The opioid epidemic: helping rheumatologists prevent a crisis
Anne-Priscille Trouvin, Francis Berenbaum, Serge Perrot

To cite this version:
Anne-Priscille Trouvin, Francis Berenbaum, Serge Perrot. The opioid epidemic: helping rheumatologists prevent a crisis. RMD Open: Rheumatic & Musculoskeletal Diseases, EULAR; BMJ, 2019, 5 (2), pp.e001029. 10.1136/rmdopen-2019-001029. hal-02413259

HAL Id: hal-02413259
https://hal.sorbonne-universite.fr/hal-02413259
Submitted on 16 Dec 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.
VIEWPOINT

The opioid epidemic: helping rheumatologists prevent a crisis

Anne-Priscille Trouvin,1,2 Francis Berenbaum,3,4 Serge Perrot2,5

ABSTRACT

An endemic increase in the number of deaths attributable to prescribed opioids is found in all developed countries. In 2016 in the USA, more than 46 people died each day from overdoses involving prescription opioids. European data show that the number of patients receiving strong opioids is increasing. In addition, there is an upsurge in hospitalisations for opioid intoxication, opioid abuse and deaths in some European countries. This class of analgesic is increasingly used in many rheumatological pathologies. Cohort studies, in various chronic non-cancer pain (CNCP) (osteoarthritis, chronic low back pain, rheumatoid arthritis, etc), show that between 2% and 8% of patients are treated with strong opioids. In order to help rheumatologists prescribe strong opioids under optimal conditions and to prevent the risk of death, abuse and misuse, recommendations have recently been published (in France in 2016, the recommendations of the French Society of Study and Treatment of Pain, in 2017, the European recommendations of the European Federation of IASP Chapters and the American Society of International Pain Physicians). They agree on the same general principles: opioids may be of interest in situations of CNCP, but their prescription must follow essential rules. It is necessary to make an accurate assessment of the pain and its origin, to formulate therapeutic objectives (pain, function and/or quality of life), to evaluate beforehand the risk of abuse and to get a specialised opinion beyond a certain dose or duration of prescription.

INTRODUCTION

Since the 1990s, strong and weak opioids have been prescribed in a field that is increasingly extensive, including acute pain and also chronic cancer and non-cancer pain. Since 1985, and the WHO classification of analgesics for cancer pain, strong opioids were prescribed beyond the initial scope of the WHO recommendations to treat non-cancer pain, including chronic pain, which, if we rely on the judicial claims in the USA, was helped by deceptive companies business practices’ made false representations the opioid addictiveness, its efficacy, in order to delude authorities, prescribers and patients. Twenty years ago, the first US recommendations were published to reinforce proper opioid prescription practices in chronic non-cancer pain (CNCP). Despite this, the problem has only become more pronounced.

CURRENT ISSUE

Clear increase in sales

In the USA, between 2002 and 2012, the number of opioid prescriptions has doubled.3 In Europe, there is the same trend with a slight time lag compared with the North American continent. In the UK and in France, opioid prescriptions grow regularly and in particular, strong opioid users doubled between 2004 and 2017.4,5

‘Epidemic’ of deaths from prescription opioids

Despite numerous recommendations, guidelines and preventative measures, many studies over the last 20 years show a significant increase in mortality related to prescribed opioids. The latest figures show an increase of 345% of all deaths attributable to opioids from 2001 to 2016 and an estimate of 1.68 million person-years of life lost in 2016.6 In Europe, data on opioid mortality follow the same trend as for the North American continent, especially for Northern Europe. In England and Wales, the number of opioid deaths increases of 425% in 20 years.7,8 In France, opioid-related deaths increased by 146% between 2000 and 2015 (table 1).4

