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ORIGINAL ARTICLE

Evaluation of Drug Abuse Relapse Event Rate Over Time in Frailty Model

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Abstract

Objectives: Drug dependence as a chronic disorder is reversible over time and has a cost burden for individuals, families, and society. An individual who has stopped taking drugs for a long time may start taking drugs again. The variables affecting the reuse of drugs are not well known. Therefore a study of the factors that increase the length of time away from drugs is essential.

Methods: This study used data collected by the Bushehr addiction treatment centers (Tolloe and Pasargadae) from 100 men with drug addiction from March 2006 to September 2010. The shared frailty model was used to study the influence of variables on the duration of time away from drug use. The most common method for entering intra-class (personal) correlation is the survival frailty model, which uses parametric survival data for the evaluation of recurrent events. A Weibull distribution for time to event with gamma shared frailty was used.

Results: The mean (standard deviation) age and age at onset of opium use of the sample were 33.85 (8.11) and 20.65 (6.87), respectively. About 30% of the men studied had chronic disease and 36% had a mental illness. The mean (frequency mean) of the amount of opium used were 4.73 (3.8) g and 2.54 (1.14) times per day. The desire to end drug use was 97% and 3% for the men with drug addiction and their families, respectively, at the time when the men stopped using opium. The age at onset of opium use [$p = 0.046$, hazards ratio (HR) = 1.30], history of chronic disease ($p = 0.005$, HR = 249.635), and marital status ($p = 0.06$, HR = 0.027) are important in the reuse of opium.

Conclusion: We found that opium addiction is related to other chronic diseases and to the age at onset of opium use. A prospective study following up individuals with drug addiction who try to stop drug use in addiction treatment centers could help to determine the risk factors of resuming drug use.

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1. Introduction

Drug dependence is a known social disorder and has become a major problem in some communities in recent years. Drug dependence causes long-term and recurrent suffering for individuals, families, and communities and a cure has not yet been found. Although an individual may stop using drugs for a long time, he or she may begin to use drugs again. Demographic and social factors and familial influence affect the start of drug use, continuing drug use, and return to drug use after time away from drugs [1]. During the addiction review process there is a fundamental problem in that individuals often have several unsuccessful attempts to stop drug use prior to when they are successful in finally stopping taking drugs [2]. It is therefore necessary to determine the factors which can prolong the period away from drugs.

The addiction process can thus be seen as a recurrent event. Recurrent events data have often been analyzed using standard survival analysis methods with an adjustment for events occurring for each person that leads to a marginal model or a frailty model [3].

As a result of the increasing use of survival analysis in medical research, there is now a need for a more flexible and efficient model for survival data. Standard methods of survival analysis in clinical research are based on the assumption that the sample is a homogeneous group. Thus survival models assume that the survival of individual patients is independent of each other and the patients' survival time distributions are the same. However, in many instances the study group cannot be assumed to be homogeneous and individual group members have different risk factors [4−6]. In many instances the importance of some factors associated with the disease are still unknown, e.g., economic factors. It is very difficult or impossible to measure all the effective and appropriate factors related to an event [7]. Ignoring unknown shared risk factors may lead to dependency between survival times and bias estimation of parameters. In these situations, we use frailty models to solve these problems. Frailty models are the most common methods for entering the intra-class (personal) correlation in survival analysis. These models formulate the variation of survival times as two sources. The first source is the natural variation explained by hazard function and the second source is the shared variation between individuals in a group (individual) expressed by the shared frailty variable [5,8,9].

There have been many studies on cigarette smoking and its prevalence in Iran [10,11], but few studies about ending drug and cigarette addiction. Li et al [12] used a cure fraction frailty model to study smoking cessation. Multiple regression using proportional hazards frailty models was applied to identify independent predictors and correlates of the duration of repeated abstinence episodes [13]. It is important to know the risk factors affecting the recurrence times of drug addicts who attempt toend their use of drugs. In this study we used the frailty model to determine these risk factors. We used a gamma distribution with finite mean because the risk function is always positive for the frailty. We also used the frailty model to consider the heterogeneity in individuals with drug addiction and we considered the mean of the frailty variable to be equal to one [8,9].

2. Materials and methods

This study used data collected from 100 patients admitted to two addiction treatment centers in Bushehr (Tolloe and Pasargadae). The data were recorded from March 2006 to September 2010. The available covariates, demographic information, and drug use data were collected. The time frame of this study was divided into 3 month intervals. Smoking status was defined by questions about the use or non-use of drugs at 3 month intervals.

Participants were allowed to indicate that during the previous 3 months: (1) they had not used drugs at all; (2) they had used drugs, but had stopped at some time during the interval; or (3) they had used drugs continuously. For the individuals who indicated (2), the time of stopping drug use and the duration of cessation were unknown. It is difficult to distinguish between groups (2) and (3) and we considered them as "users since last visit." Individuals who answered (1) positively were treated as non-users since their last visit.

In this study we only considered use of opium and non-use of opium; use of other drugs was not considered. In addition to demographic questions and questions about employment status, three questions were asked about the age of onset of the use of opium, the history of chronic disease, and mental and psychiatric illnesses. The following questions were also asked at each 3 month time interval: (1) amount of opium used and frequency of opium use per day; (2) the use or non-use of other drugs (including heroin, crack cocaine) at least once a week; (3) whether the decision to stop drug use was made by the individual or with their family; and (4) whether alcohol was consumed at least once a week.

We used a parametric shared frailty analysis for recurrent events. This included proportional hazards, a Weibull distribution for time events, and gamma shared frailty frequency dependence on time. We defined a model based on the hazard of the kth individual in the jth event and the a_k frailty for this individual. Frailty is the multiplicative risk effect of the hazard function $[h(t|x_{jk})]$. This assumed a gamma distribution with a mean of 1 and variance θ. Also, we assumed that $h(t|x_{jk})$ had a Weibull distribution. Therefore: