levels in smokers and nonsmokers, found that nonsmokers who eat Mediterranean diet had a high concentration of adiponectin; It was decreased in patients eating Mediterranean diet and were moderate smokers (10

to 20 cigarettes / day) and high (30 cigarettes / day or more) also it was found high serum adiponectin in former smokers (Al-Attas *et al*., 2013).

Another study evaluated the effects of smoking on the activity of rheumatoid arthritis found that smokers had low serum levels of IGF-I, adiponectin and leptin compared with nonsmokers, and that the period of disease activity and himself it associated with decreased adiponectin and leptin (Erlandsson, Doria Medina, Töyrä Silfverswärd, & Bokarewa, 2016)..

Discussion

This systematic review demonstrates the association between smoking and its effect on the reduction of circulating adiponectin, be it by active or passive consumption, dipper, ie smoke or not dipper, with smoke; but according to the studies reviewed and analyzed, tobaccos that are chewy and do not produce smoke (by immersion) decreases more serum adiponectin levels. In addition, patients who did not smoke and even those who were former smokers had higher levels of serum adiponectin that were currently smoking; likewise in the group of patients who smoked actively and currently persist; compared those with body mass index, cholesterol levels and normal triglycerides, with others who had factors of obesity and dyslipidemia, likewise the reaction of this protein was studied among whom were smokers young healthy with those who were older and added medical history to it. It was demonstrated in this way that reduced adiponectin levels are significantly lower in healthy young smokers than in those who had risk factors, medical history, and regardless of age.

Within the set of components of snuff, nicotine is producing a mostly detrimental effect because it inhibits gene expression of adiponectin from adipocytes, also it causes oxidative stress and inflammatory cytokines, causing deterioration of the vessel walls, causing adiponectin buildup and therefore reduces blood amounts, all together increases the chances of cardiovascular and metabolic diseases. Many studies reveal high prediction atherosclerosis due hypoadiponectinemia.

According to various studies found on the effect of hypoadiponectinemia caused by the consumption of snuff in pregnant women, they coincide with the consequences caused by nicotine in the mother and fetus, mainly because it crosses the placental barrier, causing vasodilation and causes hypertension the mother and the fetus decreased flow together with the deposit of adiponectin in the umbilical cord, resulting in many cases, abortion, congenital malformations, chronic fetal distress and mostly low birth weight.

After explaining the most frequent and relevant in relation to snuff and hypoadiponectinemia studies, a study reveals the possibility and increased risk of asthma due to these serum decreases, just as the expression of the genes studied is adiponectin, concluding that the expression of the promoter-11377 gene raises the risk of nonalcoholic hepatic steatosis (NASH).

Other study showed that people who eat Mediterranean diet and are moderate and strong smokers, have a high percentage of hypoadiponectinemia as well as those suffering from rheumatic arthritis and are constant smokers. Furthermore, a study reported that the decreased serum adiponectin is associated with an increased risk of developing renal cell carcinoma in male smokers.

Conclusion

The findings of this study suggest that decreased serum adiponectin levels represent a significant relevant factor in humans, mainly in which they are immersed or exposed to smoking; causing such effects that lead people to be susceptible to cardiometabolic diseases, cancer or other comorbidities.

This highlights the importance of developing the intervention of the population to reduce the use of snuff.

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