Abuse and misuse

Beyond the increase in deaths, studies note a strong trend towards the emergence of drug abuse with prescription opioids. Thus, in a cohort of 32 499 patients who initiated a strong opioid treatment for CNCP, 11.4% progressed to a chronic intake of more than 3 months.9 Vowles et al, in a meta-analysis, found that in long-term opioid-treated patients for CNCP, rates of misuse averaged between 21% and 29%.10 In a German cohort study, the pooled 1-year prevalence of abuse/addiction of prescribed opioids (defined by hospital stays because of mental and behavioural disorders due to alcohol, opioids, tranquillisers,
multiple substances and intoxication by narcotic agents) was 0.56%. Abuse/addiction of prescribed opioids was associated with younger age, diagnoses of somatoform pain disorder, depression and prescription of tranquilisers. Moreover, in an international survey, Morley et al investigated opioid analgesic misuse and abuse in participants from the Global Drug Survey 2015 who had used at least one prescription opioid analgesic medication in the past year. In this survey of 5670 participants from UK (N=1199), France (N=1258), Germany (N=866), USA (N=1334) and Australia (N=1013), between 8% and 22% of participants who had not used any illicit drugs or benzodiazepines in the past year reported misuse or abuse of codeine, hydrocodone, oxycodone, or tramadol.

**CURRENT USE, EFFECTIVENESS AND INEFFICIENCY OF OPIOIDS IN MUSCULOSKELETAL PAIN**

**Current use in musculoskeletal pain**

In an English cohort of 703 patients with chronic musculoskeletal pain, 59% of the participants were prescribed opioids during the 12 months follow-up. For rheumatoid arthritis (RA), a German cohort of 3140 patients showed that 6% with no or mild pain received opioids and 32.6% with severe pain. Moreover, in spondyloarthritis (SpA), one cohort study reports 21.7% of patients with intermittent opioid use and 9.5% chronic use. For fibromyalgia, cohort studies found that between 11.3% and 12.5% of the patients were treated with opioids. For back pain, an evaluation of trends in treatments over a 12-year period showed an increase in the use of opioids from 19.3% to 29.1%. Finally for osteoarthritis, DeMik et al showed that approximately 11.5% of patients with osteoarthritis will be prescribed an opioid in a given year.

**Evidence of opioid effectiveness or inefficiency in musculoskeletal pain**

Most of the literature reviews in various musculoskeletal conditions are moderate in their conclusions regarding the benefit of opioids in chronic pain. In osteoarthritis, both the Cochrane review in 2014 and Smith et al concluded to a small benefit on pain but with questionable clinical relevance, this with contrast to significant risk of adverse effects. Smith et al even concluded that nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids have comparable pain relief. The 2014 Osteoarthritis Research Society International (OARSI) guidelines for non-surgical management of knee osteoarthritis came to the conclusion of uncertain appropriateness for opioid. In chronic low back pain, reviews and meta-analysis reach the same conclusion of short-term benefit of opioids with a moderate effect on pain and small effect for function. In chronic inflammatory rheumatism the sole review is the Cochrane review from 2011, conclusion is that weak opioids may be effective for painful RA patients but evidence is limited and there is not enough evidence to conclude for long-term opioid therapy or the benefit of strong opioids. In the 2016 SpA ASAS-EULAR recommendations, opioids analgesics, might be considered for residual pain after previously recommended treatments have failed, are contraindicated and/or poorly tolerated. In fibromyalgia (FM), in a large cohort of 1700 patients, no improvement on pain, function and quality of life was shown. In the latest EULAR recommendations, the committee made a ‘strong against’ evaluation regarding the use of strong opioids in FM.

These results are to be weighed, taking into account the population included in these different trials. In fact, psychiatric pathologies, including depression, are almost always a non-inclusion criterion, and patients with pre-existing risks of abuse or misuse are commonly also excluded. These patients are, however, regularly met in consultation, mandating that we transpose the results of publications for these patients and analyse the benefit-risk balance carefully.

