Acute pain management in patients with opiate maintenance treatment in primary care: a qualitative study

CURRENT STATUS: POSTED

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DOI:
10.21203/rs.2.24203/v1

SUBJECT AREAS
General Biochemistry

KEYWORDS
acute pain, qualitative research, opiate maintenance treatment, primary care
Abstract

**Background:** Opiate use disorders are a worldwide disease. In the last 30 years, opiate maintenance treatment prescription changed patients’ and also changed physicians’ practice. General practitioners (GPs) have to deal with patients on OMT who are in acute pain. Both clinically and pharmacologically, the treatment of acute pain in patients with an opiate use disorder and an OMT (opiate maintenance treatment) differs from that given to patients with other conditions. As this situation is complex, it was important to explore whether GPs recognised this problem and whether they managed it effectively.

**Objective:** To investigate how GPs identify and manage situations of acute pain in patients with opiate use disorders and OMT.

**Methods:** semi-structured interviews were used as a data collection technique with a purposive sample of practising GPs. Data collection continued until saturation was reached. Analysis was undertaken using a thematic analysis method. Two independent researchers, working blind and pooling data, carried out the analysis.

**Results:** The maximal variation of the sample and saturation of data were reached with 11 GPs. The thematic analysis resulted in 4 main themes: (1) the importance and difficulties of professional links, (2) the specific clinical reasoning, (3) the importance of the doctor-patient relationship and (4) the particular characteristics of OMT patients.

**Conclusion:** The complexity of pain and opioid dependence represents significant challenges for GPs. It is hard to achieve a balance between pain relief and opiate use disorder treatment. These questions are particularly important in general practice, where the practitioner may feel insufficiently trained, and isolated. Existing protocols do not seem to be in line with general practice. The number of patients on OMT has increased since it was first marketed; GPs will increasingly have to deal with these situations and will have to issue their own recommendations.

**Background**

Opiate dependence, whether as a result of taking licit or illicit opiates, is a major public health issue
worldwide. Opioid dependence accounts for about 15,479,000 individuals around the world (1). In Europe, the mean prevalence of problem opiate users is estimated to be between 3.6 and 4.4 per thousand inhabitants (15-64 years of age). Opiate maintenance treatments (OMTs) such as methadone, buprenorphine or buprenorphine/naloxone have amply demonstrated their effectiveness (2, 3). This system proved to be efficient in terms of public health, access to care and risk reduction (1,5). 170,000 patients are currently being treated for opiate dependence, of whom 65% are on BHD, and 35% on methadone (7). OMT is a long-term treatment, sometimes maintained for life. This population requires specific care: opiate-dependent patients present more comorbidities than the general population, and have an especially heightened susceptibility to acute pain. First, opiate-dependent subjects present medical history with higher risks of infectious diseases (4-6), traumatic events, medical complications, such as serious cardiac abnormalities, a higher rate of epileptic seizures (7-10), liver disease and chronic pain (11, 12). Second, they present psychological vulnerabilities, such as depression and anxiety, that may be associated with a higher risk factor for pain and are also morbidity and mortality risk factors (13). Third, pharmacologically, two pharmacological phenomena can lead to more difficult management of acute pain in opiate-dependent patients: opiate tolerance, and also opioid hyperalgesia (14-16). These two phenomena lead to a resistance to pain in opiate-dependent subjects, and pain management in opiate-dependent subjects requires significantly higher doses of pain medication (17).

Many studies show that opiate medication treatment is mainly managed by GPs. Pain is a complex phenomenon and, in a large majority of cases, it is managed by GPs. We hypothesise that GPs who prescribe OMT are frequently exposed to situations of acute pain management for patients on OMT. There is very little literature about acute pain management in patients on OMT, especially in general practice. Consequently, the objective was to explore how GPs manage acute pain in patients receiving OMT.

Methods
Inclusion criteria were: GPs practising in the administrative region of this study (Finistere, Brittany, France) with personal experience of OMT management. A research committee, including GPs, a
psychiatrist specialised in addictive disorders and methodologists was recruited. First, 3 GPs were recruited, having been identified as OMT prescribers from a local panel, identified by a local research committee of the University Department of General Practice. In the second stage, starting from these first three GPs, a snowball method was adopted. Recruitment stopped when saturation was observed. No one declined because of lack of interest in the study. Participants were contacted only for the study by phone, and the interview was face-to-face in GPs workplace, without any other participant. They were told that the study concerned management of OMT.

Data collection:

The research committee (GPs, psychiatrist – specialised in addictive disorders, methodologist, all trained and experimented in qualitative studies) constructed a qualitative interview guide consisting of 6 questions. It was tested on GPs and the duration if the interview was 1 hour. A GP researcher (MD, woman, trained on qualitative studies) interviewed all the participants in the study, between 24th April and 25th June 2015. All the interviews were recorded and transcribed in a second time by the interviewer. Transcripts were sent back to participants, none made any comments. It was his first experience of the GP researcher in qualitative studies, she was not particularly experienced on this specific topic.

Insert table 1.

