

Credibility of a smoking questionnaire based on urine cotinine level for patients with bladder cancer – a preliminary report

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KEY WORDS

bladder cancer ▶ smoking ▶ cotinine

ABSTRACT

An analysis of the reliability of a questionnaire on smoking in 96 patients with transitional cell carcinoma (TCC) of the bladder. The credibility of the questionnaire was evaluated based on the detection of cotinine, an objective marker of tobacco smoke exposure, in urine. It was confirmed that approximately 18% of smokers did not admit to smoking, did not comply with recommendations to stop smoking, and about 4% of non-smokers were exposed to tobacco smoke unknowingly.

INTRODUCTION

Bladder cancer is the second most common cancer in the urogenital tract. In about 85% of cases at the time of diagnosis of cancer is limited only to the urinary bladder in the remaining 15% of the observed expansion beyond the urinary bladder [1]. An association of bladder cancer and smoking was confirmed. Carcinogenic factors contained in tobacco smoke influence the occurrence of bladder cancer. The first confirmed carcinogenic factors were the aromatic amines: o-toluidine, 2-naftylamine, 4-aminobiphenyl, and many other chemicals contained in tobacco smoke [2].

In recent years, smoking has become a serious social problem. Currently there are about 1.1 billion smokers. In Poland, there are about 9.5 million people smoking, including 43% of men and 22% of women. Passive smoking is also becoming a widespread social phenomenon, mainly at home (47% men & 52% women) and work (55% men & 27% women) [3].

In Poland, smoking is considered a shameful habit so patients asked about their smoking history do not readily admit to active smoking or they say they quit smoking just before evaluation. Most patients know that smoking is harmful since they are ashamed to admit to active smoking (embarrassed for their ignorance). They do not realize that it is possible to assess the reliability of the collected information about the history of smoking. We do not consider smoking danger warnings placed on cigarette packs and media-advocated smoking cessation as helpful to the no-smoking cause. The International Agency for Research on Cancer predicts that by 2020 the number of deaths related to smoking will rise to 10 million per year, of which 70% will be in developing countries. At present approximately 20% of cancer deaths are associated with smoking [4]. In this the lung cancer.

It is, however, satisfying that recently administrative rulings managed to limit the number of public places where smoking is

permitted. Research was carried out, which allegedly confirmed the positive results of this reduced smoking.

OBJECTIVE

The aim of this study was to assess the reliability of a subjects smoking history, and assess compliance with the recommendations of smoking cessation on the basis of a questionnaire and the measurement of cotinine, a marker of exposure. The study protocol was approved by the local ethics committee. The study is a part of the long-term study conducted in our department funded by the National Research Committee, grant No. N403-601138 awarded in 2010.

MATERIAL AND METHODS

The evaluation of patients treated in the department of General, Oncologic and Pediatric Urology of Collegium Medicum Nicolaus Copernicus University in Bydgoszcz in the period from June 2009 to December 2010 who had confirmed primary or recurrent bladder cancer by histopathological examination was undertaken. Every patient who agreed to participate in the study signed an informed consent form and completed a questionnaire on smoking history and tobacco smoke exposure. It was asked whether the patient smokes, if so, how many cigarettes per a day and for how many years. Smokers were asked when they stopped smoking, how many cigarettes were smoked per day, and for how long.

A model questionnaire on the history of smoking:

1. Non-smoker and non-exposed to the tobacco smoke

Never smoked	Stopped smoking		
	<1 year ago	2-5 years ago	>5 years ago

2. Smokers

The number of cigarettes smoked, packages (1 pack = 20 pieces)	Since I smoke?

3. Exposed to tobacco smoke "passive smoking"

Place of exposure to tobacco smoke	Home	Work	Another place
The residence time in tobacco smoke (hours)			
Number of smokers			

Each patient had their urine cotinine levels determined immediately after admission to the hospital to reduce the number of false-negative results arising from the discontinuation of smoking during hospitalization. Cotinine (name of the synthetic (S)-1-methyl-5-(3-pyridinyl)-2-pyridyna) is an objective indicator of exposure to tobacco smoke and is found in the urine, even several hours after smoking; with a half-life of 20-40 hours [5]. In the body, it can be detected at very low concentrations in the limit 0.57 nmol/l = 0.1 ng/ml (6). The analysis of cotinine, the main metabolite of nicotine, were determined by high performance liquid chromatography (HPLC / DAD) [7]. Application to the markings cotinine HPLC / DAD allowed the side to ensure adequate sensitivity of determination (ng/L) also identify the compound, determined by analysis of mass spectra. Downloaded from those covered in the study sample of urine (about 50 ml) for analysis were stored at minus 20° C. Cotinine extraction from urine was carried out in alkaline (pH = 11.1 mol NaOH). The extraction was carried out using dichloromethane in an ultrasonic bath for 30 minutes. After evaporation of organic solvent in a nitrogen atmosphere the dry residue was dissolved in methanol and analyzed by HPLC / DAD with the following conditions: liquid chromatograph f-my Agilent Technologies (binary pump & autosampler) column Eclipse XDB C8 Zorba (150x4, 6 mm, 5 µl) at 25° C, injection volume 20 ml. The mobile phase was methanol / ammonium buffer pH = 3.5 with a flow of 0.8 ml/min. Detection wavelength λ = 260 nm.

