

Addictive behaviors related to opioid use for chronic pain: A population-based study



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ABSTRACT

The growing body of research showing increased opioid use in patients with chronic pain coupled with concerns regarding addiction encouraged the development of this population-based study. The goal of the study was to investigate the co-occurrence of indicators of addictive behaviors in patients with chronic non-cancer pain in long-term opioid treatment. The study combined data from the individual-based Danish Health Survey in 2010 and the official Danish health and socio-economic, individual-based registers. From a simple random sample of 25,000 adults (16 years or older) living in Denmark, 13,281 individuals were analyzed through multiple logistic regression analyses to assess the association between chronic pain (lasting ≥ 6 months), opioid use, health behavior, and body mass index. Six potential addictive behaviors were identified: daily smoking; high alcohol intake; illicit drug use in the past year; obesity; long-term use of benzodiazepines; and long-term use of benzodiazepine-related drugs. At least 2 of the 6 addictive behaviors were observed in 22.6% of the long-term opioid users with chronic pain compared with 11.5% of the non-opioid users with chronic pain and 8.9% of the individuals without chronic pain. Thus, a strong association was demonstrated between long-term opioid use and the clustering of addictive behaviors. An intricate relationship between chronic pain, opioid use, and addictive behaviors was observed in this study, which deserves both clinical attention and further research.

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1. Introduction

Over the past 2 decades the use of opioids to treat patients with chronic pain has increased dramatically and epidemiological data from the US and Denmark have shown that 3–5% of the population use opioids for treatment of chronic pain conditions [22,46,80].

Long-term use of opioids not only may cause “classic” opioid-induced adverse effects (eg constipation, nausea, dizziness, cognitive deficits), but also may cause serious consequences such as addiction, opioid-induced hyperalgesia, cognitive disorders, and suppression of the immune and endocrine systems [34,41,47]. Addiction is a chronic neurobiological brain disease, which may occur in biologically and psychosocially susceptible individuals when exposed to reward-producing drugs such as opioids. Previous studies have shown that addiction may occur in patients with chronic pain treated with long-term opioids [2,33,53], although a substantial number

of studies does not recognize that addiction is a major problem in this population [11,12,30,37,44,50,56,58,60–62,78,84,86]. A cross-sectional study has shown that, among opioid-treated patients with chronic pain at a tertiary pain center, the prevalence of addiction was 14% when ICD-10 criteria for addiction were used and 19% when Portenoy’s criteria were used [32].

Opioids, benzodiazepines, nicotine, alcohol, and cannabis all act on the brain reward system [14,24,69,77], and recent research implies that compulsive overeating behavior also may involve the same reward center observed in the drug addiction model [1,25]. Hence, overeating and especially binge-eating disorders share common neurobiological features with substance disorder and may be understood, at least partly, as addiction behaviors [3,16].

Thus, risk factors for developing addiction during pain treatment with opioids include genetic predisposition, personal psychosocial profile, personal or family history of addiction, psychiatric disorders, including depression and anxiety, younger age, high opioid doses, use of short-acting opioids, high pain level, multiple pain complaints, self-reported craving, and concurrent use of tobacco, alcohol, and benzodiazepines [32,33,35]. In population studies,

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the long-term use of opioids in patients with chronic pain has been shown to be associated with use of benzodiazepines [52,66,67], other hypnotics [52], smoking [21,49,68], concurrent substance use disorders [18,19], and mental health disorders such as depression and anxiety disorders [20]. Chronic pain is also associated with obesity [31,64,80], but as far as we know no studies have investigated a possible association between opioid use in patients with chronic pain and obesity. Addictive behaviors such as smoking, drinking, and the use of other addictive substances and over-eating constitute a substantial part of the risk factors, and in population-based studies it seems feasible and highly relevant to extract indicators of these behaviors. Thus, the aim of the present population-based study was to investigate the associations between addictive behaviors, chronic pain, and opioid use.

2. Methods

Data were derived from the Danish National Cohort Study (DANCOS). DANCOS is a nationally representative health survey administered by the National Institute of Public Health, University of Southern Denmark [15]. The current study combines individual-based information from the Danish Health Survey in 2010 and official Danish health and socio-economic, individual-based registers. All the selected individuals were sent a questionnaire and a letter of introduction, which briefly described the objectives and content of the survey. Furthermore, it was emphasized that participation was voluntary. A mixed-mode approach was used to collect the survey data. The letter of introduction invited the selected individuals either to fill in the web questionnaire or to complete the enclosed paper questionnaire. The invited individuals received a unique username and password in order to access the web questionnaire. The study was approved by the Danish Data Protection Agency.