**Table 1. Interview guide**

| Question |
|----------|
| Could you tell us about the last patient on OMT you saw who was suffering from pain? |
| What are your thoughts about the pain experienced by patients on OMT? |
| Which difficulties do you encounter when evaluating the pain experienced by patients on OMT? |
| Do you change your pain management when patients are receiving OMT? |
| How do you feel about this type of patient consultation? |
| Do you have anything further to add on this topic? |

**Ethical approval**

Ethical approval was given by the ethical committee of the “Université de Bretagne Occidentale”.

**Data Analysis**

As the research group was investigating GPs’ thoughts about pain management for patients on OMT,
a critical theory paradigm appeared to be the best possible research perspective [22]. The data analysis technique was based on a thematic analysis with an open coding followed by an axial coding and a selective coding [23]. A pair of researchers working blind, coded the transcripts independently and compared the results at each step of coding. Any discrepancies which occurred were forwarded to the research committee to be sorted out. When the axial coding had been completed, at least one third of the verbatim accounts for each axial code were translated to provide clear examples. This was undertaken to ensure the completeness and the consistency of the coding process. A selective coding was subsequently proposed.

Results

Participants

Eleven GPs were interviewed in France (Finistere region). The social and professional profiles of the GPs are presented in Table 2.

Table 2. Participants interviewed

| Number of patients on OMT, already seen or currently being seen | Number of years’ experience as a practising GP | Gender | Type of medical practice | Place of medical practice |
|---------------------------------------------------------------|-----------------------------------------------|--------|--------------------------|--------------------------|
| 15                                                            | 9                                             | F      | Solo                     | Rural / Urban            |
| 65                                                            | 35                                            | M      | Solo                     | Urban                    |
| 70                                                            | 38                                            | M      | Solo                     | Rural                    |
| 7                                                             | 10                                            | M      | Medical group            | Urban                    |
| 20                                                            | 26                                            | M      | Medical group            | Urban                    |
| 7                                                             | 10                                            | M      | Solo                     | Urban                    |
| 14                                                            | 26                                            | M      | Medical group            | Urban                    |
| 10                                                            | 36                                            | M      | Medical group            | Urban                    |
| 11                                                            | 14                                            | M      | Medical group            | Urban                    |
| 5                                                             | 23                                            | M      | Medical group            | Urban                    |
| 3                                                             | 29                                            | M      | Medical group            | Urban                    |
| 10                                                            | 1                                             | M      | Medical group            | Urban                    |

Data extraction and analyses:

Data were analysed by 2 researchers with an iterative and interactive process of coding and recoding which permitted the aggregation of codes into 13 sub-themes and subsequently 4 themes. They are collated in Table 3.
Table 3. Description of subthemes and themes

As it was impossible to describe all the qualitative data: only the main themes and sub-themes are described. Where the themes and sub-themes that emerged had been described in detail, they were illustrated by selected verbatim accounts drawn from all the countries involved. Verbatim accounts are in italics.

FIGURE 1. Heuristic map of different themes and subthemes

Professional links

GPs identified **difficulties in medical training** and **difficulties in network coordination**.

Difficulties in medical training

References for OMT management differed significantly, according to GPs. Some followed pain management using WHO levels (WHO, 1997) « *I respect the levels (...) in whatever: doliprane (...) codeine, tramadol and, and opiates* ». Most of them reported having no references. GPs reported the lack of consensual data on this subject « *there is a lack of consensual attitude concerning acute pain management in patients on OMT* " .

They developed empiricism. Many mentioned that pain management in patients on OMT was founded on their personal experience of treatment management "*I've developed my own methods, I've done things this way, that's how it works*" and for communication management "*now I know a lot about it, I know how to take them* ".

Some GPs identified lack of training on this subject « *I think we lack training on this subject* " and described the desire for specific training to develop their knowledge about OMT and pain
management. On the other hand, other authors were at ease with pain management for patients on OMT “I'm not a pain specialist at all, but it's not a problem for me.”

Many of them reported lack of time for training. They also found that being confronted with intense pain was a rare situation “the really intense, acute pain, (...) we don't necessarily see it in our surgery; people will have gone beyond that. They will have called(...) they will have called an ambulance, they will have gone to A & E”. They said that, if they were not particularly involved with opiate-dependent patients, they did not need to spend time in training on this subject « it is more (...) for the colleagues who are much more involved, who have the time to get training in the field of drug addiction care in particular, because the problem for us is that we have a wide range of problems to deal with ».

Difficulties in network articulation

GPs reported on pain management which was not tailored to the patients during their hospitalisation. This concerned pharmacological treatment and meant that GPs needed to change the treatment after the patient had been discharged: "the pain management had not been satisfactory (...) in the hospital for example (...) so we had to review the whole scheme". Making medication changes is hard for GPs because of the sanctity of hospital doctors' prescriptions versus GPs' prescriptions. Moreover, "if something has been said to a patient in hospital and the general practitioner starts to contradict what the hospital has said, it makes management difficult." Relationships with pharmacists were also defined as difficult, with conflicting information between GPs and pharmacists, "Comments are inconsistent, and ultimately run counter to good care". However, they stressed the importance of a professional network and reported informal and evolving networks. The limits of networking were availability of the network, and the negative perceptions that some professionals might hold of opiate-dependent patients: "clichés (...) "the addict is manipulative, (...) he is addicted for the rest of his life", (...) You can't trust him".

