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Mini Review

Analysis of Smoking in Chronic Kidney Dialytic Patients and Cardiovascular Events

Lara Maria Bottino Vizzotto Tosato Martino[1], Guilherme Akiiti Ikeda[1], Nícolas Costa de Oliveira Ferreira e Silva[1], Ana Paula Pantoja[3], André Luis Valera Gasparoto[3], Vitória G Hernandes[3], Anita LR Saldanha[3], Francis Lopes Pacagnelli[3], Suelen Umbelino da Silva[1], Luciana Kelly de Camargos Batista[1,2], Tereza Luiza Bellincanta[3], Daphnne Camaroske Vera[3], Henrique Andrade Fonseca[3], Tania LR Martinez[3]*, Milena KM Silva[3] and Margaret Assad Cavalcante[1,2]

[1]*Universidade do Oeste Paulista–Unoeste, Brazil*

[2]*Hospital Regional de Presidente Prudente – HRPP, Brazil*

[3]*BP=hospital Beneficiencia de Sao Paulo, Brazil*

***Corresponding author:** Tania LR Martinez, BP=hospital Beneficiencia de Sao Paulo, Brazil.

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Abstract

Introduction: Chronic kidney disease (CKD) is an important public health issue with an estimated worldwide prevalence of 8 to 16%. It is responsible for high morbidity and mortality rates, but many of the risk factors for its development and progression are said to be modifiable. Systemic arterial hypertension (SAH) and diabetes mellitus (DM) are the main etiologies. Recent studies have demonstrated the role of smoking, also. The delayed perception that smoking impairs renal function as hypertension is due to the silent response of the kidney to vascular lesions. The risk of death in general and from cardiovascular events in chronic kidney smokers is twice as high as in the rest of the population.

Objective: To verify the prevalence of hypertension, smoking, DM and cardiovascular events in patients with CKD in a large hospital in São Paulo.

Methodology: This is a multicenter, clinical epidemiological, observational, analytical and quantitative cross-sectional study conducted between January and May 2019 with 134 patients on hemodialysis and peritoneal dialysis. Data were collected through medical records and the application of a questionnaire.

Results: SAH was the most prevalent etiology followed by DM: respectively 49.7% and 11.3% alone and in 12% of the sample concomitantly. After: undetermined causes (12.8%), Nephrotic Syndrome (6%), HIV (4.5%), Glomerulonephritis (2.3%) and Lupus (1.5%). The prevalence of smokers and former smokers were 6.7% and 39.6%; 53.7% said they had never smoked. Only 23.1% of the sample never came into contact with tobacco, actively or passively; 34% had cardiovascular events and the most prevalent were CAD (24.6%) and stroke (12.7%). Active and/or passive smoking was present in the previous history of 76% of these patients.

Discussion: The onset's age of dialysis was 49.7±14.6 years in opposition to the 2015 literature of 60 years: there is an earlier dialytic dependence of the population due to high rates of chronic disease diagnoses in younger individuals by today's modern lifestyle.

Conclusion: SAH and DM were the most prevalent etiologies of CKD in the sample, and tobacco was remarkable in the previous history of these patients, showing a positive association between active and/or passive smoking and the occurrence of cardiovascular events: public awareness policies. The harm of tobacco, including to the kidney, is necessary, in addition to encouraging the suspension of its use in CKD.

Keywords: Smoking; Chronic kidney disease; Cardiovascular events; Dialysis; Cardiovascular risk factors

Introduction

Chronic kidney disease (CKD) is currently considered an important public health issue [1]. It is estimated that its prevalence worldwide is around 8 to 16% and that the numbers tend to increase, as has been happening over the last years [2]. It is responsible for high morbidity and mortality rates due to numerous associated complications - cardiovascular, bone and mineral disorders, anemia, among others - and is a costly disease for the system, mainly due to the fact that several of the risk factors responsible for

its development. and progression are said to be modifiable [1-4]. In Brazil, as well as in other countries considered underdeveloped or developing, prevalence data are uncertain and heterogeneous [1]. In developed countries, the expectation of CKD cases growth is even higher: conditions such as diabetes and hypertension, for example, which may lead the patient to this outcome, are increasingly common [5]. Currently, hypertension and diabetes are known to be the main causes of CKD, and factors such as gender, age, socioeconomic conditions, proteinuria, hypercholesterolemia, hyper uremia and renal failure influence its pathogenesis [2,4,6]. In the 1970s, the main conditions responsible for CKD were chronic glomerulonephritis and pyelonephritis, evidencing a change in the pattern of the dialysis population [7].

In recent years there has been an increase in the number of studies that have demonstrated the role of smoking - another modifiable risk factor - both in the development and progression of chronic kidney disease [6]. The idea that smoking may impair renal function is recent, unlike its contribution to the development of cardiovascular diseases and cancer, especially lung cancer, which is already well established [4]. According to Alba et al. [7] the delay for nephrologists to perceive smoking as a potent renal aggressor in the same way as hypertension and diabetes are due to the silent manner in which the kidney responds to vascular injury: there is no "renal angina", for example, as it happens in the heart. In addition, the heart still has the possibility of manifesting itself through sudden signs such as acute myocardial infarction, which is no longer a reality for the kidney [7].

By inhaling smoke from tobacco, the individual is exposed to numerous particles and gases. Among them, in relation to renal toxicity, we highlight the lead and cadmium heavy metals, in addition to the already known nicotine [3]. The first two, once in circulation, have a tendency to accumulate in the renal cortex, exerting a toxic effect on tubular cells even in low amounts, especially when there is already a predisposition to renal injury: according to the study by Orth et al. [5], diabetic individuals exposed to minimal amounts of cadmium may progress more rapidly to diabetic nephropathy. In relation to nicotine, it is known that it has hemodynamic effects such as stimulating vasoconstriction, increased heart rate, blood pressure and peripheral vascular resistance, the latter having direct consequences on the kidney, reducing the filtration rate reduction. glomerular and renal blood flow [8]. Also, due to the presence of nicotinic acetylcholine receptors in the kidney, it induces mesangial cell proliferation, increasing fibronectin production by 50% [5,8]. An increase in vasopressin secretion is also observed, which in turn contributes to renal failure [9]. Finally, pro-inflammatory and pro-oxidant activities induced by tobacco are considered of utmost importance in worsening renal function [8].

Other factors related to smoking that should be considered are smoking, smoking status and time of exposure to this factor. It is known that the use of more than 20 cigarettes a day increases the chances of end-stage renal disease, and that individuals considered active smokers have a higher risk of developing CKD when compared to former smokers [4]. over the years [8]. Regarding exposure time, there is a deleterious cumulative effect throughout life: according to some studies, continuous smoking contributes to accelerating the decline in glomerular filtration rate [10]. According to Van Laecke et al. [10] In individuals exposed to tobacco, epigenetic changes appear to influence renal function, which may be responsible for unfavorable outcomes even in former smokers: such changes take time to recover [10]. However, when ceasing such a habit proteinuria tends to reduce around 50% of its levels, supporting the importance of this attitude to improve the prognosis of patients with kidney injury [11]. The harms arising from cigarette use also extend to individuals who underwent kidney transplantation. It has been evidenced that patients with a history of smoking have a higher chance of graft failure and rejection when compared to never exposed individuals [8,12] and that the cessation of such habit brings a greater survival for both the patient and the patient. the graft [8]. This event may bear some resemblance in the future to the prerequisites for liver transplants in alcohol patients: despite the existence of evidence proving the harm of smoking to the kidney, it is still permissible to apply for individuals who use it. tobacco in the waiting list for transplantation, and this issue is still a matter of debate [8].

And it doesn't stop there: according to the study by Makadia et al. [13] individuals exposed to cigarette smoke while in utero due to their mothers' smoking habits tend to have reduced size kidneys, as well as lower glomerular filtration rates when compared to those who were not exposed to smoke [13]. The risk of death in general and from cardiovascular events in patients with CKD who use tobacco is twice as high as in the rest of the population [8,14]. Given this, the present study is relevant given the need to elucidate an important issue that is still on the fringes of discussion and acceptance in the midst of nephrology, helping to sediment the harms of cigarette smoke both in the development and progression of the disease. renal disease, either passively or actively, by smoking analysis as a highly prevalent factor in patients with chronic kidney disease undergoing hemodialysis.

General purpose

To analyze smoking as a factor of high prevalence in patients with chronic kidney disease undergoing hemodialysis.

Specific objectives

Verify the number of patients on current dialysis regimen at the Presidente Prudente Regional Hospital - SP / HRPP who made and/or use tobacco;

Correlate smoking load and smoking exposure time with the development and progression of chronic kidney disease;

Methodology

This is an epidemiological, observational, analytical and quantitative cross-sectional clinical study conducted from January to May 2019. The study sample consisted of dialysis patients (hemodialysis and peritoneal dialysis) from the Presidente

Prudente Regional Hospital - HRPP during the period in question. Inclusion criteria were being on continuous dialysis treatment due to chronic kidney disease and consenting to participate in the research by signing the informed consent form (ICF). The researchers went to the HRPP facilities in the dialysis sector and applied the questionnaire during the procedure after signing the consent form. In total, the study had 134 participants.

Data collection strategy

Data were collected in two stages: first, the researchers applied a questionnaire to patients. Then, the questionnaire was added to information collected from the dialysis records of the patients in question.

The relationship between the number of patients and the scale of the times and days of the week they perform the respective procedure were provided by the head of the dialysis department of HRPP.

Data collection instrument

The instrument - questionnaire - used in this study was jointly elaborated by the researchers, aiming to gather information considered relevant to elucidate the research objectives. Among the researchers were two medical specialists: one in nephrology and one in cardiology. The questionnaire consisted of the following information (ANNEX 1): identification (name and age), risk factors for cardiovascular disease, start date of dialysis, etiology of CKD, active relationship with smoking (if current or previous, substance used, exposure time, smoking burden), passive relationship with smoking (current or former cohabitation with smokers, time, smoking status of smokers), previous cardiovascular events (coronary artery disease, aneurysms, ischemic stroke, deep vein thrombosis), practice of physical activity present or not, blood pressure at the beginning of treatment and laboratory data at the beginning of treatment (total cholesterol, LDL, HDL and triglycerides).

Ethical aspects

The study was submitted to the National Research Ethics Committee (CONEP) of Plataforma, Brasil and was approved under the following number: 02501018.0.0000.5515. From this, the researchers started applying the questionnaire to the participants.

Data analysis

Data were tabulated in Microsoft Excel software. Then, a descriptive analysis was performed, based on frequency counting for discrete variables and calculation of descriptive measures for continuous variables, with the aid of Action Stat software, version 3.5.152.34. To test for differences in TC, LDL, HDL and TG between smokers and non-smokers, the Student's t-test was used when the assumption of normality was verified (by means of the Shapiro-Wilk test), and the Mann-Whitney test when not. normality is verified. The next step in the analysis was to test the hypothesis that the age of the patient at the onset of dialysis differs between smokers and non-smokers. At this stage an ANOVA was performed to compare the groups, as well as the Tukey test for multiple comparisons. These same tests were also used to verify whether the smoking load of smokers and former smokers influences the age at which they begin dialysis. The significance level adopted in all tests was 5%.

