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Are patients' pejorative representations of buprenorphine associated with their level of addiction and of misuse?

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ABSTRACT

Background: In France, buprenorphine is at once the most widely prescribed and the most commonly misused opioid maintenance treatment (OMT). Unlike other medicines, it is seldom prescribed as a generic drug. Several studies have underlined the influence of the patient's representations when choosing brand-name rather than generic forms. We aim to prove a link between these pejorative representations and misuse, a higher degree of addiction and a preference for brand-name products.

Methods: An observational study carried out at 11 sites in France using self-assessment questionnaires filled out in dispensing pharmacies by patients having come to them for buprenorphine delivery.

Results: Analysis was based on 806 usable questionnaires. There indeed exists a significant correlation between pejorative representations of OMT by means of buprenorphine, and a higher degree of addiction and misuse ($p < .0001$ for each). Preference for the brand-name product is correlated with the representation of OMT as a "trap" ($p = .020$).

Conclusion: Our results underscore the existence of a link between patients' negative representations of their OMT and their drug-taking behavior. Prescribing physicians should consequently take these representations into account to more precisely identify the relevant behaviors and help their patients to evolve positively.

1. Introduction

Opioid maintenance treatments (OMT) have largely modified opiate dependency management procedures. They have been shown to efficaciously diminish the health risks associated with opioid use (Cornish et al., 2010; HAS, 2014; Kampman and Jarvis, 2015) by contributing to improved quality of life, lower mortality (Auriacombe et al., 2001; Ponizovsky et al., 2010) and social rehabilitation (Bilal et al., 2003). The two molecules currently used are buprenorphine (BUP) and methadone (Kampman and Jarvis, 2015; Mattick et al., 2014). By acting on the opiate receptors, they nullify cravings and thereby help patients to reduce their consumption and improve their lifestyles. By limiting cardiorespiratory depression, the partial agonist activity of BUP ensures greater safety than methadone (Auriacombe et al., 2001; Pinto et al., 2010; Srivastava and Kahan, 2006). However, and contrarily to methadone, its galenic form renders it more easily injectable (Lavonas et al., 2014). Only high dose sublingual formulations are currently available in France: brand name Subutex™ (0,4 mg, 2 mg and 8 mg), commercialized since 1996 (Nordmann et al., 2012) with 73% market share (MS) in 2013; the generic form (0,4 mg, 2 mg, 4 mg, 6 mg and 8 mg), which first appeared in 2006, (MS = 24%); and BUP (8 mg, 2 mg)/Naloxone (2 mg, 0,5 mg) (Suboxone™) (MS = 3%) (Brisacier and Collin, 2014).

In France, BUP is prescribed by 78% of general practitioners (GP) (Binder et al., 2015; Thirion et al., 2012), its distribution is highly uneven inasmuch as a mere 26% of GPs treat 75% of OMT patients (Feroni et al., 2004). While prescription of generic BUP reached a maximum in 2008 (MS = 32%), it markedly declined in 2013 (Turner et al., 2015), even though mean MS in France for the other generic drugs is 82% (Nordmann et al., 2012). Several studies have underlined the importance of the patients' preferences in their choices of galenic form (Birebent et al., 2014; Lavonas et al., 2014). Indeed, even though bioavailability of brand name and generic drugs remains similar (MHRA, 2008; Nordmann et al., 2012), differences exist as regards

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industrial packaging, the nature of the excipients, and the taste and size of the tablets. Moreover, generic products are less soluble, and consequently less easily injectable, than brand-name products (El-Haïk et al., 2014). It should be added that the generic form is administered at a lower dosage than the brand name, which is often prescribed when there are psychiatric comorbidities, insecurity factors (Nordmann et al., 2012) and more severe addiction (Binder et al., 2016). Finally, it would seem that they are less easily divisible, and leave a disagreeable aftertaste; moreover, their exceedingly rapid sublingual melting is suggestive of lessened absorption (El-Haïk et al., 2014). Taken together, these factors help to explain why patients often consider the generic form to be less effective than the brand-name form, which is better appreciated and more commonly implicated in misuse (Julians-Minou et al., 2010; Lavonas et al., 2014; Nordmann et al., 2012). In point of fact, BUP overdosage and misuse by nasal route or injection are more widespread (Johanson et al., 2012; Obadia et al., 2001; Pradel et al., 2004; Yokell et al., 2011) than is the case with any other drug, including methadone (Brisacier and Collin, 2014), whether it be in the USA (Thirion et al., 2012) or in Europe (Casati et al., 2012; Feroni et al., 2004).