**RECOMMENDATIONS FOR SAFE PRESCRIPTION OF OPIOIDS IN NON-CANCER PAIN**

In this context of complex benefit-risk balance with a moderate short term expected benefit on the one hand, and the risk of abuse or misuse with sometimes deadly consequences, several recommendations of good practice have been issued. In 2016, the French Society of Study and Treatment of Pain (SFETD) published French recommendations on good prescribing practices for strong opioids in non-cancer pain and the Centers for Disease Control and Prevention (CDC) published guidelines in the USA in 2016 SpA ASAS-EULAR recommendations, opioids analgesics, might be considered for residual pain after previously recommended treatments have failed, are contraindicated and/or poorly tolerated. In fibromyalgia (FM), in a large cohort of 1700 patients, no improvement on pain, function and quality of life was shown. In the latest EULAR recommendations, the committee made a ‘strong against’ evaluation regarding the use of strong opioids in FM.

All recommendations remind us to introduce strong opioids only after failure of recommended first-line drug treatments given at maximum tolerated effective doses; and as part of the comprehensive care of the patient, including at least a psychological evaluation in the case of depressive or anxious comorbidities, social, professional and rehabilitative management for osteoarthritis pain and chronic low back pain, expected benefits should outweigh risks. French and American guidelines highlight clinical contexts for which expected benefits of opioids are unlikely to overbalance the risks: fibromyalgia and headaches.

Some key principles: before any prescription of opioids is given, one must first establish an assessment with a clear and documented diagnosis, a physical examination, a psychological assessment, and finally a determination...
of the impact of pain in all aspects of the patient’s life.29–31 On the other hand, it is necessary to evaluate pain and function.29–31 The three publications recommend establishing therapeutic goals with the patient and anticipating with clear explanation, the adverse effects and potential inefficiency.25–31 It is important to define for the patient the different modes of action of the prescribed treatments and the difference between prolonged release and immediate release forms. Symptomatic treatment for the most common adverse reactions (constipation, nausea/vomiting) should be systematically prescribed.

Treatment should be initiated at low doses with progressive titration.29–31 There is no evidence in the literature to recommend one molecule over another.29–31 Avoid dose greater than (morphine milligram equivalents) 150 mg/day of morphine.29–31 Avoid co-prescription of benzodiazepines.

Regular reassessment (with regard to previously set goals of pain relief, and/or functional improvement, and/or quality of life improvement) should be systematically performed.29–31 Evaluate risk factors for opioid-related harms.

The risk of abuse should be evaluated before the initiation of treatment. The main risk factors are personal and family history of substance abuse; age; history of preadolescent sexual abuse; and certain psychological diseases. To assess this risk, the Opioid Risk Tool can be used. It is a quantitative tool with a stratification of the risk according to the scores: 0–3 (low risk), 4–7 (moderate risk), ≥8 (high risk).32

Once instituted, the treatment must be regularly re-evaluated, especially with regard to previously set goals of pain relief, and/or functional improvement, and/or quality of life improvement. Indicative thresholds of 30% or two out of 10 improvement of pain rating are considered clinically significant for the SFETD.29 Similarly, at each prescription renewal, it is important to look for signs of abuse or misuse in order to be able to quickly refer the patient for specialist advice. The Prescription Opioid Misuse Index can be used.33

CONCLUSION

Strong opioids can bring a moderate benefit in chronic non-cancer musculoskeletal pain. However, their prescription should be done in a reasoned way with increased monitoring of both efficacy and adverse effects, with special attention to the risk of abuse and misuse.

Contributors A-PT wrote the draft, SP and FB revised it critically for important intellectual content; all three authors gave the final approval of the version to be published.

