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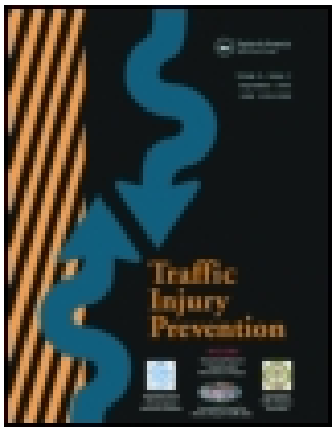

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Opium Consumption and the Risk of Traffic Injuries in Regular Users: A Case-Crossover Study in an Emergency Department

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Opium Consumption and the Risk of Traffic Injuries in Regular Users: A Case-Crossover Study in an Emergency Department

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Objective. *The cause-specific annual death rate due to traffic injuries is around 30 in 100,000 in Iran. On the other hand, this country has the highest proportion of opiate users in the world. Little is known about the transient effect of opium on traffic injuries. The objective of this study was to explore the effect of opium consumption on traffic injuries in drivers who use opium.*

Methods. *Seventy-five regular opium users who suffered traffic injuries were studied in a case-crossover investigation. The study subjects had been admitted to the single trauma emergency department in Kerman, a city in southeast Iran. The relative risk (RR) of short-term opium effect was estimated by considering frequency of driving after opium consumption during 6 hours before the accident in comparison to the usual frequency of driving after opium consumption by the same persons. Stratified data analysis was performed by the Mantel-Haenszel method.*

Results. *The opium consumption of drivers up to 6 hours before the accident was associated with an increased RR = 3.2, 95 percent confidence interval (CI): 1.9, 5.4. The third hour after consumption had the greatest magnitude of effect considering RR = 4.29, 95 percent CI:2.65, 6.95.*

Conclusions. *These results suggest a heightened risk of traffic injuries after opium consumption in regular users. The RR in the third hour after consumption could be explained by considering the greater probability of driving compared to the immediate hours after use, rather than peak effect time of opiates. The results indicate necessity of regular assessment of all common drivers, especially truck and bus drivers, regarding use of opium.*

Keywords Iran; Opium; Substance Withdrawal Syndrome; Traffic accidents

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INTRODUCTION

Based on the Ministry of Health and Medical Education death registry data, in 23 out of 28 provinces of Iran, road traffic injuries caused 31,800 deaths in 2003, which accounted for 9.9 percent of total deaths and 17.4 percent of years of life lost (YLLs). The cause-specific death rate due to traffic injuries is 47.8 in 100,000 (76.5 and 17.9 in males and females, respectively). The victims' average age is 35.6 years (Naghavi 2003).

Though alcohol is the major substance related to traffic injuries, all drugs that affect the central nervous system can decrease driver performance (Hunter et al. 1998), although strong evidence still cannot be found to support the latter condition (Peden et al. 2004). Meanwhile, studies have shown an increasing trend toward the use of illicit drugs among drivers (Mørland et al. 1995), and research that can determine the relationship of illicit drugs, other than alcohol, and traffic injuries is among the main priorities in this field (Peden et al. 2004).

According to the UN World Drug Report for 2005, with a population of about 70 million, Iran has the highest proportion of opiate users in general terms in the world: 2.8 percent of 15 to 64-year-olds in 1999 (United Nations Office on Drugs and Crime [UNODC] 2005). A recent study showed an 8 percent average increase in the annual incidence of drug abuse during 1978–1998 in Iran. In other words, the total population of drug users has doubled every 12 years (Rahimi-Movaghar et al. 2002).

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There is a belief among some people that opium use not only does not contraindicate driving but can also improve consciousness during driving. This explains why opium consumption is not uncommon among professional commuting drivers (including truck and bus drivers). Consistently, one road survey showed 14.4 percent (95% confidence interval (CI): 12.4, 16.4) prevalence of opiate misuse among truck and bus drivers in Iran (Motevalian et al. 2004). It is interesting and under question that though the Iran Road Traffic Act has allowed alcohol testing in case of police suspicions, this is not the case for opium.

A review of studies on the relationship of drugs to driver performance disclosed a wide diversity of approaches. Where some focused on cognitive and/or emotional characteristics as outcomes in laboratory settings (Bruera et al. 1989), others looked at drug effects in situations such as driving in simulators or roads (Galski et al. 2000). Based on basic research, both chronic and acute opium consumption can be considered as risk factors for traffic accidents (Krystal 1995; Lyvers and Yakimoff 2003). In other words, people who are addicted to opium may have a greater risk of traffic injuries in comparison to the non-opium-using population, and their baseline risk is increased after a single use as well. This issue has not been tested in field situations. Most epidemiological studies have dealt solely with drug consumption prevalence in drivers who suffered from fatal and/or nonfatal traffic injuries and were not targeted on the acute influence of opium usage on traffic accidents.