It is consequently of pronounced interest to analyze patients' representations of their opioid maintenance treatments. Several user profiles have been observed: “conformists”, “innovators”, “ritualists” and “deviants” (Langlois and Milhet, 2012). However, few studies have dealt with how patients view their OMT, of which their representations range from medicine to drug (Langlois and Milhet, 2012), from therapeutic maintenance to a legal narcotic, from way of coping to means of entrapment (Guichard et al., 2007). At the positive pole, as a medical treatment OMT is viewed as worth continuing; at the negative pole, discontinuation is deemed imperative.

Are the pejorative representations frequently encountered in general practice associated with misuse, a particularly high degree of addiction, and a pronounced preference for brand-name products? These are the questions we decided to addressed in a cross-sectional study conducted in direct contact with users.

2. Methods

2.1. Study design

We carried out a multicenter observational study of patients who had come to pick up their BUP in dispensing pharmacies. The study was conducted by 11 corresponding teams covering 13 departments throughout France in the vicinity of the towns of Bordeaux, Poitiers, Rochefort, Cognac, Niort, Nancy, Limoges, Rennes, Reims, Besançon and Lille. At least 30 observations were to be performed by site and at most 25 by pharmacy. Each of the local correspondents was tasked with meeting pharmacists and requesting their participation in the survey, the choice of pharmacies being left to the discretion of the correspondent. Once a pharmacist agreed to participate, he signed up and received all relevant documents: pharmacist questionnaires, anonymous self-assessment patient questionnaires, blank envelopes for the patient questionnaires, an explanation of the study to be given to the patient (study objective, responsible parties…) and, finally, a large envelope to contain the envelopes given back by the patients with their completed questionnaires inside. The procedure was validated by the local ethics committee.

2.2. Recruitment

Over the course of 3 weeks, all patients coming to a pharmacy for delivery of generic BUP, BUP/Naloxone or brand-name BUP were deemed eligible to participate in the study. Patients who came for methadone or low-dosage buprenorphine analgesic treatment (TemgesicTM) were excluded. It was up to the pharmacist to make sure that they had not registered elsewhere for the same study. He kept a 6-item observation book on participants: gender, type of medicine delivered, prescribed dosage, presence of a co-prescribed psychotropic substance, function of prescribing physician, consent to take part in the study. The pharmacist then asked eligible patients to participate; once they accepted, they were given a numbered, anonymous self-assessment questionnaire and a confidential envelope. Only one number ensured a link between the questionnaire itself, and the pharmacist's observations. The patient filled out the questionnaire in an isolated and confidential area, placed it in the envelope, and handed it back to the pharmacist, who continued to apply this procedure until there was no longer a single questionnaire left. Once this phase of the study was over, the local correspondent came back to pick up the completed documents.

2.3. Questionnaire

The questionnaire consisted of two pages; while the first explained the study objective and showed how to fill out the document, the second contained the questions themselves, each one of which called for only a single response. They were grouped together as follows: one set of questions on the patient (gender, age, resources, universal health care coverage); two on the form of BUP being used (product name, duration of use); two on his or her experience with other forms of BUP; four on his or her perception of the treatment (less effective, provokes disorders, less practical, less easy to sniff or inject); and, finally, three on his or her representation of the treatment (a trap that does me harm, a treatment with which I feel normal, a drug that makes me feel better). The grouping of questions was carried out according to the profiles identified in several qualitative studies (Guichard et al., 2007; Langlois and Milhet, 2012). Misuse was assessed by questions on its incidence over the preceding month and on possible involvement in illicit trafficking. Degree of addiction was determined from eleven binary items according to the relevant DSM 5 criteria (American Psychiatric Association, 2013).

The questionnaire and the modus operandi were tested during a feasibility study involving 149 patients in 17 pharmacies (Muscat, 2013). The testing helped to optimize the questionnaire, to enhance comprehension and to upgrade the modus operandi. Following the reception, the data were captured by two independent operators.

2.4. Index calculation

Three indexes of pejorative representation, misuse, and addiction, were calculated as follows:

2.4.1. Pejorative representation

Questions exploring patients' representations were graded on a 4-point Likert scale from 0 for the least pejorative (not at all) to 3 for the most pejorative (yes indeed). Two questions explored the profiles consistent with their addiction (Guichard et al., 2007):

- “A trap that does me harm”.
- “Like a drug that does me good”.

There was also a question exploring profiles that seemed inconsistent with addiction (Guichard et al., 2007): “An ordinary treatment with which I feel normal”.

2.4.2. Misuse

To our knowledge, there exist no validated studies through which level or degree of misuse could be measured. To fill this gap, we have built an index of misuse obtained by combining user’s responses about the misuse of the product during the preceding month and possible involvement in illicit trafficking. The index was graded from 0 (no misuse) to 4 (maximum misuse).

- “During the past month I was involved in illicit trafficking”: no, 1 or 2 times, more than 3 times