Table 2 Summary of major recommendations for prescribing opioids for non-cancer pain

| Recommendation                                                                 | SFETD | EFIC | CDC |
|--------------------------------------------------------------------------------|-------|------|-----|
| First establish an assessment with a clear and documented diagnosis, a physical examination, a psychological assessment and finally a determination of the impact of pain in all aspects of the patient’s life. | ✔     | ✔    |     |
| Failure of first line recommended treatment given at maximum tolerated dose     | ✔     | ✔    | ✔   |
| Global comprehensive care of the patient (psychological, social, professional and rehabilitative management) | ✔     | ✔    |     |
| Expected benefits of opioid treatment should outweigh the risk                  | ✔     |      |     |
| In fibromyalgia expected benefits of opioids are unlikely to overbalance the risks | ✔     | ✔    |     |
| Establish therapeutic goals with the patient and anticipating with clear explanation, the adverse effects and potential inefficiency | ✔     | ✔    |     |
| Define for the patient the different modes of action of the prescribed treatments and the difference between prolonged release and immediate release forms | ✔     | ✔    |     |
| Symptomatic treatment for the most common adverse reactions (constipation, nausea/vomiting) should be systematically prescribed | ✔     | ✔    |     |
| Treatment should be initiated at low doses with progressive titration           | ✔     | ✔    | ✔   |
| There is no evidence in the literature to recommend one molecule over another  | ✔     | ✔    | ✔   |
| Avoid dose greater than (morphine milligram equivalents)                       | 150   |      | 90  |
| Avoid co-prescription of benzodiazepines                                       | ✔     | ✔    | ✔   |
| Regular reassessment (with regard to previously set goals of pain relief, and/or functional improvement, and/or quality of life improvement) | ✔     | ✔    | ✔   |
| Evaluate risk factors for opioid-related harms                                 | ✔     | ✔    | ✔   |

EFIC, European Federation of IASP Chapters; SFETD, French Society of Study and Treatment of Pain.
Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests A-PT reports personal fees from Pfizer, from Menarini and from Astellas, outside the submitted work; FB has received consulting fees from Grunenthal, personal fees from BMS UPSA, outside the submitted work.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No additional data are available.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