Results

The sample consisted of 134 individuals with a mean age of 54±14.1 years, of which 78 were male (58.2%) and 56 females (41.8%). The prevalence of smokers and former smokers at the time of data collection, respectively, was 6.7% and 39.6%. Thus, the prevalence of active exposure to cigarettes corresponded to 46.3%. Still, 53.7% of patients said they had never smoked. Of the entire sample, more than half (62.7%) have lived or live with someone who smokes, while only 23.1% of individuals have never been in contact with tobacco, either actively or passively. Among the individuals who smoke, in relation to the period of exposure, the average time they have already been smoking was 31.4 ± 17.7 years, and all reported smoking classic tobacco. Of these, 77.7% smoke up to 10 cigarettes a day and 11.1% more than 20; 33.3% have tried to quit, 55.6% say they want to quit and 88.9% said they know the harm that cigarettes do. In relation to former smokers, 86.8% smoked classic tobacco and 9.4% straw smoke; 45.3% had a smoking load of more than 15 cigarettes / day. The most prevalent primary causes of dialysis CKD were hypertension and diabetes mellitus, which together with other reasons or alone, were responsible for the prevalence of 61.7% and 46.26% of cases, respectively. Then there are undetermined causes (12.8%), Nephrotic Syndrome (6%), HIV (4.5%) Glomerulonephritis (2.3%) and finally Lupus (1.5%). Regarding cardiovascular events, the results revealed that 65.7% of patients never presented any complications contemplated in the questionnaire applied by this study. The most prevalent events were, respectively, Coronary Artery Disease - CAD (24.6%) and Ischemic Stroke - AVEi (12.7%). Moreover, the relationship of patients who presented such events with tobacco was verified, classifying them as smokers, former smokers, passive smokers, only and finally, without active or passive contact with the substance. Smoking - active and / or passive - was present in the previous history of 76% of these patients.

The following cardiovascular risk factors were investigated in patients: Hypertension, diabetes, dyslipidemia, obesity, male gender and smoking. Hypertension was 81.3%, while dyslipidemia was present in 38.8% of the sample. Of all respondents, 94.8% had at least 1 risk factor for cardiovascular disease, and 14.9% had four factors simultaneously.

The next variables analyzed were the TC, LDL, HDL and TG levels referring to the beginning of the dialysis treatment of the sample patients, and the values were taken from the medical records of that service. It is noteworthy that the adopted LDL values come from the laboratory report. However, according to the p-values, these differences were not considered statistically significant at a significance level of 5. %. Only TG were lower among non-smokers. We sought to correlate tobacco exposure - actively or passively - with the period in which individuals began dialysis treatment

in their chronology. We hypothesized that the age of initiation of dialysis treatment differs between smokers and non-smokers. To perform this test, patients were classified as smokers, non-smokers, former smokers and passive smokers. For former smokers who were also passive smokers, they were allocated in the first category. Mean dialysis initiation ages of smokers, passive smokers and nonsmokers are close (around 46 years), whereas former smokers appear to have started treatment a little later, around 54 years old of age, contrary from what expected, and no reason was found to explain it. With a p-value of 0.0368, it can be concluded that the ages of onset of dialysis differ between groups at the 5% significance level. Thus, to identify in which group (s) this difference was significant, the Tukey test, with multiple comparisons of each group pair, was run. Only the groups of passive smokers and former smokers were considered significantly different. From this it can be concluded that patients on dialysis who are former smokers start it about 7 years later than those who are passive smokers and that this age difference is considered significant. To finalize the analysis, a test was performed to verify whether the smoking load of smokers and former smokers influences the age at which they began dialysis. According to the p-value of the test, there were no significant differences between the ages of onset of dialysis in relation to the smoking load.

Discussion

Data on smoking prevalence in chronic dialytic renal patients are uncertain and scarce [1]. According to Liebman et al. (2011) more recent information suggests that 6.2% of dialysis patients are smokers. This study initially had the hypothesis that dialysis patients have a high prevalence of smoking. In this sense, it was found that 6.7% of the sample were smokers at the time of the interview, while 39.6% were former smokers. Thus, 46.3% of patients already actively exposed themselves to cigarettes at some point in their lives, confirming the previous hypothesis of the study. A higher prevalence of CKD was found in males - 58.2% - compared to females - 41.8% - a fact previously observed in the study by Sarmento et al. [2]. The average age of the patients was 54±14.1 years, and the average age when they started dialysis was 49.7±14.6 years. According to Thomé et al. [23] Most individuals on dialysis in Brazil are aged 45 to 64 years, a fact consistent with the findings of the present study. However, it is worth mentioning the change that this scenario has undergone in recent years, since in 2015 the census of the Brazilian Society of Nephrology published that the predominant age group in the country was from 60 to 69 years [2]. From this, it can be inferred that there is currently a trend towards earlier dialytic dependence of the population. One of the possible explanations may be the high rate of chronic diseases such as hypertension and diabetes in the population, two of the main globally recognized etiologies of CKD, which are increasingly diagnosed in younger individuals, as a consequence of the current lifestyle of society. modern: sedentary lifestyle, fast food, high stress levels, high consumption of processed products, etc. From this perspective, the most prevalent etiology of CKD in the sample was hypertension (48.9%), followed by diabetes (11.3%). Such results were expected given the previously described reality.

