

Short Communication

Reliability and Validity of Opiate Use Self-Report in a Population at High Risk for Esophageal Cancer in Golestan, Iran

Christian C. Abnet,¹ Mitra Saadatian-Elahi,^{2,3} Akram Pourshams,⁴ Paolo Boffetta,² Ali Feizzadeh,⁴ Paul Brennan,² Philip R. Taylor,¹ Farin Kamangar,¹ Sanford M. Dawsey,¹ and Reza Malekzadeh⁴

¹Cancer Prevention Studies Branch, Center for Cancer Research, National Cancer Institute, Bethesda, Maryland; ²International Agency for Research on Cancer and ³Department of Biochemistry, Eduard Herriot Hospital, Lyon, France; and ⁴Digestive Disease Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Objective: To assess the reliability and validity of self-reported opium use in a rural Iranian population at high risk for esophageal cancer in preparation for a large cohort study. **Method:** 1,057 subjects ages 33 to 84 years were recruited from Gonbad city and three surrounding villages in Golestan province of Iran and completed a questionnaire and provided biological samples. The history and duration of using opium, smoking tobacco, chewing nass, and drinking alcohol were measured by questionnaire in the entire cohort. A subgroup of 130 people was reinterviewed after 2 months to assess reliability. Validity of the opium question was assessed by comparing the questionnaire responses with the presence of codeine and morphine

in the urine of 150 selected subjects. **Results:** Self-reported opiate use is reliable and valid in this population. The reliability of ever opium use and duration of opium use had κ 's of 0.96 and 0.74, respectively. The validity of self-reported opium use was also high. Using urine codeine or morphine as the gold standard for use of opium, self-report had a sensitivity of 0.93 and a specificity of 0.89. **Conclusions:** The self-reported use of opium can provide a reliable and valid measurement in this population and will be useful for studying associations between opium use and occurrence of esophageal cancer and other diseases. (Cancer Epidemiol Biomarkers Prev 2004; 13(6):1068–70)

Introduction

The population inhabiting the northeastern section of Iran near the coast of the Caspian Sea and the Turkmenistan border (mainly of Turkmen ethnicity) has some of the highest rates of esophageal squamous cell carcinoma in the world. Annual age standardized incidence rates of 93 per 100,000 in men and 110 per 100,000 in women were reported in the 1970s in the area around Gonbad (1), and the high rates have been confirmed in more recent surveys (2). The cumulative mortality rate for the entire population approaches 1 in 6 (1), which is equivalent to the lung cancer rate in very heavy tobacco smokers in Western populations. The cause of these extraordinary rates has been investigated (3–5). The main risk factors suggested by these studies included a poor diet (marked by a reliance on tea and bread and a deficiency in fresh fruits, vegetables, and meat), consumption of hot tea, and

opium consumption. However, current evidence does not allow definitive conclusions.

Opium is widely used in this population and has traditionally been consumed in Iran as a treatment for pain, diarrhea, and insomnia. Opium use was prohibited in 1955, and methadone and buprenorphine are available to registered addicts as part of treatment programs. Illicit opium use is thought to remain common. In Iran, opium is typically either eaten or smoked in one of three forms: (1) raw opium; (2) *sukteh* or opium dross, the pyrolyzed opium residue that is scraped from opium pipes; or (3) *shireh*, a refined opium product made by boiling either raw opium or *sukteh* and collecting the residue. An ecologic study across the northern part of Iran showed that areas with higher prevalence of opium use are coincident with higher rates of esophageal cancer (6). This study showed that among inhabitants over age 50 years in high esophageal cancer incidence areas, 58% of men and 32% of women had >0.3 g/mL morphine in their urine. In low esophageal cancer incidence areas, the corresponding percentages were 14% in men and 12% in women. Within villages, opium use was more common among household members of esophageal cancer cases than among household members of noncases.

Received 12/10/03; revised 2/4/04; accepted 2/10/04.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked advertisement in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Requests for reprints: Christian C. Abnet, Cancer Prevention Studies Branch, Center for Cancer Research, National Cancer Institute, 6116 Executive Boulevard, Room 705, Bethesda, MD 20892. Phone: 301-594-1511; Fax: 301-435-8644. E-mail: abnetc@mail.nih.gov

Table 1. Selected characteristics of study subjects overall and those with urine opiate measurements

Variable	Total Cohort	Urine Subcohort*
No.	1,057	150
Age, median (range)	49 (33-84)	46 (36-80)
Sex, female <i>n</i> (%)	610 (57.7)	30 (20.0)
Place of residence, rural <i>n</i> (%)	619 (58.6)	128 (85)
Ethnicity		
Turkmen, <i>n</i> (%)	665 (62.9)	130 (86.7)
Fars, <i>n</i> (%)	288 (27.3)	15 (10)
Turk, <i>n</i> (%)	68 (6.4)	2 (1.3)
Sistani, <i>n</i> (%)	21 (2.0)	0 (0)
Other, <i>n</i> (%)	15 (1.4)	3 (2.0)
Opium, <i>n</i> (%) ever	93 (8.8)	75 (50)
Alcohol, <i>n</i> (%) ever	38 (3.8)	7 (4.7)
Tobacco, <i>n</i> (%) ever	163 (15.4)	51 (34.0)
Nass, <i>n</i> (%) ever	54 (5.1)	28 (18.7)

*Subjects selected for the urine cohort were stratified on age, sex, place of residence, ethnicity, and whether they admitted opiate use by questionnaire.

Self-reported illicit drug use has been widely investigated and found to be reliable and usually valid (7, 8). Reliability, the likelihood of getting the same answer on two or more occasions, is typically high, ranging between 0.80 and 0.95 (9). Validity, the accuracy or truthfulness of the answers received, can also be good but is lower than the range seen for reliability and can be very dependent on the setting (e.g., criminal justice vs. drug rehabilitation/treatment) and the population studied.

Recently, the IARC, the National Cancer Institute, and the Digestive Disease Research Center of Tehran University of Medical Sciences have begun joint studies to reexamine the etiology of esophageal cancer in northeastern Iran. In preparation for a large cohort study, we conducted a pilot study to test the recruitment of community members for an assessment of lifestyle and habits and the feasibility of collecting biological samples. In this article, we examine the reliability and validity of self-reported opium use to determine if it is sufficient for use in association studies.

Methods

Study Subjects and Recruitment. This study was conducted under the aegis of the ethical review panels of the IARC, the National Cancer Institute, and the Digestive Disease Research Center. Subjects for the study were selected from Gonbad city and three rural villages in the surrounding region of Golestan province. In Gonbad, 645 adults were sent a letter via their local health house informing them of the study and asking them to participate by attending their health house at a specific time for interview. Subjects (*n* = 438) subsequently attended and provided interview information and biological samples. In the three rural villages, 619 individuals were successfully interviewed from the 682 invited to visit the health house. In total, 1,057 subjects were enrolled into the study, an overall participation rate of 80%. The higher response rate among the rural inhabitants was thought to be due to their working close to home in agricultural occupations, which allowed greater flexibility to visit the health house.

Questionnaire and Sample Collection. A broad-based questionnaire was administered to each participant by a local doctor recruited and trained by the study staff. The questions regarding opium (and tobacco, alcohol, and nass) use were "Have you ever used opium at least weekly over a 6-month period?" If the subject responded yes, they were asked to indicate the amount consumed in five categories from once a week to more than six times a day. The amount consumed was collected for distinct periods, by age, as defined by the respondent. Other variables were sex, place of residence (rural vs. urban), ethnicity. To assess reliability, 130 random subjects (80 rural, 50 urban) were reinterviewed 2 months after the initial interview.

Laboratory Analysis. At the time of recruitment, a spot urine sample was collected from all subjects and frozen. Subsequently, they were transferred from the cohort recruitment center to the biorepository at IARC, where they were kept at -20°C . Anonymized urine samples, from 150 cohort members comprising 75 admitted opium users and an age, sex, residence, and ethnicity-matched group of 75 nonusers, were shipped to a commercial laboratory (American Toxicology Institute, Las Vegas, Nevada) on dry ice. Samples were screened for codeine and morphine using a proprietary immunoassay, and positive results were verified using gas chromatography-mass spectroscopy. Subjects with >500 ng/mL urine for either analyte were considered positive. All subjects positive in the first-stage immunoassay were above the 500 ng/mL cutoff in the gas chromatography-mass spectroscopy assay.

Data Analysis. Data were tabulated for the total cohort and for members of the urine subcohort. We assessed reliability of questionnaire responses, using κ , by comparing the first and second reports in the subgroup of 130 subjects with repeated measurements. We assessed validity of self-reported opium use by comparing the results of the questionnaire to the results of the urine analysis (the gold standard) in the subgroup of 150 subjects who had both measurements.

Results

Table 1 presents the characteristics of the 1,057 persons included in the study and the subgroup of 150 subjects

Table 2. Reliability of self-reported substance use and duration of use

Substance	Agreement (%)	Expected agreement (%)	κ
Opium, ever use	99.3	83.5	0.96
Opium, duration of use	83.3	35.4	0.74
Tobacco, ever use	92.8	74.7	0.97
Tobacco, duration of use	85.0	20.8	0.81
Alcohol, ever use	99.3	89.7	0.93
Alcohol, duration of use	71.4	26.5	0.61
Nass, ever use	99.3	85.9	0.95
Nass, duration of use	80.0	34.0	0.70

Table 3. Validity of self-reported opiate use comparing questionnaire responses to urinalysis

	Urine Positive for Codeine or Morphine	
	No	Yes
Self-reported use of opiates		
No	67	5
Yes	8	70
Operating characteristics of self-report		
Sensitivity (95% confidence interval)	0.93 (0.87-0.97)	
Specificity (95% confidence interval)	0.89 (0.83-0.93)	

included in the urine test cohort. Use of four different substances, all potentially associated with esophageal cancer, were assessed, including use of opium in any form, smoking tobacco, drinking alcohol, and chewing nass. Ever use of opium was reported by 8.8% of the study population. Smoking tobacco was reported by 15% of subjects, and use of alcohol or nass was rare.

We assessed the reliability of the questionnaire for assessing self-reported substance use by reinterviewing a subgroup of 130 cohort members 2 months after the initial interview. The percentage agreement and the κ statistic for ever use and duration of use of opium, tobacco, alcohol, or nass are reported in Table 2. All of the κ statistics for ever use were >0.9 (excellent agreement), and all of the κ statistics for duration of use were >0.6 (very good agreement).

We tested the urine of 150 cohort subjects selected equally from subjects who did and did not report opiate use and who were matched on the age, sex, place of residence, and ethnicity to the users. We found a concordance rate of 91% (137 of 150) between self-report and urine positivity (Table 3). The sensitivity (95% confidence interval) and specificity (95% confidence interval) of self-reported opium use were 93% (0.87-0.97) and 89% (0.83-0.93), respectively.

Discussion

Opium use was reported by 8.8% of all cohort members. Previous studies from this area reported that opium use in rural inhabitants ranged from 12% of females in the low cancer incidence area to 58% of men in the high incidence areas (6). The prevalence of use among rural men in the current study was 21%. Whether the apparent reduction in the prevalence of opium use during the last three decades is real cannot be assessed in this data set. However, other analgesics are now freely available through the network of health houses, and opium has become more difficult and expensive to obtain, so the reduction may be real.

In our study, self-reported use of opium was very reliable, with a κ of 0.96 between measurements sep-

arated by 2 months. Self-report of opium use was also valid. Using urine analysis of opium metabolites as a gold standard, we found that the questionnaire had a sensitivity of 93%. The lower specificity of self-reported opium use (89%) could be due to the relatively short time opium metabolites are present in the urine (2 to 4 days). The important conclusion from this analysis is that using a simple questionnaire produces a reliable and valid assessment of recent opium use in this population.

Because opium is a traditional medicine in this population, and possibly because of the setting and personnel completing the interview, we suspect that there was little social pressure to deny use. The simplicity of the question favors a finding of high reliability and validity but may undermine our understanding of the association between opiate use and esophageal cancer, which may depend on the dose, form of opium used, and route of administration. Further work is warranted to determine our ability to assess other facets of opium use (i.e., opiate form, route of administration, etc.) by questionnaire. For our purposes, if we assume a 10% frequency of opium use among the controls and set the true odds ratio for the association between opium use and esophageal squamous cell carcinoma at 2, 4, or 10, a 93% sensitive assessment of opiate use would reduce the apparent odds ratio to 1.99, 3.91, and 9.34, respectively. These small changes in the estimates for the disease association would not change the inference drawn from the results.

Our finding that self-reported use of illicit drugs can be both reliable and valid is similar to reports from other populations (7, 8). Questionnaires should allow the investigation of the association between opiate use and diverse diseases in our population-based study and others.

References

- Mahboubi E, Kmet J, Cook PJ, Day NE, Ghadirian P, Salmasizadeh S. Oesophageal cancer studies in the Caspian Littoral of Iran: the Caspian cancer registry. *Br J Cancer* 1973;28:197-214.
- Saidi F, Malekzadeh R, Sotoudeh M, et al. Endoscopic esophageal cancer survey in the western part of the Caspian Littoral. *Dis Esophagus* 2002;15:214-8.
- Kmet J, Mahboubi E. Esophageal cancer in the Caspian Littoral of Iran: initial studies. *Science* 1972;175:846-53.
- Joint Iran-IARC Study Group. Esophageal cancer studies in the Caspian Littoral of Iran: results of population studies—a prodrome. *J Natl Cancer Inst* 1977;59:1127-38.
- Cook-Mozaffari PJ, Azordegan F, Day NE, Ressicaud A, Sabai C, Aramesh B. Oesophageal cancer studies in the Caspian Littoral of Iran: results of a case-control study. *Br J Cancer* 1979;39:293-309.
- Ghadirian P, Stein GF, Gorodetzky C, et al. Oesophageal cancer studies in the Caspian Littoral of Iran: some residual results, including opium use as a risk factor. *Int J Cancer* 1985;35:593-7.
- Darke S. Self-report among injecting drug users: a review. *Drug Alcohol Depend* 1998;51:253-63.
- Harrison L. The validity of self-reported drug use in survey research: an overview and critique of research methods. *NIDA Res Monogr* 1997;167:17-36.
- Hser YI. Self-reported drug use: results of selected empirical investigations of validity. *NIDA Res Monogr* 1997;167:320-43.