The present study was designed to compare the risk of traffic accidents immediately after consumption of opium with other periods of time in one of the high opium prevalence areas of Iran with a case-crossover design. Case-crossover design is a type of designs that for each case one or more preceding time periods are selected as control period. In this instance, the opium consumption of the case at the 6 hours before traffic injury—that is, the hazard period—is compared with the distribution of exposure status for that same individual in the control periods. The advantage of this methodology is the control of confounders on an individual basis (Maclure 1991). This study design has been used for other exposures associated with traffic accidents such as mobile use (McEvoy et al. 2005) and alcohol (Borges et al. 2004; Cherpitel et al. 2005; Gmel et al. 2009) and cannabis use (Gmel et al. 2009).

METHODS

This study was conducted in the emergency department of Shaheed Bahonar Hospital in Kerman, a city in southeast Iran. Kerman is the capital city of Kerman province, the largest province of Iran, with more than 400,000 inhabitants. This emergency department is the only trauma emergency service in the city. The eligibility criteria were involvement in accidents resulting in traffic injuries, using opium almost daily during the past year, age over 18 years, and a valid driver's license. Consumption of other substances, such as alcohol, heroin, and marijuana, on the accident day was considered as exclusion criterion.

Two hundred and thirty-seven injured drivers were screened for regular opium use. Among them, 7 percent (17 persons) were not interviewed due to patient refusal (n = 2), clearance from hospital with personal consent before filling the questionnaire (n = 2), patient death (n = 5), and a Glasgow Coma Scale score below 7 at admission (n = 8). Five others used illicit drugs other than opium on the same day. Among the remaining 220 drivers, 65 and 80 were occasional and never opium users, respectively. Finally, 75 were admitted as regular opium users in the study.

A questionnaire was employed for data gathering. The average time for questionnaire completion was 20 minutes. The study variables were time of accident, history of illicit drug use, time of the last drug dose consumed, frequency of consumption during the past month and year, frequency of driving time in hours per day, and confounding factors such as weather conditions and demographic variables.

A complementary study was undertaken to assess the negative predictive value of opium consumption responses. The positive predictive value of responses was not assessed based on the assumption that all who reported recent opium use must have been truthful for judicial reasons. Urinary samples were gathered anonymously from 20 subjects who claimed that they did not use opium during the week before their accident. In 2 cases, morphine metabolites were detected by thin-layer chromatography (TLC). The estimated negative predictive value of this question was 90 percent (95% CI: 75, 99) based on this complementary study.

Trained interviewers were responsible for filling out the questionnaires after asking consent from the study subjects. Respondents were informed that in the complementary study, with urine sampling and TLC, the samples would remain anonymous.

The hazard period was determined by tracing maximum risk for first to the sixth hour before the accident separately (first, second, third hour and so on). For this calculation, 18 hours were considered as the maximum daily activity of study subjects (excluding 6 hours for sleep), then considering the maximum of three opium consumptions a day among regular users; the sixth hour before the accident was considered as the upper margin of the hazard period.

The usual frequency approach was adopted for analysis. This approach had been used in a similar case-crossover study on alcohol consumption and traffic injuries (Borges et al. 2004). Two sets of data were needed for this analysis. The first data set was time of last opium consumption, if any, during 6 hours before the traffic accident (the aforementioned hazard period). The second data set was the usual frequency of opium consumption and driving experience from the same injured patient in the past year. Since the exposure was driving under pressure of opium (and not solely using opium), the overlap between the driving hours and the hours after opium consumption was considered as person-hours exposed in the past year. Thus, driving hours without opium consumption was considered as unexposed person-hours.

The exposure was driving under the influence of opium before the accident (and not using opium solely), and the overlap between the driving hours and the hours after opium consumption until traffic accident (at most 6 hours) was considered as person-hours exposed for the hazard period. Then, driving hours without opium consumption were considered as unexposed

Table I Description of screened subjects who admitted to traffic injuries for the selection of study subjects and final, eligible regular opium users admitted to Shaheed Bahonar Hospital, Kerman, for traffic injuries.