Surprisingly, HIV was responsible for 4.5% of CKD cases. Pre-existing data suggest that about 3.5% of the causes of CKD correspond to HIV infection, and according to Bonotto et al. [24] effective antiretroviral therapy can reduce the risk of developing CKD by 46% [24]. It was found that 46.3% of the patients on dialysis were already actively exposed to cigarette smoke, while passively, the prevalence found was 62.7%, and only 23.1% of the sample never came into contact with this substance, noting the remarkable figure of smoking in the early history of these chronic kidney. There are several known mechanisms by which tobacco promotes deterioration of the circulatory system including renal microcirculation, mainly due to nicotine: besides stimulating vasoconstriction and increasing vasopressin levels, this substance acts directly on the kidney, causing mesangial proliferation [3,8]. Smoking has also been related to the increased likelihood of CKD [21], especially in individuals who are pre-disposed to kidney injury: heavy metals present in tobacco - cadmium and lead - accumulate in the renal cortex even in small amounts. exert toxic effects on this tissue [3]. That said, such prevalence data relative to such exposure should not be considered casual, since in recent years many studies have associated the role of tobacco - as well as high blood pressure levels, race, prevalence of cardiovascular disease, among other factors - with a serum creatinine increase, and consequently, a decline in renal function [21].

Analyzing the ages at which study subjects were introduced to dialysis, it was found that former smokers started it later than all other individuals, including passive smokers and smokers. It is noteworthy that in the division of groups, former smokers who were also passive smokers were allocated together to smokers for comparison purposes. Thus, this data refers exclusively to former smokers, and is in agreement with what Laecke et al. [8] published about smoking and the development of CKD: the risk of developing it decreases over time after smoking cessation, whereas it increases through active use and prolonged exposure [4,8]. Therefore, the fact that former smokers in the sample started dialysis about 7 years more trade than other individuals may indicate a cause / effect or dose-dependence relationship with this substance. The study, however, did not correlate exposure time with this result. However, these results suggest that smoking cessation encouragement should be given at all ages. It is interesting to note that other authors have already alluded to age, CKD and tobacco, and there are reports in the literature that the impact of smoking-related mortality is greater among younger dialytic chronic kidney than older ones [25]. According to what was stated by Stack et al. [25], in addition to the high prevalence, complications arising from atherosclerosis have a massive effect on increased mortality of patients with dialytic chronic kidney disease. Therefore, the control of cardiovascular risk factors is extremely important, especially in these patients. In the present study, 14.9% and 23.1% of patients had, respectively, four and three risk factors simultaneously for cardiovascular disease, a considerably critical percentage considering that 81.3% of the sample was hypertensive, 38, 8% dyslipidemia and 32.1% diabetic, chronic diseases that have a detrimental effect on blood vessels. In addition, it is noteworthy that only 33% of diabetics, 29% of

dyslipidemias and 22% of hypertensive patients had no active and / or passive contact with tobacco, a known and modifiable cardiovascular risk factor, highlighting the importance of raising awareness. the population of the harm caused by this substance in this group.

Because it is characterized as a modifiable risk factor and evidence suggests that smoking is responsible for increased mortality, number of cardiovascular events, post-transplant graft rejection rate, and acceleration of atherosclerosis in chronic renal patients. [25] The poor approach to this issue, especially of passive exposure to tobacco, is remarkable, as this contact appears to be common: among the 46 patients who reported cardiovascular events, only 11 (24%) never came into contact with this substance, while that in the group that was already actively and / or passively exposed, the prevalence of these events was 76%, identifying a positive association between tobacco and the occurrence of such events (prevalence ratio 3.1), besides to reiterate it. CAD was the most prevalent cardiovascular complication in the sample (24.6%) followed by stroke (12.7%). According to Zhou et al. [26] Nicotine, through mechanisms that include macrophage activation and increased oxidized LDL uptake has pro-atherogenic effects, justifying a higher prevalence of CAD in the group exposed to it, as found in this study. In addition, the reduction in HDL levels promoted by cigarettes, making the picture described even more conducive. In this study, however, the HDL differences between active and passive smokers compared to non-smokers, although they existed were small and with a significance level of 5%. Triglyceride levels, however, were higher in smokers.

It is pertinent to point out that in this study, although lipid levels were not as expected when compared between smokers (active and passive) and nonsmokers, such result does not negate three facts; The first refers to the harmful action of tobacco to the dialytic chronic renal, and smoking at the beginning of dialysis, by itself, already increases the risks inherent to this individual regarding mortality regardless of the previous existence of cardiovascular disease. Second, as reported by the KDIGO Clinical Practice Guideline for Lipid Management in Chronic Kidney Disease (2013), dialysis patients constitute a group with the highest absolute risk for coronary heart disease, with higher or lower LDL levels. they are not a criterion of greater or lesser severity, respectively, nor are they a criterion for pharmacological treatment. Finally, the present study reveals that regardless of the comparisons, these individuals had a low mean HDL value (38.7). On the other hand, only 55.2% of individuals stated that they practiced some type of physical activity, and the frequency and duration of this activity were not investigated. 22.4% of the sample had a diagnosis of obesity recorded in the medical chart, except for overweight individuals. Based on the above and respecting the inherent limitations of the underlying disease, a need for guidance and reinforcement regarding the importance of lifestyle change is identified, especially before dialysis treatment is needed.

Among the weaknesses of the study, we highlight the quality of the etiological records of CKD of patients, as well as the memory bias at the time of application of the questionnaire to the sample. An important aspect of the survey was the size of the sample and the correlations performed, since there are not many publications on the subject.

Conclusion

The prevalence of active exposure to cigarettes was 46.3% and passive exposure to 62.7%. The real implication of smoking - both actively and mainly passively - in patients with CKD is not well established. The present study reveals a high prevalence of active and passive exposure to tobacco in the past history of patients on current dialysis, reinforcing the important role of this substance in their previous history, a fact that should not be ignored by public health. Thus, studies to further elucidate this relationship become crucial for a better understanding of the harmful effects of this substance on renal function. The most prevalent etiology of CKD in the sample was hypertension followed by diabetes, causes already recognized and expected as the main in this regard. However, a higher than expected prevalence of HIV was observed. Regarding the average age of the patients, this study supports the reasoning that patients are starting younger and younger dialysis treatment (mean age 49.7±14.6 years), a fact that should be attributed to the diagnosis each time. early on of hypertension and diabetes, as well as the lifestyle change of modern satiety. This study demonstrated a positive association between active and passive tobacco exposure and the occurrence of cardiovascular events, where only 24% of individuals with a history of an event had never been exposed to tobacco. Noting that former smokers tend to start dialysis later than active and passive smokers, the study in question makes its major contribution: endorsing the discourse that smoking cessation should be encouraged as soon as possible, especially in the renal group, in order to prevent the progression of the disease and the occurrence of cardiovascular events that further increase the mortality of these individuals. Finally, it is concluded that active and passive smoking is related to CKD and its outcomes, and it is necessary to invest in public policies that seek to raise awareness of the harmful effects of smoking, including on the kidney, and encourage smoking cessation. regardless of age for all chronic renal.

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Conflict of Interest

No conflict of interest.

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