REVIEW

Can the Use of Smokeless Tobacco Products Be Accepted as a Harm Reduction Method in Tobacco Addiction?

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Abstract

The goal of smoking cessation treatment is to keep the patient completely away from tobacco and tobacco products. The aim of harm reduction strategies in tobacco control is to reduce the risks associated with tobacco use. In order to turn it into an opportunity, tobacco companies have developed smokeless tobacco products. Some epidemiological studies have reported that smokeless tobacco products are safer than tobacco smoke. However, this method is not completely harmless. In this review, we will discuss all aspects of tobacco harm reduction methods.

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INTRODUCTION

Harm reduction strategies in the field of tobacco control aim to reduce the risks associated with tobacco use. In this context, the term "harm reduction" is used to define minimizing the unfavorable effects of tobacco use on health in individuals that continue to use tobacco. In this review, information on the definition of harm reduction and studies conducted on this subject will be summarized.

Harm Reduction

In 2006, the American Council on Science and Health has officially promoted "tobacco harm reduction", in other words "smokeless tobacco", on the grounds that it is a much safer nicotine source for smokers that were unable to quit nicotine/tobacco [1]. Some epidemiological studies report that smokeless tobacco (ST) products are safer than cigarette smoke. Moreover, it has been asserted that using smokeless tobacco products has no effect on starting cigarette smoking.

In fact, the following questions should be answered in terms of whether the use of smokeless tobacco products for harm-reduction could actually be a "treatment method":

- 1. What are the effects of smokeless tobacco products on health?
- 2. What are the influences of these products in replacing cigarettes?
- 3. What are the effects of smokeless tobacco products on starting cigarette smoking?
- 4. Does concurrent use of smokeless tobacco products and cigarette have an effect on quitting smoking and reducing cigarette-related harms on health?

Epidemiological studies and data of meta-analyses point out that the use of smokeless tobacco products enhances the risk of oral cavity and pancreatic cancers [2,3]. Likewise, it is reported that smokeless tobacco products mildly enhance the risk of prostate cancer and the risk of fatal myocardial infarction is increased in the subjects using such products. The use of such products also enhances the risk of cerebrovascular accident [4,5]. The use of smokeless tobacco products in pregnant women results in increased risk of low birth weight, premature birth, stillbirth and preeclampsia [6].

On the other hand, it is observed that most of the data about the influence of these products in replacing cigarettes are from developed countries. For example, it has been reported that the risk of becoming a daily cigarette smoker is



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decreased and the probability of quitting smoking is increased with the use of ST in Sweden [7]. Likewise, in Norway, the increased incidence of using "snus (moist snuff)" whilst decreased cigarette consumption in the last 20 years and the preference of smokeless tobacco products more commonly than pharmacological therapies for quitting smoking have attracted attention [8]. However, although there are evidence that the use of such products may be a key factor in decreasing cigarette-related diseases and cigarette smoking rates in the developed countries like Sweden, the fact that these products decrease the incidence of cigarette smoking could not be proven in other countries [1]. Therefore, recommending/using smokeless tobacco products as a way of "harm reduction" depending on data from a few developed countries such as Sweden and Norway while disregarding data from other countries would lead to irreparable public health problems in the future.

Whether smokeless tobacco products have an effect on starting cigarette smoking is another question to be answered, because smokeless tobacco products may be a gate for starting cigarette smoking in the future [9,10]. Although some studies from the United States of America and Sweden suggest just the opposite of this trend, it is not possible to make a positive prediction on smokeless tobacco products depending on these limited numbers of studies [11].

In a very few studies investigating the effect of using smokeless tobacco products together with cigarette on quitting smoking and reducing cigarette-related health hazards, the success of quitting smoking were lower in the subjects using smokeless tobacco products as compared to the subjects using cigarette alone even though the subjects that use smokeless tobacco products together with cigarette consumed lesser number of cigarettes than the subjects not using smokeless tobacco products. That is to say, the use of smokeless tobacco product has not motivated them for quitting cigarette smoking.

Despite the unfavorable effects of smokeless tobacco products on health and their insufficient success in quitting smoking, why does the incidence of using these products is increased in time and, moreover, why do these products are being brought into the forefront as a kind of method for quitting smoking?

Through the global perspective, it is known that worldwide one billion people and Turkey-wide 15 million people are dependent on nicotine in the cigarettes and the majority of these people do not want to quit smoking in the near future. On the other hand, young people continue trying harmful and addictive tobacco products because of tactics and strategies of tobacco industry. Thereby, some scientists think that "the lesser of two evils" is a good choice and they display an approach that an individual can use smokeless tobacco products, which are less harmful than cigarette if she/he will be addicted to cigarette or decide to try tobacco.

However, the main argument for this approach is the concern that marketing strategies of tobacco industry cannot be prevented. On the other hand, recommendation of products that would kill one billion people in 21st century, which are manufactured by tobacco industry and, tobacco industry

earn money by selling them as a kind of "treatment method" is an inadmissible approach in terms of ethics.

Actually, when worldwide tobacco consumption in years is analyzed, it attracts attention that global tobacco market has changed in time. Within this context, it is known that 92% of the revenue in global tobacco market in 2010 was generated from cigarettes [12]. Moreover, annually a 4% increase was observed in global tobacco consumption between 1960 and 2000. However, especially after 2000, the annual growth in tobacco market has been less than 1%. Such deceleration in growth is quite conspicuous. Probably, effective tobaccocontrol policies put in practice in many countries until today and the saturation due to successful expansionary fiscal consolidation policy of the industry have led to a recession in tobacco consumption. However, despite decelerated growth and recessed cigarette sales, the most remarkable change in the recent years is the increase in the pricing power of tobacco products. For example, 84% increase has been observed in global cigarette sales in the last decade despite restricted growth rate [13]. At this point, the efforts of tobacco industry to achieve volume growth, i.e. seeking developing markets, is striking. Tobacco industry seeks for ways of accessing new markets and new opportunities and increasing consumption in order not to decrease the profit margin. Therefore, tobacco industry use professional tactics on the "right product", "right cost", "right place", "right subject (consumer)" and "right promotion" issues in the newly established markets. At just this point, the key "new" theme of the last few years "harm reduction" and, in this context, "smokeless tobacco products" has been brought to the agenda. And, in a way that could not possibly be a coincidence, the interests of British American Tobacco (BAT), Philip Morris International (PMI), Japan Tobacco International (ITI) and Imperial Tobacco Group (ITG) in smokeless tobacco products rapidly increased [14]. The most basic reflection of this increased interest is the faster growth in sales of smokeless tobacco products than cigarette. For example, whilst the increase in global cigarette volumes was 8% between 2001 and 2010, it was 51% for smokeless tobacco products. The market share of smokeless tobacco products reached to 2% of global tobacco market in 2010 [15]. In fact, the documents of BAT and PMI clearly reveal how they consider smokeless tobacco products. In this context, it should never be disregarded that the approach of the tobacco industry to "harm-reduction" is in the way "it may allow freedom for marketing and provide development in brand resources via political support and legal regulations". Likewise, the statement made by tobacco industry as "Cigarette category should establish the profitability pool in the international tobacco world, but we must always be one step ahead" is striking although the industry is not voluntary for joint venture with snuff producing companies for now [16,17].

On the other hand, 2001 report of the National Academy of Sciences Institute of Medicine expresses that there is not adequate evidence on these products' being less harmful than normal cigarette [18]. Again, many health institutions with the Surgeon General's Office is the leading, strongly emphasize that the information that smokeless tobacco products are less harmful than cigarette is not true and must be corrected.

In brief, expectations of the tobacco industry from the investments in the field of smokeless tobacco products can be listed as follows:

- To provide a new market, increase in the pricing power, and more limited competition environment in tobacco sector in favor of itself
- To provide a potential growth rate for smokeless tobacco products inversely with cigarette in the long term and thus provide a guarantee to the investors
- By means of harm reduction discourse, to maintain an appropriate basis for the industry in the future in terms of safe access to market and permanent effect

In conclusion;

- As many implementations performed in the past (filter, light, etc.), implementations supporting the use of smokeless tobacco products under the name of "harm reduction" are, in fact, public relations tactics of the industry.
- The solution is not introducing less harmful forms of a substance known to be harmful but completely removing it.
- Aggressive efforts of the tobacco industry to enhance cigarette smoking are ongoing.
- If smokeless tobacco products become an alternative that could compete with cigarette in time under the name of "harm reduction", the threat would become an opportunity for the industry.

Smokeless Tobacco Products

In the recent years, studies in the literature conducted on smokeless tobacco products under the topic of harm reduction have begun to attract attention. In fact, although some authors consider smokeless tobacco products as an option in quitting smoking, this should never be the treatment targeted for the patients, as, for tobacco companies, harm reduction refers to creating markets for new products.

The first paper on harm reduction was written in Lancet in 1974 by Michael A.H. Russell, who was the addiction specialist of British Tobacco Company [19]. Thereafter, interest in this subject has been enhanced when Russell and colleagues put the smokeless tobacco, which they called as nasal snuff, into use for cigarette smokers and subsequently papers on this subject have been written [20-23]. However, the term harm reduction was scientifically first used in 2001 in the report of the National Academy of Sciences Institute of Medicine, United States of America [18].

Harm reduction comprises all methods performed to reduce mortality and morbidity caused by toxic substances that a patient is exposed to because of cigarette smoking.

In fact, many years before the harms of cigarette have been defined in the literature, scientists and tobacco companies imagined that toxic effect can be prevented by reducing the amount of nicotine thinking that nicotine is the only toxic substance in tobacco. For this purpose, a German scientist named Paul Koenig obtained patent for the cultivation of tobacco plant containing less nicotine for the first time in 1933 [24]. Within this context, according to the data from Patent Searching and Inventing Resources, 12,196 tobacco-related patents have been obtained until today, of which 206 were the interventions for harm reduction [25]. On the other hand, as the harms of tobacco were identified, pressure on tobacco companies notably increased, particularly in 1970s. At this point, tobacco industry considered harm reduction method as a field to be converted into opportunity and developed new relevant products. These products are cigarette forms defined in English as Potential Reduced Exposure Products (PREPs). These products were presented to the users as less carcinogenic cigarettes including less nicotine and less tar under the name of "special-filter", "light", "mild" and "ultra light" expressing that they would help quitting smoking and pose less damage [26,27].

Tobacco industry has been defending for 80 years that they are working thoroughly to reduce the toxic substances as much as possible while processing tobacco in the factory and these products are less harmful. Smokers took these claims seriously and believed that they really could quit smoking and would be exposed to less harm by means of these products but the result was always just the opposite [28-30]. However, tobacco industry specifically targeted female smokers by writing phrases on cigarette packages asserting that they are less harmful, and smoking such cigarettes have been supported by advertisements.

A type of tobacco that has been asserted to be less harmful is the Smokeless Tobacco Products (STP), which, in fact, has been known since the "discovery" of America. These products are products used via oral or nasal route in many countries in the world with USA, North European Countries, Middle-Eastern Countries and India are the leading [9]. In some countries, different herbs are also mixed with tobacco products. In our country, the plug tobacco known as "Maras powder" is a sample for these.

These products, which are usually of USA and Sweden origin, are traditionally found in three forms including powdered dry snuff, loose leaf chewing tobacco (snuss), and moist snuff [29]. Initially, less amount of tobacco-specific nitrosamines (TSNA) were added to the Swedish products, since different methods were used in the manufacturing of American and Swedish products. However, in the last 25 years, the amount of TSNA in these products have been gradually reduced and pulled down to the same level [31].

On the other hand, the prevalence of using these products is not close to that of cigarettes since these products are not available in all countries. For example, the prevalence of using these products in the USA was 5.6% (4.8 million) in adult males and 0.6% (533 000) in females in 1991, whereas it was decreased to 4.4% in males and 0.3% in females in 2000 [32,33]. Nevertheless, in the 2001 report of the National Academy of Sciences Institute of Medicine, it has been stated that there is not adequate evidence that these products are less harmful than cigarette [7]. Again, many

health institutions with Surgeon General's Office is the leading, insistently emphasize that the information about smokeless tobacco products' being less harmful is not true and must be corrected [9,34,35].

In addition to tobacco, smokeless tobacco products are sweetened with additives such as sugar, water, sodium chloride, ammonium chloride, menthol, liquor, paraffin grease and glycerol. Additionally, they contain TSNA, small amount of metal, polycyclic aromatic hydrocarbon (PSAH) and small amount of formaldehyde [36,37]. However, the amount of these substances changes depending on the method of processing STP. Moreover, frequency of using these products, duration of keeping them in the mouth or nose, oral flora of the user, amount of saliva, other habits (alcohol, drug use), comorbid conditions and the background of the individual are the other probable causes that facilitate the development of harmful effects [38-40].

