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Literature Review of the Contravention Relation between Smoking and Parkinson's Disease

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Abstract:
Researchers have found that cigarette smoking reduce risk of Parkinson disease (PD) by half for heavy smokers compared to non-smokers persons. Cigarette smoking is confirmed as risk factor for various diseases such as heart disease, lung cancer, and COPD. However, beneficial effects of cigarettes have been discussed over the years. It was in the late 1950's studies reported an adverse association between smoking and Parkinson's disease. More recently, several epidemiological studies supported the negative relation between cigarette smoking and PD. These findings suggested that patients who smoke are 50% less likely to have PD when compared to the non-smoker colleagues. This indicates that nicotines, which is the addictive substance of cigarette have a "neuroprotective" effect on PD. That may lead to totally new types of treatments for the disease and potentially reduce the side effects of existing drugs.
In this literature review we summarized the years of studies and researches in PD, and its link to smoking with a clear statement that smoke is still number one killer in our society. This study is to introduce the relation between PD and smoking to our local researcher, and PD care provider as another field of research for the interested health care, and research centers in Saudi Arabia.
we used key words such as cigarette hazards and benefits, smoking and PD relation, PD. We used many search engines for example pubmed, google, and others. The review study will discuss many published papers that reported this unique relation between smoking and PD. Papers are discussed from older to newer published date.

Keywords: *Cigarette smoking, DAT SPECT, Parkinson's disease*

1. Introduction

Parkinson's disease (PD), is a neurodegenerative disease of the brain affect nerve cells that associated with control normal movement and balance. The mechanism of PD starts when loss of dopamine neurons that's produced by nerve cells in substantia Nigeria. Dopamine is a neurotransmitter or chemical messenger that helps in transmission of signals between neurons in the brain. The etiology of PD is idiopathic, and it is supposed to be due to many risk factors such as, mutation in gene, age and exposure to some pesticides (1-15).

The symptoms appear only when around 80 percent of the dopamine neurons in the brain are destroyed. The earliest symptoms are a fine tremor of the hands while rest (shaking disappear when the part of the body that shakes being used), rigidity where the muscle stiffness in the neck and other body parts become hard to bend in the legs or arm over time, this muscle stiffness may lead to muscle aches. In advance stage of PD muscle stiffness can leads to stooped posture. Moreover, PD cause movements of the body to slowed and this is termed bradykinesia, slow in facial expressions which lead to condition called poker face which shows no emotions in the face, and PD cause difficulty in maintaining balance (16).

The diagnosis of Parkinson disease needs an effectiveness medical Imaging to distinguish PD from essential tremor and other diseases that have the same symptoms because its normal in elderly ages to lose some of these cells as part of the normal senility process (17). The most important modality to distinguish the disease is by performing a DaT SPECT scan that's measure dopamine transporter in the brain, therefore help the doctor to diagnose these cases and realize if the changes are due to normal senility or due to PD.

DaT/SPECT scans used to show the function of the brain because the brain anatomy of a Parkinson's disease patient appears normal. These types of scans based on the ACTIVITY of the dopamine transporter (19). The new DaT scans use a material that influence a part of a neuron in the brain where dopamine binds to it, displaying the density of healthy dopamine neurons. Thus, the more of the picture that lights up the healthier brain cells. If the dopamine cells part on the brain remain dark in the scan, an early brain degeneration may be diagnosed by expert reader. This could mean Parkinson's disease (20). There are scan patterns that may appear. The more widespread the decrease in uptake on the scan, the more developed the degeneration (21).

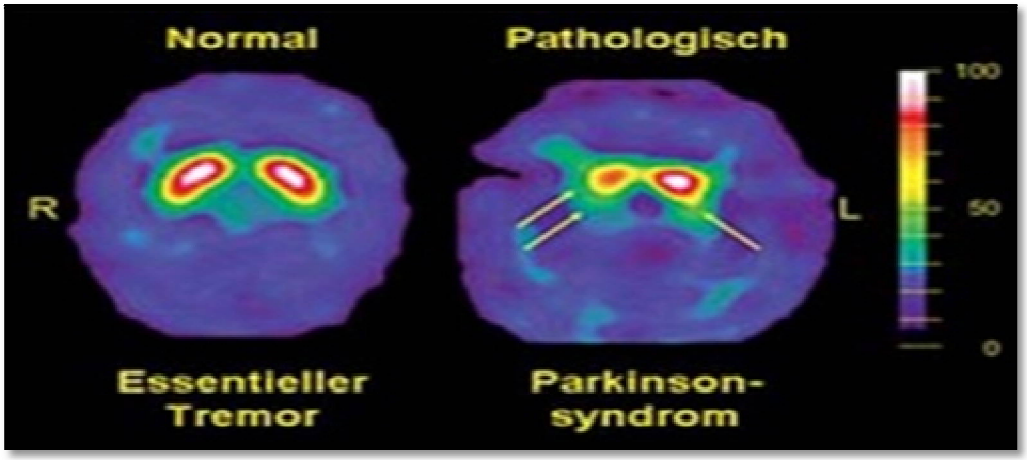

Figure 1: A SPECT Camera Showing DAT Scan and It Displays Essential Tremor on the Left (Normal DAT), and a Parkinson Syndrome on the Right (Decreased DAT)