Clinical reasoning

Subthemes identified were pain evaluation, difficulties in prescription management and lack of evaluation of efficacity or treatment.
For **pain evaluation**, some used the visual analogue scale systematically, but most stated that they used no systematic scales. They said that they used a global clinical evaluation and the functional consequences of the evaluation. Their evaluation was also based on the patient's description: "if the patient told me he was in pain, I thought, that's it, he's in pain, if he's in a lot of pain, he's in a lot of pain". Some GPs identified no difficulties at all in pain evaluation; others described 4 specific difficulties: 1. The reduced pain threshold: "as they have a slightly lower threshold (...) it could possibly be misleading (...) for pains rated higher than 5 (between 0 and 10)"; 2. The self-increasing of OMT by patients limits pain evaluation; 3. The context of psychological suffering: "often there is a psychological component (...) anxiety, stress, (...) between psychological pain and nociceptive pain (...) the boundary between the two is not always easy to determine"; 4. The risk of supplying patients who are only in search of the ‘high’ effect of opiates "it is hard to make the distinction between what is real pain and what is simply a demand for, for a product".

GPs stressed the need to look for the aetiology of the pain, which guides the choice of treatment “you need to know what the cause is if you can, (...) which will also guide the choice of analgesic ».

**Difficulties in prescription management**

With regard to **prescribing analgesics**, a wide variety of practices were described by physicians:

Non opioid painkiller analgesics (paracetamol) were the most frequently cited. Weak opioids were widely used by some doctors, and not at all by others: "I felt that pharmacologically it could not work, that we would not have a satisfactory result, because of the competition from substitution treatments, so a priori with the receptors being saturated, it did not seem appropriate to me". Strong opioid painkillers were also described in various ways: Many of the doctors interviewed avoided this prescription. In contrast, there were others who used morphine in combination with MSOs. However, one reported using lower doses. Others still preferred to stop buprenorphine to prescribe morphine.

As mentioned above, doctors also prescribed multimodal analgesia, with extensive use of anti-inflammatory drugs, and sometimes antidepressants, for neuropathic pain.

Regardless of their prescription, doctors stressed the importance of using a second category of medication for analgesic treatment. The reasons given were:
- Clarification of the indications: "I prefer to prescribe analgesics; ultimately, I prefer to dissociate the use of analgesics for analgesic purposes, from a specific analgesic, used for withdrawal, (..) the buprenorphine retains its status as a substitution treatment ".

- Clarification of the provisional aspect of this prescription: "the fact that a (..) second molecule (..) has been prescribed indicates the provisional nature of the treatment".

Some physicians described prescribing OMT fractionation, with or without an increase in daily dosage. Others associated a Non opioid painkiller or weak opioid analgesic with OMT: "when you have to give them morphine, to be sure that methadone is effective I divide it in 2, and then I add either tramadol, or Acupan â, or another level 2 medication, avoiding level 3 analgesics".

However, many doctors mentioned their reluctance to split MSO for analgesic purposes. Many of them stressed the inconsistency of this practice in their efforts to observe the considerations of OMT provision: "That's what is so complicated, explaining to them that all the medication must be taken in one dose, that...". Some doctors feared destabilising the background treatment: "I think my fear would be that they would say afterwards, 'I still have pain, I have a lot of pain', knowing that if we don't treat the cause of the pain, and that the cause is not resolved, I am afraid that, afterwards, we will go from 8mg to 12-16mg for weeks". They also reported patients' reluctance to split medication doses. They fear that they might not be able to reduce the dose frequency of MSO back to once a day after the pain had subsided: "She says 'I could never have split my Subutex' because she would have felt that, by splitting her daily dose, she might become reliant again on something she had been fighting to be free of for a long time." As a result, those doctors felt that fractionation of OMT for pain management could only be used with stabilised patients. "I felt that she was ready to hear that she could divide her daily dose in case of pain".

They mentioned the health and lifestyle advice they provided to reduce pain when they saw patients. They also described the importance of supportive psychotherapy: "I am one of the old doctors who think, yes, that conversation has therapeutic value". They mentioned the need for patient reassurance, which they believed depended on providing sound information. They nevertheless deplored the lack of time available to provide this information: "we don't have 1 hour ahead of us, eh,
we have to understand that an appointment in general practice lasts 15 minutes, for which 23 euros are reimbursed by social security, that's basically the average, okay? So, in 15 minutes we will have everything to deal with, well, but that's what you have to keep in mind, and that's the problem in general practice”.

Many doctors spoke of the need to call on colleagues in difficult therapeutic situations. They first mentioned the colleagues in the same general practice: "the fractionation of buprenorphine which I had already done, but then found, after discussing it with colleagues, that they would have done the same". They also mentioned the use of addiction networks "the centre for drugs, of course, for the whole aspect of toxic side-effectives and drug treatment", the pain centre ("pain centres of the La Cavale Blanche, the maritime hospital, are quite likely to help us with this issue" and hospitalisation "if the pain is so severe that she cannot sleep, well I hospitalise her".

– Lack of evaluation of care effectiveness

Most of the doctors interviewed described the effectiveness of their pain management as good: "Well, they are in less pain. They are better, so they are happy". Some physicians evaluated the effectiveness of pain management through the use of a pain scale and they re-evaluated it after treatment. However, many of them described an evaluation which was based on the absence of repeated requests for painkillers: "I don't get much feedback but, if I don't see them again, I assume that is because they are fine".

They described difficulties in assessing the effectiveness of their management because of the lack of feedback from patients "I rarely get feedback" and there is not enough time to see them again in a timely consultation "we would have to be able to see the patient again the next day, the day after, and in current practice, that's almost impossible in town or city practices, they don't come back, or they move on".

Finally, opinions were divided regarding the effectiveness of codeine. Some physicians described variable patient feedback. Others said they had noticed codeine efficacy: "so it's true that, pharmacologically, it shouldn't work except that it can actually work". In addition, they did not
observe withdrawal syndrome by combining codeine and buprenorphine: "in my daily professional life, I have never had codeine-Subutex withdrawal, never, ever..".

**Complex therapeutic relationship**

A relationship that is often of high quality

Most physicians described a relationship of trust with patients: "it is a relationship of trust that is established over time".

The doctors were more confident with patients known to the practice: "someone who is followed up, with whom there is trust, it goes smoothly, it's not too stressful". They then described trusting patients complaining of pain: "if they tell me they have pain, I believe them". In return, the patient trusted the doctor and particularly valued the doctor's non-judgemental approach: "as things stand, we are quite open about what we say, I always ask them what they have, if they have taken anything, what they do not have, and so they say, they tell me".

Doctors also stressed their attention to pain. They noted the importance of letting the patient know "so that they can also see that their pain is being taken into account".

This idea was in line with that of the overall management of the patient in general medicine: "the patient who comes to me I take as a whole person, not just as a drug addict, but as a patient, and so a patient on substitution treatment, can also have toothache, (..) or chronic bronchitis, (..) or hypertension.. ".

Sometimes difficult relationship.

Doctors' lack of trust: Many doctors mentioned their mistrust of certain patients. They explained it as the fear of being manipulated in the context of trafficking or in misuse of OMT or analgesics. They also mentioned a greater mistrust if the patient was unknown to them.

Complex contact: The doctors interviewed mentioned patients with complex psychological profiles: They were described as having "a particular psychological profile".

There was a distance between them, maintained by the patient: "year after year we still manage to discuss a little bit when we know their history, but for those whose history we don't know, who come to us, they never, or very rarely, tell us what has happened...".
At the time, the GPs being interviewed deplored the role of the doctor, which sometimes boiled down to merely prescribing: "they see us a supplier in some ways".

They also mentioned a difficulty in maintaining a link with these patients because of cancelled appointments and medical nomadism.

Finally, the doctors described the difficulty of providing care in response to a patient’s request to be treated solely by their GP: "And often the difficulty comes from the fact that, just because they are causing you problems and you feel your competence is being stretched to its limit in caring for them, they do not want to leave you... you are their only contact and you remain so, therefore you have to solve things that are sometimes much more complex than you would like".

**A specific patient population.**

**A young population**

Doctors agreed that this is quite a young patient population: "it is often patients who are still quite young".

**Relationship between consumers**

They mentioned links between consumers in the context of trafficking or misuse of OMT: "they gave their capsules to everyone".

**Perception of their own bodies**

One doctor mentioned patients having a different perception of their own body compared with the general population: "they have notions about their own body which are not be the same as other people’s".

**Pain experienced**

Opinions about pain were divided. Thus, some doctors did not observe any specificity in the pain: "I do not get the impression that they suffered more pain than other patients".

Other doctors referred to their knowledge of acquired hyperalgesia, and described having observed this lowering of the pain perception threshold: "They feel increased pain".

On the other hand, the doctors mentioned a more important psychological aspect of the pain: "In terms of pain, we are just as concerned about understanding emotional pain, the mental component
of the physical pain."

Others, on the contrary, mentioned a better tolerance of pain: "that's what it says, that they would be hypersensitive to pain compared with a standard population, I admit that I didn't particularly experience that, I even saw some who were quite resistant to pain".

**Relationship to drugs and meds**

Immediate satisfaction: The physicians interviewed described a request for immediate pain relief from patients: "these patients are often still at the...the impetuous stage of expecting rapid results". In this context, they observed excessive consumption and the search for repeated and symptomatic medication in relation to painkillers: "it is precisely (...)the addictive attitude that I am trying to remove with regard to medication, and that is the main difficulty".

**Patient knowledge of pharmacology**

Interviewees reported a good understanding of pharmacology by patients: "They know, they can generally manage pharmacology, many of them at least know which drug to use and how to use it, in the normal way, that is ".

**Perception of meds and drugs**

The physicians interviewed agreed that these patients had a specific attitude towards drugs: "they also have a somewhat specific attitude towards drugs". Thus, one doctor stated that the prescribed drugs were considered a highly addictive risk by some patients: "the drugs they are prescribed are often ultimately experienced as even more addictive, more addictive than their own substance of choice". They had a strong awareness of tolerance to painkillers: "Yes, but I am addicted to drugs, I don't like taking products anymore". In this context, they described frequent refusals of paracetamol.

**Self-medication**

Opinions were divided on the frequency of self-medication. One doctor noted an uncontrolled and indiscriminate use of products by some patients. Another mentioned a modified intake of analgesics adopted by stabilised patients: "those who are really well stabilised or who take small or regular
doses and who are consistent (.) take analgesics more easily”.

They observed self-medication with OMT: “those who overuse for analgesic purposes tend not to take it, or to take it in 2 doses easily, morning and evening, or in case of pain which is a little more acute, they split the medication, also for analgesic purposes"

They mentioned guilt expressed by patients on this subject: "I don't know if they feel guilty (.) But (.) they justify their increase in buprenorphine and they apologise for taking it (.) or try to clear themselves of the pain by taking, buprenorphine, that's it, and they don't necessarily think about taking anything else, other than buprenorphine".

*Potential for misuse:*

Physicians described difficulties arising from the misuse of several analgesic active ingredients, such as nefopam, tramadol and morphine.

*Low investment in care*

*Care provision seemed constrained*

The doctors interviewed spoke of patients who felt the treatment they received was holding them back “patients with OMT follow-up in specialized care constantly talk, among themselves, about how they are being kept drug-dependent”.

*Observance*

One doctor mentioned that some patients adhered somewhat better to treatment than the general population. However, most of the doctors interviewed mentioned that it was difficult to obtain compliance: "I try, of course, to ensure that they take buprenorphine once a day in the morning and not on demand, which is complicated".

They went on to mention the need for a more important framework for prescribing: "Some patients had a rather unusual attitude towards drugs so, for these people, prescribing needed to be extremely precise ".

*Delays in providing somatic management :*

The physicians interviewed agreed about the delays that patients were experiencing in their somatic management. They identified delays for acute pathologies (“he broke his metatarsus, he only came 4
days later because he was in pain”), dental care (“they had to go to the dentist for 6 months”) and check-ups requested by their general practitioner ("we make them have check-ups, most of the time they do not go for them").

Discussion

**OMT and pain in general practice**

In this study, GPs identified specific difficulties and limits in the management of acute pain in patients on OMT treatment in primary care. Pain is a frequent intercurrent event, destabilising the theoretical observance of OMT (14, 17). Opiate maintenance treatment management requires a core that corresponds to that at the heart of general practice (18). Two thirds of OMT are prescribed by GPs in France (19). In general practice, among a population of patients on OMT, over 25% had associated somatic disorders (20). In this study, GPs reported that it was a rare situation. However, they were aware of the acute pain in opiate-dependent patients and were concerned about the specificities in this patient population. They reported a lack of training and a lack of recommendations, or guidance for modifying treatment in these complex situations. These findings correspond to the deficiencies identified in literature, where very few articles dealt with the management of pain in patients on OMT, and the majority were only concerned with methadone (21). France is an exception, among the world, in allowing buprenorphine to be prescribed by any practitioner (22), and therefore GPs have to handle the management of long-term buprenorphine treatment, including management of pain in patients with buprenorphine.

**Empiricism**

GPs stated that decisions about prescribing were based on empiricism rather than protocol which probably induced interpersonal variability in pain management, as reported in a study conducted in an A & E department (23). Moreover, beyond the absence of consensual pain-management guidelines for opioid-dependent patients, the preconceptions of caregivers about this addictive disorder, and about patients on OMT, are another limiting factor. GPs in this study described a
complex relationship, with mistrust of certain patients and a fear of being manipulated in a trafficking or misuse of OMT or analgesics scenario. These negative representations probably hinder medical reasoning and reduce the effectiveness of management (24-26). These negative representations were also described as a limiting factor in professional network relationships, between GPs and pharmacists. Case-by-case management should have an evolving network of professionals available, and consistent guidance to patients, especially between the prescribing GPs and the pharmacists, but also between hospital and primary care, to improve the management of these situations.

However, despite these limitations, management of pain in opiate-dependent patients on OMT corresponds to the central core of general practice. GPs have to be involved in patient follow-up, to improve access to OMT and a patient-centred program, as recommended by European consensus (27). One GP mentioned developing a closer relationship with the patient through managing the patient's pain, with an evaluation centred on the patient, including variables not directly linked to opiate-dependence.

**Modalities of acute pain management for patients on OMT**

Evaluation

GPs did not report any exploration of the intensity of pain using a visual analogic scale, as recommended by many protocols. They said that they used a global clinical evaluation and the functional consequences of the evaluation. Their evaluation was also based on patients’ descriptions of the types of pain experienced and distinguished between psychological and nociceptive components of pain. This corresponds to literature: a study in general practice in 2014 showed that only 50% of GPs in the survey used a validated pain assessment scale for a patient on OMT, and 94% of them relied mainly on questioning patients (28).

The GPs interviewed interpreted the absence of a new consultation or complaint at the next consultation as an indication that the initial management had been effective. However, when faced with patients in pain, they found that 40% of patients on OMT did not ask for help compared with 28% in the general population (29). Moreover, GPs identified patients who had a specific perception of
their own bodies; they identified the care required for patients on OMT, for patients with hyperalgesia and also for those patients who had a greater tolerance of painful symptoms; they identified a lack of investment in care which frequently caused a delay in accessing treatment. The lack of pain reassessment is particularly problematic in this patient population on OMT. The risk of pain being undertreated is significantly high (30) and acute pain, that is not sufficiently relieved, exposes the patient to a 2.3 times higher risk of premature discontinuation of treatment (31).