		Injured drivers admitted to the emergency department ($n = 220$)		Regular opium users eligible for study participation ($n = 75$)	
		n	%	*n*	%
Age (years)	18–24	76	34.5	4	5.3
	25–34	64	29.1	22	29.3
	35–49	61	27.7	33	44.0
	50 and above	19	8.6	16	21.3
Sex	Female	21	9.5	2	2.7
	Male	199	90.5	73	97.3
Marital status	Single	91	41.4	6	8.0
	Married	129	58.6	69	92.0
Education	Illiterate	22	10.0	16	21.3
	Primary and secondary	99	45.0	45	60.0
	High school and diploma	76	34.5	13	17.3
	University	23	10.5	1	1.3
Type of vehicle at accident	Car	83	37.7	28	37.3
	Motorcycle	124	56.4	35	46.7
	Truck and/or bus	13	5.9	12	16.0

person-hours. A similar approach was considered for usual frequency of driving after opium consumption for the past year.

Data analysis was performed by stratification of each person's data in one stratum, and relative risk (RR) was estimated by the Mantel-Haenszel method (Greenland 2008).

This study was approved by the institutional ethics review board of the Tehran University of Medical Sciences that followed the Helsinki declaration.

RESULTS

Table I describes all 220 people screened for eligibility criteria in this study as well as 75 regular opium users.

Algebraically, two numbers are sufficient for calculation of RR in a case-crossover study. The sum of unexposed person-hours over the past year among those who consumed opium during 6 hours before the accident was 25.5, and the sum of person-hours exposed to the exposure effect over the past year among those who did not have exposure during the hazard period was 7.9. Therefore, the RR of traffic injury resulting in emergency department admission for opium consumption was 3.2 (95% CI: 1.9, 5.4).

Table II shows the results of separate analyses performed according to different durations for the hazard period and the number of consumptions per day. The results revealed that the third hour after consumption with RR = 4.29 (95% CI: 2.65, 6.95) had the greatest RR and this hazard period—that is, the third hour—is the only statistically significant hour if different hours were considered separately. Those who used opium three times a day had the lowest RR and analysis considering different hours for this group of opium users illustrates that the RR is not significant in any separate hours.

DISCUSSION

The RR of traffic accidents resulting in hospital admission becomes 3.2 (95% CI: 1.91, 5.45) during 6 hours after opium consumption among regular users.

Morphine and heroin are parenterally and orally well absorbed. Orally rapid conjugation prevents significant blood

Table II Relative risk of traffic injuries after single dose of opium by the number of opium consumptions per day and for separate hours after opium usage.

Hours after opium usage	Number of opium consumptions per day							
	1 ($n = 32$)		2 ($n = 18$)		3 ($n = 25$)		Total ($n = 75$)	
	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)
1	**2.95**	**(1.20–7.30)**[a]	1.13	(0.26–4.97)	0.53	(0.14–1.99)	1.32	(0.70–2.51)
2	2.10	(0.85–5.17)	0.58	(0.08–4.28)	0.70	(0.21–2.31)	1.24	(0.66–2.33)
3	**6.90**	**(3.32–14.40)**[a]	**5.60**	**(2.07–15.2)**[a]	2.10	(0.84–5.22)	**4.29**	**(2.65–6.95)**[a]
4	0.34	(0.05–2.41)	1.36	(0.31–6.01)	0.96	(0.29–3.26)	0.79	(0.34–1.83)
5	0.33	(0.04–2.50)	1.48	(0.35–6.29)	[b]		0.40	(0.13–1.23)
6	0.69	(0.16–2.95)	2.15	(0.63–7.29)	1.90	(0.69–2.26)	1.44	(0.73–2.85)

[a] Statistically significant ($P < 0.05$).

[b] No exposed study subject was observed in this category.

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levels. The duration of action is 3 to 6 hours. Due to heroin's lipophilic nature, it crosses the blood–brain barrier within 15 to 20 seconds and achieves significant brain levels. Heroin and 6-acetylmorphine peak at 10 minutes after IM injection. Morphine peaks at 15 minutes after IM. The important point to present study is that no evidence exists on the peak level of morphine after opium inhalation (Micromedex Drug Evaluation Database [MDED] 2007). Therefore, the 6 hours were selected arbitrarily to investigate the hazard period after single opium use. Hazard period is the time interval from an exposure to an event. Though the times to the plasma peak for major compounds of opiate were reported less than an hour after usage, Table II illustrates that the third hour after consumption had the highest RR. This could be explained not by the pharmacological effect of opiates per se but also by considering the greater probability of driving at this time, compared to the immediate hours after use. Although this figure could overestimate the RR for the third hour, this is not the case for computation considered for the whole 6-hour period. Case-crossover studies could stand for determination of the hazard period in an empirical setting. It could be traced with finding greatest magnitude of effect—for example, RR and or odds ratio (OR).