There are some medications can minimize the symptoms of PD. The main types of drugs that used are Levodopa, Dopamine agonists, MAO-B inhibitors, COMT- inhibitors, Amantadine and Anticholinergics (22-24)**.** Levodopa (also called L-dopa) is the most effectiveness drug to control the symptoms of PD, particularly bradykinesia and rigidity. If medications are not sufficiently effective surgery may advise (24). There is very strong evidence that nicotine is preventive of Parkinson's disease. Future research based on these findings could lead to discover new types of drugs for the disease and potentially reduce some of the side effects of existing drugs (25-27)

Previous studies reported that there is a relationship between smoking and Parkinson disease where they link heavy smoking reduction in the probability of having PD by half compared to non-smokers (1,28-31). This was elucidated by the effect of chemical compounds in cigarette including nicotine which is the addictive substance of cigarettes, and carbon monoxide which induce dopamine release and up-regulate nicotinic receptors through nicotine which lead to prevent the damage of free radical damage to nigral cells through carbon monoxide, also protect against toxic neuronal damage by inhibition of monoamine oxidase B,enzyme which is breakdown the dopamine in the brain, or competitive inhibition of neurotoxins.

This beneficial effect of cigarette smoke is rarely discussed due to the hazards of smoking and the diseases. The major diseases caused by cigarette smoking were discussed many times such as chronic obstructive lung disease (COPD), cardiovascular disease and cancer. For that, when comparing between the risk and benefit of smoking we have to remember that smoking can harm all the organs in the body and cigarette smoking kills and PD not. Death related to smoking is higher than car crashes, alcohol, AIDS, suicide, homicide, and illegal drugs all combine (32-35).

The knowledge of Parkinson Disease side effect and its reflection on patients and their families is very limited in Saudi society due to lack of information on this disease. There are no regular programs from health care systems and civil societies to educate Saudis regarding this problem and to raise awareness among families of PD member. This deficiency of community service lead to poor social care for PD patients in our society and do not help families with best ways in how to deal and communicate with their PD patient member. In this literature review we summarize the decay of studies and research in PD and its link to smoking with a clear statement that smoke is still number one killer in our society. This study is to introduce the relation between PD and smoking to our local researcher and PD care provider as another field of research for the interested health care and research centers in Saudi Arabia.

2. Methods

In this literature review we reviewed some of published papers from 1950-2014 about relation between smoking and Parkinson disease. We searched Medline, google, and yahoo by these key words: Parkinson disease, cigarette smoking, and nicotine. We are going to discuss these papers based on the date of publishing.

3. Discussion

There are many questions required to be answered about the relation between smoking and PD. The main questions include the importance of smoking doses vs period, the effect of age of starting or quitting, the period after smoking cessation and before disease beginning, and the type of tobacco use. Furthermore, there is no single PD study has

had adequate sample size or diversity and it seems to be, there is no effect of age, sex, education and race on PD as the observed smoking effects(31,36,37).

There are nearly 40 epidemiological studies that have been published about this topic. In the late 1950's the first report about negative association between smoking and Parkinson's disease is done by Dorn, 1959(5)who reported decreased PD occurrence among smokers after conducting mortality studies. Later on, several epidemiological studies have found that the relation between cigarette smoking and PD in patients who smoke are 50% less likely to have PD when compared to the non-smoker counterparts. This point out that cigarette smoking may have a "neuro-protective" effect on PD (29). In the 1970's more studies, both case-control and longitudinal were achieved, and mostly supported the negative association and protective effect of smoking in PD (38). That is also the same result achieved on the case control study conducted in 1984 and in 1990(39,40).

Most research in PD relation to smoke has focused on nicotine because it protects from a variety of toxic effect in cell that damage nigral neuron. Also, there are Numerous studies state that cigarette smoke contains more than 10^{14} radicals per puff- reactive substances damage lung tissue by chemically reaction with DNA, cell membrane and other molecules in the lung(41,42).a comprehensive study was conducted in 1992by taken group of 14,436 twins from the National Academy of Sciences-National Research Council World War II Veteran Twins Registry to test the hypothesis that cigarette smoke protects against the development of PD. Examine the relation of cigarette smoking behaviors and PD. The study revealed that the risk of PD is inversely correlated to the dose or pack-years smoked. These results proven that there is a biologic protective effect of cigarette smoking on PD and suggest that nicotine stimulates dopamine release*(26)* and this is not just an epidemiological theory. A study in 1994 supported this relation in Manhattan, NY and concluded that PD reduces by smoking(43).