The place of painkillers

The GPs interviewed were concerned by the risk of destabilisation of opiate-dependent patients, about observing OMT only in terms of pain, so they focused on opiate analgesics and on the WHO levels of painkillers. The study showed level 2 painkillers (WHO) were widely prescribed and in particular paracetamol + codeine. This prescription may seem surprising from doctors skilled in prescribing OMT. Opiates are contraindicated in combination with the BHD or NX-BHD (32). The combination of level 2 painkillers (WHO) with methadone is not recommended either because it is not effective (32, 33). This use of the adjunct of an opioid analgesic to OMT varies in literature. It has been developed by specialists in addictology and pharmacology, aiming to increase the dosage with fractionation, in order to benefit the patient by means of the analgesic efficacy of OMT. These discrepancies were also identified in previous studies: in general practice, 50% of GPs reported using a level 2 analgesic prescription combined with OMT (34), and in the emergency department, 19% of physicians reported prescribing level 2 analgesics combined with OMT (31), which was comparable with yet another study (23). A two-year follow-up of 1182 patients on OMT also found that the most prescribed analgesic, after non-steroidal anti-inflammatory drugs, was a combination of paracetamol + codeine, representing 9% of the analgesics prescribed (35).

No consensus exists in literature about the management of acute pain in opiate-dependent patients on OMT, and certainly none in general practice. Some authors proposed protocols (24, 32, 33, 36) based on pharmacology. Most agreed on avoiding the prescription of level 2 analgesics and on the interest in using co-analgesics (non-steroidal anti-inflammatory drugs, antidepressants, anxiolytics...).
While it is stated that existing pain management protocols are not widely applied (19,27), the factors limiting application were not well known, and this applied particularly in general practice. The prescription of level 2 painkillers reflects a certain empiricism in a situation identified as quite rare, complex in evaluation and lacking a reference guide. However, despite pharmacological interactions and risks, physicians interviewed in this study reported their feelings on the analgesic efficacy of codeine in combination with buprenorphine and/or Methadone. However, in patients on OMT, analgesic treatment, exposes patients to an increased risk of undesirable effects, misuse, tolerance and dependence (30, 31, 37).

**OMT management**

GPs were concerned about the risk of opioid dependence in OMT management. They reported fear of treatment destabilisation and of poor compliance with treatment so they preferred to add another analgesic rather than increasing and splitting OMT during the day, as tends to be recommended in literature (38). This is in line with a previous work, where 41% of the GPs questioned were familiar with the possibility of using OMT for its analgesic effect, but only 43% of them actually used it for analgesic purposes. The reason given by physicians for not prescribing was fear of an uncontrolled resumption of MSO consumption (28). The GPs interviewed here had a global approach to the management of their patients, whom they were monitoring both for addictive disorders and for medical follow-up. In terms of addictive disorders, they described how they countered the tendency of many patients to split OMT. They felt that asking the patient to split his or her treatment in the alleviation of pain, was inconsistent with their previous discussions. They preferred to prescribe a second active ingredient to clarify the temporary aspect and indications of this treatment. This fractionation of MSO for analgesic purposes seemed to receive a varied response from the patients. Thus, in this study, the doctors interviewed described reluctance on the part of the patients. They stated that some patients were not (or did not feel) sufficiently stabilised to have the ability to split the MSO without slipping into uncontrolled consumption. However, a study showed that 61% of the patients in the survey were aware of the fractionation of OMT for analgesic purposes; 68% considered
it effective and 58% of them used it regularly (28).

**Implications**

This study highlighted a lack of medical training on the subject, with harmful consequences for the doctor-patient relationship and for the management of the patient's pain. To limit inconsistencies in information given to patients by the various stakeholders, training should be provided targeting a multidisciplinary population (private or hospital doctors, general practitioners, specialists, pharmacists, nurses, etc.). Initially, it could be necessary to organise targeted training for the most experienced OMT prescribers. These GPs, who are often the main supporters of informal networks in liberal medicine, could thus facilitate the dissemination of this training. One of the physicians interviewed spoke of improving his communication through his clinical experience. Training in communication could prove valuable in order to optimise the forming of professional relationships, even at the beginning of a physician's career. Finally, the willingness to network was unanimous among the GPs interviewed. This way of working makes it possible to obtain an opinion, and a procedure to be followed, rapidly, when the general practitioner is faced with a difficult situation.

**Strengths and limitations**

In literature, there are very few articles on this topic. The qualitative methodology helped us to get in-depth answers about the management of acute pain in patients on OMT.