RESULTS

Detection of cotinine level in urine was performed in 96 patients, of which 35 patients (36%) obtained results indicating active smoking (cotinine levels in the urine of >200 ng/ml, values range from 257 to 7929 ng/ml) and in 4 patients (4%) had cotinine levels equivalent to "passive smoking" (level between 0-200 ng/ml, range of values from 40 to 187 ng/ml) while in the remaining 57 patients (59%) had no cotinine in urine (Table 1).

We analyzed the questionnaire completed by patients and compared it with test results of cotinine in the urine. Among the 96 patients, 18 admitted to smoking (at about 19%), the remaining 78 patients said they did not smoke or to quit. In fact, in 35 (36%) patients were confirmed by cotinine levels indicating active smoking, in 4 patients, exposure to tobacco smoke at home. Among smokers, the average smoking time is approximately 33 years (range from 20 to 45 years). The number of cigarettes smoked was on average 15.6 pieces per day (range of values from 15 to 20 pieces a day)

Table 1. Subjects groups on basis cotinine level

	Active smoking	Passive smoking	No smoking
Cotinine level	36 (36%)	4 (4%)	57 (59%)
The questionnaire	18 (19%)	0	78 (81%)

Within 18 months of observation in 3 patients in the first test was confirmed in the urine cotinine (values from 2709 to 4760 ng/ml) in a subsequent study found no cotinine in 2 patients, with a group of non-smokers in another examination confirmed that indicates the level of active smoking (values from 839 to 1110 ng/ml) was not confirmed in the questionnaire.

DISCUSSION

It is widely know from numerous publications that bladder cancer and smoking are strongly linked; however, no significant

correlation between the type of tobacco smoking, nicotine content of the smoked cigarettes, and higher risk of bladder cancer was confirmed. All cigarette smoking, both "strong" (with a higher nicotine content) and "weak" (with reduced nicotine content), with or without a filter, has the same negative effect on our body without clinically important differences [8]. There are no further reports assessing how smoking affects the course of bladder cancer, the number of recurrences, and the progression of the disease. No such analysis is probably due to the limited reliability of the smoking questionnaire and due to expensive and time-consuming methods of monitoring cotinine in urine in all patients, which can only be afforded by a few university centers. The destructiveness of tobacco should always be presented to all smoking patients in an attempt to persuade the smokers to stop smoking. This study found that not all patients admit to smoking, and not all follow the recommendations to quit smoking. In the present study patients did not know that the information contained in it would be verified objectively before filling in the questionnaire. Therefore, 18% of patients admitted to active smoking and 4% of patients were unaware of the adverse effects of tobacco smoke exposure. Three smoking patients quit smoking by the 18-month follow-up while two from the group of non-smokers had confirmed active smoking in subsequent examinations, although the questionnaire strongly denied that those patients smoke.

Using a marker of exposure to tobacco smoke has allowed us to assess the credibility of such a questionnaire. Each patient was determined in urine cotinine levels immediately after admission to hospital to reduce the number of false-negative results resulting from smoking cessation during hospitalization, despite the fact that the period of persistence of cotinine in the urine is so long that it enables detection, even after several hours [9]. Detection of cotinine in urine proved to be a convenient and easy way that was acceptable to the patient and chosen by the authors of the study to eliminate the stress factor associated with the collection of a blood sample.

Cotinine analysis was performed by high performance liquid chromatography. Application to the markings cotinine HPLC / DAD allows side to ensure adequate sensitivity of determination (ng/L) also denoted the identification of compound [10]. Statement and determine the levels of cotinine in the urine of patients who do not smoke tobacco will allow the realization of risks arising from the presence in tobacco smoke to those who reside there but involuntarily and unknowingly risk individuals [11, 12]. In our study, people exposed to tobacco smoke, "passive smoking" was not aware that being in smoky areas are directly exposed to the harmful effects of tobacco smoke. Satisfactory is the fact that in recent years through administrative rulings have managed to limit the number of public places where smoking is permitted. Still, smoking in enclosed areas, especially in households causes harmful substances that remain after combustion of nicotine on the surfaces of various objects for many hours and adversely affect people who are in such areas, in particular, children [4]. On the question how smoking affects of bladder cancer evaluation will answer the study conducted in our clinic during the long observation of patients with bladder cancer.

CONCLUSIONS

1. Detection of cotinine level allows for credible assessment of medical history related to tobacco smoking.
2. Questions and answers indicated that the credibility of the questionnaire is limited to the disclosure and does not accurately relate smoking by the patients.
3. Assessment of active and passive smoking should be carried out based on evaluation of the questionnaire and measurement of the nicotine metabolite in the urine.

4. Monitoring of cotinine level allows for an objective assessment and to effectively convey the recommendations for quitting tobacco smoking.

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