REFERENCES
1. Haftfajee RL, Mello MM. Drug companies’ liability for the opioid epidemic. N Engl J Med Overseas Ed 2017;377:2301–5.
2. American Academy of Pain Medicine and American Pain Society. The use of opioids for the treatment of chronic pain: a consensus statement. Glenview, Ill: American Academy of Pain Medicine and American Pain Society, 1997.
3. Dart RC, Surratt HL, Cicero TJ, et al. Trends in opioid analgesic abuse and mortality in the United States. N Engl J Med 2015;372:241–8.
4. Chenal C, Kaboré J-L, Delorme J, et al. Prescription opioid analgesic use in France: trends and impact on morbidity-mortality. Eur J Pain 2019;23:124–134;124–34.
5. Mordecai L, Reynolds C, Donaldson Lj, et al. Patterns of regional variation of opioid prescribing in primary care in England: a retrospective observational study. Br J Gen Pract 2018;68:e225–33.
6. Gomes T, Tadrous M, Mamdani MM, et al. The burden of Opioid-Related mortality in the United States. JAMA Netw Open 2018;1:e180217.
7. Giraudon I, Lowitz K, Dargan PI, et al. Prescription opioid abuse in the UK. Br J Clin Pharmacol 2013;76:823–4.
8. Office for National Statistics. Deaths related to drug poisoning in England and Wales: 2014 registrations. Available: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtordrugpoisoningenglandandwales/2015-09-03#toc [Accessed 27 May 2019].
9. Kaplovitch E, Gomes T, Camacho X, et al. Sex differences in dose escalation and overdose death during chronic opioid therapy: a population-based cohort study. PLoS One 2015;10:e0134550.
10. Vowles KE, McIntee ML, Julnes PS, et al. Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. Pain 2015;156:569–76.
11. Manschall U, L Hoest H, Radbruch L, et al. Long-term opioid therapy for chronic non-cancer pain in Germany. Eur J Pain 2016;20:767–76.
12. Morley KJ, Ferris JA, Winstock AR, et al. Polysubstance use and misuse or abuse of prescription opioid analgesics: a multi-level analysis of international data. Pain 2017;158:1138–44.
13. Ashaye T, Hounsme N, Carnes D, et al. Opioid prescribing for chronic musculoskeletal pain in UK primary care: results from a cohort analysis of the COPERS trial. BMJ Open 2018;8:e019491.14. Jobbási K, Luque Ramos A, Albrecht K, et al. Pain, depressive symptoms and medication in German patients with rheumatoid arthritis-results from the linking patient-reported outcomes with claims data for health services research in rheumatology (RMD Open) study. Pharmacoeconomics and Outcomes Research 2019;7:665–74.
15. Dau JD, Lee M, Ward MM, et al. Opioid analgesic use in patients with ankylosing spondylitis: an analysis of the prospective study of outcomes in an ankylosing spondylitis cohort. J Rheumatol 2018;45:188–94.
16. Painter JT, Ford LL, Talbert J. Geographic variation of chronic opioid use in fibromyalgia. Clin Ther 2013;35:303–11.
17. Wolfe F, Walitt BT, Katz RS, et al. Longitudinal patterns of analgesic and central acting drug use and associated effectiveness in fibromyalgia. Eur J Pain 2013;17:581–6.
18. Mafij NJ, McCraghtyn EF, Davis RB, et al. Worsening trends in the management and treatment of back pain. JAMA Intern Med 2013;173:1573–81.
19. DeMik DE, Bedard NA, Dowdle SB, et al. Are we still prescribing opioids for osteoarthritis? J Arthroplasty 2017;32:3587–82.
20. da Costa BR, Nüssch E, Kasteler R, et al. Oral and transdermal opioids for osteoarthritis of the knee or hip. Cochrane Database Syst Rev 2014;30.
21. Smith SR, Deshpande BR, Collins JE, et al. Comparative pain reduction of non-opioid anti-inflammatory drugs and opioids for knee osteoarthritis: systematic analytic review. Osteoarthritis Cartilage 2016;24:962–72.
22. McAlindon TE, Bannuru RR, Sullivan MC, et al. OARSI guidelines for the non-surgical management of knee osteoarthritis. Osteoarthritis Cartilage 2014;22:1599–615.
23. Chaparro LE, Furlan AD, Deshpande A, et al. Opioids compared with placebo or other treatments for chronic low back pain: an update of the Cochrane Review. Spine 2014;39:556–63.
24. Koes BW, Backes D, Bindels PJ.E. Pharmacotherapy for chronic non-specific low back pain: current and future options. Expert Opin Pharmacother 2018;19:537–45.
25. Whittle SL, Richards BL, Husni E, et al. Opioid therapy for treating rheumatoid arthritis pain. Cochrane Database Syst Rev 2011;23.
26. van der Heijde D, Ramiro S, Landewe R, et al. Update of the ASAS-EULAR recommendations for the management of axial spondyloarthritis. Ann Rheum Dis 2016;2017:978–91.
27. Peng X, Robinson RL, Mease P, et al. Long-term evaluation of opioid treatment in fibromyalgia. Clin J Pain 2015;31:7–13.
28. Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis 2017;76:318–28.
29. Moisset X, Trouvin A-R, Tran V-T, et al. [Use of strong opioids in chronic non-cancer pain in adults. Evidence-based recommendations from the French Society for the Study and Treatment of Pain]. Presse Med 2016;45:447–62.
30. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain--United States, 2016. JAMA 2016;315:1624–45.
31. O’Brian T, Christrup LL, Drewes AM, et al. European pain Federation position paper on appropriate opioid use in chronic pain management. Eur J Pain 2017;21:3–19.
32. Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the opioid risk tool. Pain Med 2005;6:432–42.
33. Knisely JS, Wunsch MJ, Cropsy KL, et al. Prescription opioid misuse index: a brief questionnaire to assess misuse. J Subst Abuse Treat 2008;35:380–6.