This study has several biases. First, there is a selection bias. The sample was selected on the basis of five criteria (number of patients on OMT being monitored, number of years of practice, gender, type of practice: solo or in a group, rural, semi-rural or urban practice setting). The maximum variation was obtained on these criteria. There was also an information bias: during some interviews, the investigator perceived discomfort in some responses. This could be a type of social desirability bias. It should be noted that this bias is described in many qualitative studies. Saturation was obtained at the 6th interview. This is a type of information bias. However, the rarity of the situation explored may have contributed to this early saturation. Finally, none of the physicians interviewed was a prescriber of BHD NX. As a result, it was not possible to assess the difficulties associated with this drug.
Conclusion

This study showed that GPs’ overall care has specific characteristics in the context studied. The complexity of pain and opioid dependence represents significant challenges for clinicians and patients. It is hard to achieve a balance between pain relief and opiate use disorder treatment. These questions are particularly important in general practice, where the practitioner may feel insufficiently trained, and isolated. Moreover, clinical reasoning may be influenced by the stigma associated with opiate-dependent people, and by the misinterpretation of an opioid request by the patient as a “way of obtaining drugs” or by the perception of OMT as a separate treatment for pain or dependence. Physicians who are familiar with the recommendations for fractionation and dose increase of OMT for analgesic purposes refuse to prescribe it. The main reason is that this message is contradictory. It clashes with one of the most important messages about opiate dependence and OMT monitoring, i.e. the observance of the single daily MSO intake. Most use additional and different medication which, according to those prescribing it, enables the indications and the provisional aspect of the medication to be clearer, especially for the patient.

Existing protocols do not seem to be in line with general practice. However, obtaining clear recommendations for care will be increasingly important in the future. Indeed, the number of patients on OMT has increased since it was first marketed, and these patients experience more pain than the general population. General practitioners will increasingly have to deal with these situations and will have to issue their own recommendations. It will, therefore, be valuable to evaluate the prescribing practices of general practitioners and their effectiveness on pain, as well as the sustainability of substitution, using quantitative methods. It will then be necessary to assess the feasibility of, or need for, a set of recommendations adapted to general practice.

Abbreviations

OMT = opiate maintenance treatment OUD = opiate Use disorders
MTD = methadone BHD = buprenorphine GP = General practitioner

Declarations
Ethics approval and consent to participate

This study was approved by the ethics committee of the university of Bretagne Occidentale. This study did not include any patients. All the GP's interviewed gave their written consent to participate.

No participants were underage.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable : All the relevant data of this study are available in this article. No supplementary data available.

Competing interests

No competing interests to declare

Funding

This study was not funded

Authors' contributions

MGL , JYLR and MB designed the study, MB collected data, MB and MGL analyzed qualitative data, JYLR and DLG participated to the redaction and reviewed the article.

All authors approved read and approved the manuscript.

Acknowledgements

Many thanks for all the GP's who have accepted to answer to the study.

References

1. Degenhardt L, Whiteford HA, Ferrari AJ, Baxter AJ, Charlson FJ, Hall WD, et al. Global burden of disease attributable to illicit drug use and dependence: findings from the Global Burden of Disease Study 2010. Lancet. 2013;382(9904):1564-74.

2. Guillou Landreat M, Victorri-Vigneau C, Grall-Bronnec M, Sebille-Rivain V, Venisse JL, Jolliet P. Impact des politiques de santé publique sur les consultations en addictologie à partir d’un suivi longitudinal de 1998 à 2007. Ann Med Psy 2013;171(6):367-71.
3. Guillou Landreat M, Rozaire C, Guillet JY, Victorri Vigneau C, Le Reste JY, Grall Bronnec M. French Experience with Buprenorphine : Do Physicians Follow the Guidelines? PLoS One. 2015;10(10):e0137708.

4. Zhang L, Zhang D, Chen W, Zou X, L. L. High prevalence of HIV, HCV and tuberculosis and associated risk behaviours among new entrants of methadone maintenance treatment clinics in Guangdong Province, China. PLoS One. 2013;8(10).

5. Klepser ME, Klepser TB. Drug treatment of HIV-related opportunistic infections. Drugs. 1997;53(1):40-73.

6. Sulkowski MS, Mast EE, Seeff LB, Thomas DL. Hepatitis C virus infection as an opportunistic disease in persons infected with human immunodeficiency virus. Clin Infect Dis. 2000;30 Suppl 1:S77-84.

7. Basu D, Banerjee A, Harish T, Mattoo S. Disproportionately high rate of epileptic seizure in patients abusing dextropropoxyphene. Am J Addict Am Acad Psychiatr Alcohol Addict. 2009;18(5):417-21.

8. Manninen P. Opioids and seizures. Can J Anaesth Journal canadien d’anesthesie. 1997;44(5pt1):463-6.

9. Jovanovic-Cupic V, Martinovic Z, Nesic N. Seizures associated with intoxication and abuse of tramadol. Clin Toxicol. 2006;44(2):143-6.

10. Mattoo S, Singh S, Bhardwaj R, Kumar S, Basu D, Kulhara P. Prevalence and correlates of epileptic seizure in substance-abusing subjects. Psychiatry Clin Neurosci. 2009;63(4):580-2.

11. Amari E, Rehm J, Goldner E, Fischer B. Nonmedical prescription opioid use and mental health and pain comorbidities: a narrative review. Can J Psychiatry Revue canadienne de psychiatrie. 2011;56(8):495-502.

12. Kobus A, Smith D, Morasco B, al. e. Correlates of higher-dose opioid medication use
for low back pain in primary care. J Pain Official J Am Pain Soc. 2012;13(11):1131-8.

13. Fridell M, Bäckström M, Hesse M, Krantz P, Perrin S, Nyhlén A. Prediction of psychiatric comorbidity on premature death in a cohort of patients with substance use disorders: a 42-year follow-up. BMC psychiatry. 2019;19(1):150.