Morens and his group reviewed 46 articles in 1996 related to cigarette smoking and PD *(28,43-45).* They found that the negative relation was due to a direct chemical protective effect of smoking. This crucial review proved strong evidence for the hypothesis on the negative association with PD and disclose the need for direct animal studies

Furthermore, a population-based case-control study done by the Henry Ford Health System database in 1999*(31)* confirmed a strong negative association between smoking and PD. In 2000, many epidemiological studies have also found a beneficial effect of smoking in PD*(46,47).* This led to that nicotine may contribute to the lower incidence of PD among smokers. Cigarette smoke also inhibit monoamine oxidase (MAO) activity, known to breakdown dopamine (48).

A previous study (36) supported the important questions we mentioned above, and they precede the first ever analysis of PD. They combine individual level data from 3 cohort studies and 8 US case-control. The participants were almost white (81%-100%). In this study about half the subjects reported they have smoked cigarettes regularly and men reported smoking more often than women. Most participants started smoking in theirLate adolescence) mean age, 18 years in men, 21 years in women), and most smokers quit between the ages of 40 and 50 years. The result of this study showed that the effects not affected by sex or education and the risk reduction they observed for white and Asian patients were not seen in Latinand African American patients.

Various studies in 2003 tested the effect of cigarette smoke exposure on MPTP (1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine) induced neuronal changes. Inveterate nicotine treatment showed a serious reduction in the loss of dopaminergic neurons in the substantia nigra. They examined the neuro protective response of cigarette smoke and nicotine on a MPTP- induced in mouse model of PD. These authors submitted that nicotine and Less exposure to cigarette smoke may have a neuroprotective effect on the dopaminergic nigrostriatal system(37).

Quik et al in 2006, tested the effect of deep-rooted nicotine treatment against nigrostriatal damage in non-human primates. They found that the levels of dopamine transporter, vesicular monoamine transporter, dopamine and nicotinic receptors were greater in nicotine-treated MPTP-lesion primates than lesion primates not treated with nicotine(49).

A prior study (8) showed that there is a clear link between cigarette smoking and PD. Although the mechanism by which this occurs is un-clear, direct animal studies predict a possible protective effect of smoking on the development of PD and its symptoms. Therefore, the mechanism by which smoking may impart a neuro protective effect remains to be explained in an animal model. Deciding the underlining mechanism by which smoke announce its effects may aid in defining the etiology and pathogenesis of PD, and it may be applied in the development of aimed drug therapies for PD

Other researchers (50) support that the probability of quitting cigarette smoking it could be a marker for beginning of PD based on their several case-controls studies, and they relate the fewer available nicotinic acetylcholine receptors in the brain of patients with PD to the feeling less nicotine stimulates from cigarette smoking

Another research group (50) observed that smokers who had difficulty quitting cigarette smoking might due to the level of nicotinic receptors available in their brain, and smokers feels nicotine stimulate from cigarette smoking which is considered to be very difficult to quit smoking. This observation leads the researcher to believe that the group of smokers have lower risk of PD than who had easily quitting(31).

Regarding the relationship between smoking and low rate of PD, a significant research study (5) highlighted a very important point which is although cigarette smoking may prevent or delay PD in group of people, the risk of dying from smoking is much higher than the risk of harming due to PD. Cigarette smoking is a certain high-risk factor for various diseases such as lung cancer, COPD, cardiovascular disease and heart disease**.**

4. Conclusion

Heavy smoking might delay or prevent PD where many studies showed a reduction by half in infected by PD among heavy smokers compare to nonsmoker.Scientists have found that Chronic nicotine treatment resulted in a significant reduction in the loss of dopaminergic neurons in the substantia nigra. In the other hand, hundreds of studies proved that cigarettes are the first killers in our modern societies, for that the cigarettes company forced by law to write a

warning phrase on their product saying smoking harms your health. Health care systems in our society spend millions of riyals to treat many diseases resulted from smoking every year.

This research neither support smoking in anyway, nor trying to signify any positive value of smoking. We are just summarizing what had been written and published about medical phenomena that linking smokes to reduce PD symptoms and focus on that nicotine might be the new treatment to make life easier for PD patients. We present this summary to Saudi researchers in case if any group wants to pursue further research on this topic.

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