The imperfect negative predictive value (90% with 95% CI: 75, 99) shows that the resulting RR somehow underestimates the reality. Though positive predictive value was not estimated because of reasonable assumption—that is, the legal impact of positive answers, and to maximize their participation as well as to minimize conflict with consent of the responders—it can be counted as one of the study limitations. A study conducted in Golestan province (the northeastern part of Iran) showed that self-reported use of opium was a reliable (kappa = 0.96) and valid (0.93 and 0.89 sensitivity and specificity, respectively) measure in this population (Abnet et al. 2004).

The source of data for the time lag between opium consumption and traffic accident can be considered as a source of error in the present study. The definition of this variable in the study of mobile use and traffic accidents was objective because the time of exposure had been determined by records provided by mobile companies (McEvoy et al. 2005). Though in the setting of the present study, patients who were admitted to emergency department for medical care could improve validity of their responses, there was no objective way to validate data given by study subjects, especially because opium consumption is illegal in Iran. However, if we consider this subjectivity as a nondifferential error and/or by chance, the result should be an underestimation of the effect (RR). Therefore, the finding of this study can be far from the null hypothesis if the time elapsed between opium consumption and accident can be defined with more validity. This was the case also for other studies conducted on the effect of alcohol and/or cannabis on traffic injuries (Borges et al. 2004; Cherpitel et al. 2005).

The interesting point in Table II is that the RR is around 1 in regular users who consumped opium three times per day. This figure suggests that those who used opium three times a day were less susceptible to the short-term effects of consumption. This finding must be clarified from the chronic effect of opium usage. The comparison group for assessing the later effect must be a normal population and the baseline risk of traffic accident in opium addicts is not appropriate substitution for this effect.

Two different approaches are used for analysis of a case-crossover study; namely, pair-matched and usual frequency. The pair-matched is to contrast a time period on the day of the collision with a comparable period on a period preceding the collision (Mittleman et al. 1995). The statistical power of this approach depends on number of discordant pairs in the study. Because the probability of using opium during 6 hours is considerable among regular opium users, this approach requires a large sample size and most data must be discarded due to concordant observations. Therefore, we used the usual frequency approach. However, the latter approach is not applicable for irregular users because they do not have a consistent schedule of opium consumption and their report is not reliable and cannot be considered for person time at risk estimation. Thus, the result of usual frequency analysis must be limited to regular opium users. On the other hand, various confounding factors, including aggressive and/or risky behaviors, were controlled by the case-crossover design, which is the strength of this study.

Different studies have reported psychomotor and cognitive disorders in opium users (Darke et al. 2000; Davis et al. 2002), although a recent investigation that compared constant-dose opium users with nonuser drivers did not find a significant lack of performance with opium (Byas-Smith et al. 2005). Another study illustrated better psychomotor performance in patients with low back pain who used opioid analgesics for 90 and 180 days (Jamison et al. 2003). A case control study estimated the OR to be equal to 8.2 (95% CI: 2.5, 27.3) for exposure to opioids among traffic-injured drivers in comparison to other patients admitted to the emergency department (Mura et al. 2003).

Although similar epidemiologic approaches have not yet been taken, experimental studies that investigated the effect of a single opioid dose (by laboratory tests with repeated measurements) obtained results different from those of this work. Strain et al. (1995, 2002) concluded that a single dose of opioids does not affect the psychomotor performance of addicted patients in comparison to placebo. Although Preston et al. (1992) reported similar results, Comer et al. (1997) observed high doses of produced disturbances in two out of four psychomotor tests.

A systematic review of 48 articles concluded that there is no strong and consistent evidence of psychomotor impairment immediately after being given doses of opioid, but further research is needed in this area (Fishbain et al. 2003). None of the aforementioned studies used case-crossover methodology. This design was applied to examine the immediate effect of exposures. All other studies that focused on the short-term effect of opioids were conducted in laboratory settings, with psychomotor, visual, and/or cognitive performance considered as outcome measurements. None compared the risk of traffic injuries before and after single use, which was the objective of the present work.

Based on our results and especially 14.4 percent prevalence of opioids use by truck and bus drivers (Motevalian et al. 2004),

appropriate action must be taken to prohibit driving by opium addicts. Appropriate measures, including laws to prohibit driving under opium pressure, must be considered for control of the problem. Educational campaigns might be another approach. In this regard, drivers' beliefs and attitudes are a research priority for providing appropriate educational programs.

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