Encouraging efforts for the consumption of smokeless tobacco products have gained acceleration in the 2000s. The World Health Organization as well adopted the striking sentence "All of Tobacco Products are Fatal, Do not Pay attention to Its Costume" as the slogan for the World No Tobacco Day of May 31, 2004 to enhance the awareness of health authorities on this subject. In the same year, all health care workers tried to propagate and adopt similar messages in their own country taking this slogan as the basis.

Effects on Cardiovascular System

The effects of smokeless tobacco products on sympathetic nervous system are similar to that of normal cigarettes and they increase heart rate and blood pressure [41,42]. Prevalence of hypercholesterolemia was found to be 2.5 times higher in STP users as compared to nonusers [43]. Despite these findings, six epidemiological studies failed to find a risk for heart attack or stroke in STP users [44-48]. However, other two studies found a strong positive correlation between STP use and cardiovascular disease [49,50]. In a review in 2003, Asplund attracted attention to the absence of significant difference between STP users and nonusers in terms of heart rate, blood pressure, cardiac output, vascular wall thickening, development of atherosclerosis, as well as leukocyte, hemoglobin, fibrinogen, C-reactive protein and thromboxane levels [51]. The risk of cardiovascular disease has been shown to be high in diabetic patients that smoke cigarettes [52-55]. Person found the risk of cardiovascular disease to be high in type II diabetic patients that intensively use STP [56].

Effects on Oral Health

Oral leukoplakia is a pathology that can be seen in more than 60% of STP users and is thought to result from irritation [55,56]. The risk of transformation of leukoplakia to dysplasia is in STP users is 3% lower than that of cigarette users. Therefore, progression to cancer is less common and slower [57-61]. In a study from Sweden, 200,000 male patients using snuff were retrospectively investigated and oral cancer was detected in only one case in a year [62]. However, the relation between oral cancers and STP has been recognized in 1950s [15]. In an analysis that collected case-control studies, the risk of oral and respiratory tract cancers was found to

be significantly higher in those using powdered dry snuff, whereas it was found lower in those using moist snuff and plug tobacco [63]. On the other hand, since the results of two studies performed in 1998 in Sweden revealed no relation between oral cancers and STP, tobacco companies requested removal of the phrase "may cause oral cancer" written on the packages and made the European Union partially accept this demand resulting in the removal of the phrase "can cause oral cancer" on their products. However, the warning phrase "hazardous for your health and may cause addiction" written for these products has not been removed yet [64-66].

Cancers of Other Systems

4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (Nicotinederived nitrosamine ketone: NNK) and N' nitrosonornicotine (NNN), which are found in smokeless tobacco products and considered carcinogen, are the substances most frequently studied in animal experiments for their relation with cancer [2]. However, different from human studies, other factors such as environment and genetic factors are disregarded in animal studies performed with these molecules. Nevertheless, they are valuable as they may illuminate further studies, because the results of epidemiological studies are contradictory and show variations among regions. For example, NNK and NNN application on the cheeks of rats led to development of cancer in this region [67]. Again, experiments in rats demonstrated that NNK, NNN and their metabolite 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) causes pancreas cancer [68]. It has been found that TSNAs mixed into drinking water of rats play a role in the development of esophagus and pancreas cancer [69]. However, epidemiological studies reveal that the relation between STP use and cancers of other systems is not clear as was mentioned above [70]. But, the study published in 2008, which was conducted on 336,381 males, found increased risk of squamous cell esophageal cancer and non-cardia gastric cancer in STP users versus nonusers [71]. Again, in a study from Sweden, risk of pancreas cancer was found to be increased in snuff users among STPs, but the same risk could not be found for oral and lung cancers [72].

Effects on Fetus

As was demonstrated in animal studies, nicotine has toxic and teratogenic effects on fetus [73,74]. Exposure to STP has been found to be associated with low birth weight and inadequate ossification of bone in animal fetus [75,76]. It is difficult to say the same thing for human fetus. However, it is assumed that when the mother uses these products, the fetus would be exposed to higher amounts of nicotine as compared to medical nicotine preparations, because these products contain higher amounts of nicotine and exposure time is longer [77,78]. In a study conducted in Sweden in pregnant women that were using snuff tobacco, the risks of preeclampsia and low birth weight were found to be 1.6 fold higher [79].

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