Respondents suffering from chronic pain were identified through the question “Do you have chronic/long-lasting pain lasting 6 months or more?” with the answer categories “yes” and “no.” Complete data on sex and age were obtained from Danish Civil Registration System. Data on highest completed education level were obtained from the Population’s Education Register [38]. Missing data on highest completed education were supplemented with self-reported data from the survey when possible. Information on cohabitation status was obtained from the survey.

Alcohol habits were assessed by several questions. Initially, respondents were asked if they have used alcohol within the last year. The following beverage-specific question was used to identify individuals with a high alcohol intake: “How many alcoholic drinks do you typically have each day in a week?” The intake was measured in number of standard drinks, with 1 drink equaling approximately 12 g (or 15 ml) of pure alcohol. The Danish National Board of Health’s sensible drinking limits (21 drinks per week for men and 14 drinks per week for women) were used to define high alcohol intake in the present study. Binge drinking was assessed by the question: “How often do you have five or more drinks on one occasion?” with the answer categories: “daily or almost daily,” “weekly,” “monthly,” “less than monthly,” and “never.” The 6-item CAGE-C questionnaire was used to screen for problem drinking [88].

Smoking behavior was assessed by asking the respondent whether they smoked or not. Daily smokers were asked how much they smoked a day on average (number of cigarettes daily). Heavy smokers were defined as individuals smoking at least 15 cigarettes a day.

The use of selected illicit drugs (cannabis, amphetamines, cocaine, LSD, ecstasy, heroin, magic mushrooms, and other substances) was assessed based on the recommendations by the

European Monitoring Center for Drugs and Drug Addiction (EMCDDA) [23]. Thus, the following question was asked to all respondents: “Have you ever tried one of more of the following drugs?” with the 4 possible answer categories: “no,” “yes, during the past month,” “yes, during the past year (but not during the past month)” and “yes, previously (but not during the past year).” Body mass index (BMI) was based on self-reported height and weight (weight in kilograms divided by height in meters squared).

Data on prescription drug use were retrieved on an individual level from the Danish National Prescription Registry [42]. Opioids were identified by the Anatomical Therapeutic Chemical (ATC) Classification System codes N02A, N02BE51, N02BA51, and R05DA04. Long-term users were defined as individuals who have used at least 1 prescription per month for 6 months in the previous year. This definition has been suggested by the Danish Health and Medicines Authority. Short-term opioid users were defined as individuals who have used at least 1 prescription in the previous year (and not defined as long-term users). Benzodiazepine derivatives were defined by the ATC codes N05BA and N05CD, and benzodiazepine-related drugs were defined by the ATC code N05CF. Long- and short-term users were defined by using the same definition as for opioid users.

Since all Danes have a unique and permanent 10-digit civil registration number it was possible to link both participants and non-participants in the survey on an individual level to different administrative registers. Calibration was used to adjust for non-response as proposed by Särndal and Lundström [63]. The weights were computed by Statistics Denmark based on register information on, for example, sex, age, municipality of residence, educational level, income, employment status, marital status, country of origin, and health care utilization for all individuals who were invited. Thus, those less likely to respond were given a higher weight in the analyses to represent the larger number of non-respondents with similar characteristics. Accordingly, those more likely to respond were given a lower weight.

2.1. Statistical analysis

Multiple logistic regression analyses were used to assess the association between chronic pain (opioid treated and non-opioid treated) and health behavior. Furthermore, multiple logistic regression analyses were used to examine the association between chronic pain (opioid treated and non-opioid treated) and use of benzodiazepines and benzodiazepine-related drugs. Results are presented as odds ratios (OR) with 95% confidence intervals (CI). A χ^2 test was used to examine the association between chronic pain and the clustering of addictive behaviors.

3. Results

The survey was based on a simple random sample of 25,000 adults (16 years or older) living in Denmark using the Danish Civil Registration System [59]. In all, 15,165 individuals participated in the survey (response rate 61%), out of which 1762 respondents with a personal history of cancer were excluded from the present study. Furthermore, 21 respondents without chronic non-cancer pain, but in long-term opioid treatment, and 101 respondents with missing chronic pain data were excluded, leaving 13,281 eligible individuals.

Selected characteristics of the study population are presented in Table 1. The mean age was higher among long- and short-term opioid users (62.3 years and 57.4 years, respectively) than among non-opioid users with chronic pain and individuals without chronic pain (49.6 years and 43.6 years respectively). Approximately 2 out of 3 long-term opioid users were women (67.7%). The table also

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