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Workplace gasoline exposure increases the risk for early renal dysfunction: A case-control study in Mexico.

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Abstract

Gasoline is a solvent and exposure to it has been associated with advanced stages of kidney disease. Workers at traditional automobile repair shops and gasoline stations in Mexico are continuously exposed to gasoline. In the present study, we evaluated the association between exposures to gasoline at the workplace (in "traditional" auto repair shop mechanics and gas station attendants) with early kidney function abnormalities (microalbuminuria/proteinuria). Ninety-nine cases and 130 controls were analyzed. Subjects presenting with high blood pressure, diabetes mellitus, and acute pathologies related to kidney alterations were excluded. The quantity of excreted protein in urine was determined. A level of albumin in urine of 50 mg/l (Micral-Test) was regarded as microalbuminuria and its presence was considered early renal dysfunction. After adjustment to known risk factors (sex, age, overweight/obesity, smoking, and high cardiovascular risk), exposure to gasoline resulted in a 2.5 increase in the risk for early renal dysfunction (OR: 2.46, 95% CI: 1.1-5.7, p=0.03). In the crude odds ratio analysis, that risk gradually became greater as the years of exposure increased, but after the statistical adjustments with the known risk factors, the level of risk did not increase in relation to the years of exposure. In conclusion, exposure to gasoline in mechanics working at traditional automobile repair shops and in gas station attendants, significantly increased their risk for early renal dysfunction. Preventive measures should be implemented and diagnosis should be opportune to avoid end-stage renal disease.

Keywords: Gasoline, Microalbuminuria, Renal insufficiency, Risk factors, Proteinuria, Mexico.

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Introduction

Chronic kidney disease (CKD) is a worldwide health problem that represents a great economic expense for society in general and for the patients' families in particular [1,2]. It also produces significant deterioration in quality of life of the patients, as well as negatively affecting those close to them [3,4]. Early detection and intervention in kidney disease can help slow kidney function decline, prevent complications, and decrease cardiovascular events, thereby improving survival and quality of life. Currently, the main risk factors for kidney damage are diabetes mellitus and high blood pressure [1,2,5,6]. However, CKD etiology remains unexplained in a considerable number of patients [7]. Experimental studies suggest that many chemical products can affect the kidney, but the role of organic solvents in chronic diseases has long been the subject of debate [1,3].

Gasoline is a solvent, and exposure to it has been associated with advanced stages of kidney disease. There are a limited number of studies on the topic and none of them analyzes the risk for early renal function abnormalities. Microalbuminuria is an early alteration that serves as a predictive marker for kidney damage [8,9]. Early progressive renal function decline has been shown in a large number of patients with microalbuminuria or proteinuria (32 to 50%, respectively), despite their having normal or elevated baseline kidney function. Once the process of decline begins, it progresses until reaching impaired kidney function. Studies suggest that progressive kidney function loss does not start at the proteinuria stage, but rather 10 to 15 years earlier, during the microalbuminuria stage, or even before that [10,11]. If exposure to gasoline were to increase the risk for presenting with microalbuminuria, this would serve as a base for early detection of kidney alterations in the exposed workers. Such knowledge could help affected individuals avoid future exposure to solvents, and possibly reduce progression to terminal disease [9-13].

In different regions of developing countries, auto repair shop mechanics and gasoline station attendants are exposed to gasoline on a daily basis, generally without adequate protection. Therefore, determining the risk that those persons have for presenting with microalbuminuria is of great interest in both medical and labor contexts [9]. The present case-control study analyzed the association between prolonged gasoline exposure in the workplace and the development of microalbuminuria in a population in western Mexico.

Material and Methods

Study population

Within the time frame of January 2014 and December 2015, a total of 420 individuals were analyzed. Of those individuals, 229 were exposed to gasoline at work and 191 were not exposed to gasoline. After the elimination criteria or inconsistent results in urine samples were considered, the case group consisted of 99 individuals with prolonged exposure to gasoline and the control group consisted of 130 individuals with no such exposure (Figure 1). The cases and controls were unrelated Mexican mestizo subjects from the State of Colima (western Mexico). All the participants signed statements of informed consent and their participation in the study was voluntary. The Research Committee of the Universidad de Colima, the School of Nursing, and the Research and Ethics Committee of the Hospital General de Zona No. 1, IMSS Colima approved the evaluation protocol. The study, regarded as minimum risk research, was carried out according to the principles of the World Medical Association Declaration of Helsinki and the General Guidelines for Health Research. The anonymity of the participants was guaranteed and all were given healthcare orientation.

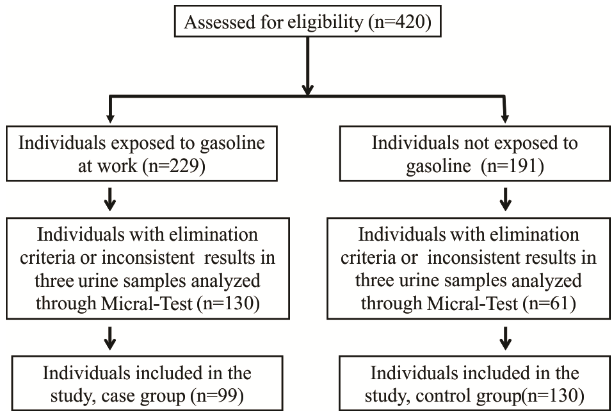

Figure 1. *Flow diagram showing the selection process of the individuals included in the study. The main elimination criteria were fasting serum glucose above 100 mg/L, high blood pressure, diabetes or any other chronic disease affecting kidney function, fever within 24 hours prior to the study, leukocyturia, hematuria, or glycosuria in the urinalysis, among others (see "Elimination criteria" in the Material and Methods section).*

The case group

A combined total of 99 automobile repair shop workers and gasoline station attendants with at least one year of gasoline exposure were included in the study. The participants worked in "traditional" repair shops, in which the mechanics come into direct contact with gasoline, oils, and grease. Workers have no protective equipment and there are no gas extractors in the workplace. Gasoline is the main hydrocarbon or derivative that the mechanics come into contact with, because it is used to clean motor pieces and is also applied directly to the skin to remove oil and grease from the body (mainly the hands). In contrast, gas station attendants usually have little direct physical contact with liquid gasoline, but they have much greater exposure to its vapors. Those workers do not wear gloves or protective masks and are in contact with gasoline fumes approximately 8 hours a day, 6 days a week.

The control group

A total of 130 clinically healthy subjects that came to the Hospital General de Zona No. 1 of the IMSS Colima, in the function of accompanying a relative with a chronic disease, were included in the study. No individual in the control group had a history of gasoline exposure at the workplace or on a daily basis, and each one was paired with a participant of the case group by sex and age (± 5 years). Elimination criteria for both groups: The following elimination criteria were applied to the initial groups exposed to gasoline (n=229) and unexposed to gasoline (n=191): individuals that presented with fever or dehydration within 24 h prior to the study, those that had eaten large quantities of meat, that had done excessive exercise, and in the case of women, those that were menstruating. Subjects that were being treated for diabetes mellitus, high blood pressure, or some other chronic disease affecting kidney function were also excluded, as were those individuals that presented with a serum glucose level of more than 100 mg/L (after 4 or more hours of fasting) [14] or at-rest blood pressure values above 140/90 mmHg. Subjects that had leukocyturia, hematuria, or glycosuria in the urinalysis were also eliminated from the study. After the application of the elimination criteria, the study population included a total of 99 subjects in the case group and 130 subjects in the control group.

Procedure

A case history was elaborated for each participant through an interview and completed physical examination. The body mass index was established (weight in kilograms, divided by height in centimeters squared) [15] and the waist-hip index was obtained by calculating the circumference of the waist in centimeters divided by the circumference of the hip in centimeters. Cardiovascular risk was determined through the waist-hip index and was considered positive when figures were higher than 0.95 for men and 0.85 for women [16]. Smoking was regarded as positive when one or more cigarettes were smoked per day.

A capillary blood glucose test with at least 4 hours of fasting was also carried out, using reagent test strips and a Roche Accu-Chek glucometer. A urinalysis using Roche Combur® reagent test strips was done to detect elimination criteria. Microalbuminuria was evaluated in urine through Roche Chemstrip Micral Albumin Test Strips. All detections were carried out according to the manufacturers' instructions [8]. The Micral-Test employs a strip upon which the color reaction is mediated by an antibody-bound enzyme [17]. This method has shown good correlation with radioimmunoassays and is a rapid screening method.

Although there are studies in which a 20 mg/l albumin concentration with the Micral-Test is considered positive [18], some authors state that said value can increase the number of false positives to 42% in diluted urine and up to 83% in concentrated urine [19]. Therefore, in the present study, a concentration of albumin in urine of 50 mg/l or more was regarded as microalbuminuria (early renal dysfunction). The quantity of protein excreted in urine was determined on an ordinal scale that was divided into four levels (0-19, 20-49, 50-99, 100 or more). To compensate for variations in urine concentration in spot-check samples, three spot samples were taken on different days within the same week. Patients were considered positive or negative when their results matched the three samples, and were eliminated from the study if their results were inconsistent. The microalbuminuria level was the median of the three samples. Patients eliminated from the study due to the detection of a disease or an elimination criterion was referred to their family doctor.

Statistical analysis

Frequencies, percentages, and means of some of the study variables were obtained. Depending on whether the data were qualitative or quantitative, either the chi-square test or the Student's t test was used to examine the differences between the cases and controls. The association between exposure to gasoline and the risk for early renal dysfunction (microalbuminuria) was estimated by OR and the corresponding 95% CI calculations (Crosstabs procedure in the SPSS version 19.0). Risk factors were controlled using a Mantel-Haenszel analysis (sex; age: 5-year strata; overweight/ obesity: presence or absence; smoking: presence or absence; high cardiovascular risk: presence or absence). The correlation between the level of protein excretion in urine (ordinal scale) and the years of exposure to gasoline was carried out using the Spearman test. All statistical analyses were performed with the SPSS version 19.0 software. Statistical significance was reached when $p<0.05$.