14. Courty P, Authier N. [Pain in patients with opiates dependence]. Presse Med. 2012;41(12 Pt 1):1221-5.

15. Yi P., Pryzbylkowski P. Opioid Induced Hyperalgesia. Pain Med. 2015;16(suppl. 1):32-6.

16. Higgins C, Smith B, Matthews K. Evidence of opioid-induced hyperalgesia in clinical populations after chronic opioid exposure: a systematic review and meta-analysis. Br J Anaesth 2019;122(6).

17. Delorme J, Chenaf C, Bertin C, Riquelme M, Eschalier A, Ardid D, et al. Chronic Pain Opioid-Maintained Patients Receive Less Analgesic Opioid Prescriptions. Front Psychiatry. 2018;9(335).

18. Loxterkamp D. Medication-Assisted Treatment Should Be Part of Every Family Physician's Practice: Yes. Ann Fam Med. 2017;15(4):309-10.

19. Drogues et addictions, données essentielles - OFDT.

20. Gentile G, Frauger E, Giocanti A, Pauly V, Orleans V, Amaslidou D, et al. [Characteristics of subjects under opiate maintenance treatment in primary care using the OPEMA data 2013]. Therapie. 2016;71(3):307-13.

21. Eyler EC. Chronic and acute pain and pain management for patients in methadone maintenance treatment. Am J Addict. 2013;22(1):75-83.

22. Fatseas M, Auriacombe M. Why buprenorphine is so successful in treating opiate addiction in France. Curr Psychiatry Rep. 2007;9(5):358-64.

23. Desplas M. Prise en charge de la douleur chez le sujet sous médicament de
substituion Toulouse: Université de Toulouse 2005.

24. Alford DP, Compton P, Samet JH. Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. Ann Intern Med. 2006;144(2):127-34.

25. Newshan G. Pain management in the addicted patient. Nurse Pract. 2000;25(4):14, 7-8.

26. Guillou Landreat M. Représentation des traitements de substitution aux opiacés et de leur arrêt. Regards croisés patients-médecins. 2013:23-44.

27. Dematteis M, Auriacombe M, D'Agnone O, Somaini L, Szerman N, Littlewood R, et al. Recommendations for buprenorphine and methadone therapy in opioid use disorder: a European consensus. Expert Opin Pharmacother. 2017;18(18):1987-99.

28. Lefevre-Mohr C. Quelle prise en soins du patient douloureux sous traitement de substituion aux opiacés ? analyse des comportements d'automédication des patients et des pratiques antalgiques des médecins Strasbourg University of Strasbourg 2014.

29. Vignas F. Douleur, souffrance et toxicomanie : évaluation et traitement de la douleur chez le patient sous traitement de substitution, enquête dans le loiret en 1999 Tours: Université François Rabelais; 1999.

30. Scimeca MM, Savage SR, Portenoy R, Lowinson J. Treatment of pain in methadone-maintained patients. Mt Sinai J Med. 2000;67(5-6):412-22.

31. Bounes V, Jouanjus E, Roussin A, al. e. Acute pain management for patients under opioid maintenance treatment : what physicians do in emergency department ? . Eur J Emerg Med. 2013;44(2):127-34.

32. Laprevote V, Geoffroy PA, Rolland B, Leheup BF, Di Patrizio P, Cottencin O, et al. [Management of opioid maintenance treatments when analgesic treatments are required]. Presse Med. 2013;42(7-8):1085-90.
33. Victorri Vigneau C, Bronnec M, Guillou Landreat M, Jolliet-Evin P. Prise en charge de la douleur aigue chez les patients sous traitements de substitution aux opiacés. Douleur Analgésie 2012;25(2):83-6.

34. Dumand E. Prise en charge en médecine générale d’une douleur aigue chez un patient toxicomane aux opiacés Grenoble université de Grenoble 2008.

35. Fredheim OM, Borchgrevink PC, Nordstrand B, Clausen T, Skurtveit S. Prescription of analgesics to patients in opioid maintenance therapy: a pharmacoepidemiological study. Drug Alcohol Depend. 2011;116(1-3):158-62.

36. Olivier M, Roussin A, Bayle P, al. e. Prise en charge des douleurs faibles à modérées et des douleurs fortes de patients substitués pas buprénorphine ou méthadone pour une pharmacodépendance majeure aux opiacés France CLUD 39; 2013.

37. Heiskanen T, Kalso E. Non-analgesic effects of opioids: interactions between opioids and other drugs. Curr Pharm Des. 2012;18(37):6079-89.

38. Koller G, Schwarzer A, Halfter K, Soyka M. Pain management in opioid maintenance treatment. Expert Opin Pharmacother. 2019;20(16):1993-2005.

39. SFETD. Utilisation des opioïdes forts dans la douleur chronique non cancéreuse chez l’adulte Recommandations de bonne pratique clinique par consensus formalisé. Paris 2016.

40. Voon P, Karamouzian M, Kerr T. Chronic pain and opioid misuse: a review of reviews. Subst Abuse Treat Prev Policy. 2017;12(1):36.

Figures
FIGURE 1. Heuristic map different themes and subthemes

Figure 1

Heuristic map of different themes and subthemes

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