Results

All participants were individuals with no chronic pathologies (diabetes, high blood pressure, hyperlipidemia, etc.). The mean age of the participants was 36.5 ± 14.8 years for the case group and 37.8 ± 14.3 for the control group (p=0.19). Microalbuminuria positivity was 39.4% in the case group and 13.8% in the control group. After adjustment to the known risk factors (sex, age, overweight/obesity, smoking, and high cardiovascular risk), exposure to gasoline resulted in a 2.5 increase in the risk for early renal dysfunction (OR: 2.46; 95% CI: 1.1-5.7, p=0.03). A crude OR analysis showed that the degree of association increased with the years of gasoline exposure. That association was statistically significant only when there were 6 or more years of exposure. However, when making the statistical adjustments with the known risk factors, the level of risk did not increase with the years of exposure (Table 1). The years of exposure to gasoline were positively correlated (r=0.25 correlation index) with the level of protein excreted in urine (p=0.03).

Table 1. *Analysis of the association between gasoline exposure at work and early renal dysfunction (microalbuminuria).*

Years of exposure	OR for Early Renal Dysfunction*			P
	Crude	P	Adjusted**	
1 to 5	2.1 (0.81-5.8)	0.10	2.4 (0.8-7.5)	0.11
6 to 10	3.3 (1.2-8.9)	0.02	3.3 (1.1-10.0)	0.03
11 or more	3.9 (1.8-8.4)	0.00	2.6 (1.1-6.6)	0.04
1 or more	3.2 (1.7-6.2)	0.00	2.5 (1.1-5.7)	0.03

*Compared with individuals having no history of exposure to gasoline at the workplace or on a daily basis. **Adjusted by sex, age, overweight/obesity, smoking, and high cardiovascular risk.

Cumulative effect of exposure to gasoline and cardiovascular risk/obesity was detected. The individuals exposed to gasoline that presented with obesity and cardiovascular risk (through the waist-hip index) had an almost 12 times greater risk for developing early renal damage, compared with the subjects that were not exposed to gasoline and that did not present with obesity or cardiovascular risk (OR: 11.8; 95% CI: 1.5-93.9, p=0.01). In individuals that were not exposed to gasoline, the presence of obesity and cardiovascular risk produced an OR that was lower, but not statistically significant, than in those unexposed individuals with no obesity or cardiovascular risk (OR: 5.6; 95% CI: 0.69-45.96, p=0.06).

Discussion

In our study, work as a gas station attendant pumping gasoline or as a mechanic at a "traditional" automobile repair shop (activities linked to gasoline exposure) increased the risk for presenting with early renal dysfunction (microalbuminuria). That risk, as well as the quantity of protein excreted, became higher as the years of gasoline exposure at the workplace increase. Repeated exposure to high concentrations of gasoline has previously been reported to cause pulmonary, brain, and renal lesions [20]. The authors of a cohort study reported that exposure to gasoline resulted in a 7.5 fold increase in the risk for end-stage renal disease [8], similar to our risk result in relation to early renal alterations. Gasoline and other organic solvent vapors have been shown to cause proteinuria [21] or high levels of urea, creatinine, and uric acid in rats, suggesting kidney involvement [22]. The exposure to massive quantities of gasoline can cause interstitial edema, as well as degeneration of the glomerulus and proximal convoluted tubule, which can explain the renal deficiencies [12].

It is important to point out that the risk for kidney damage was drastically increased in individuals exposed to gasoline that concomitantly presented with cardiovascular risk and obesity (OR=11.8). That risk was also much higher in individuals that were only exposed to gasoline or that only presented with cardiovascular risk/obesity. Such information is valuable when evaluating those risks in different populations. This interaction is congruent with previous reports on the association between cardiovascular risk and early renal damage [1,2].

Microalbuminuria is an early alteration that serves as a predictive marker for kidney damage [9,13]. In our analysis conducted in western Mexico, exposure to gasoline significantly increased that alteration in traditional automobile repair shop workers and gas station attendants. The workplace conditions of our study population could be similar to those in different parts of the world. Exposure to gasoline or other solvents should be minimized through worker protection strategies.

Furthermore, the at-risk population should be periodically checked-up to detect early renal alterations, and if found, those workers should avoid further contact with gasoline with aim to prevent the progression of kidney damage. It's worthy of mention that microalbuminuria is also present in 13.8% of clinically healthy individuals not exposed to gasoline, similar to the data reported in another Mexican population [23].

The use of a screening method to detect microalbuminuria was a limitation of our study. Micral-Test strips rapidly detect microalbuminuria, but this method has its drawbacks. Multiple measurements were performed to minimize errors. Therefore, it is suggested that future studies be performed with quantitative or functional methods, utilizing 24-hour urine samples.

In conclusion, exposure to gasoline significantly increased the risk for early renal dysfunction in mechanics at traditional automobile repair shops and in gas station attendants. Preventive measures and opportune diagnosis should be carried out to avoid end-stage kidney disease.

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