UK recommendations on opioid stewardship

A wider and more coordinated approach is necessary

Nicholas Levy,[1] consultant anaesthetist, Linda J Lord,[2] chief pharmacist, Dileep N Lobo,[3] professor of gastrointestinal surgery

[1]Department of Anaesthesia and Perioperative Medicine, West Suffolk NHS Foundation Trust, Bury St Edmunds, UK

[2]NHS West Suffolk Clinical Commissioning Group, Bury St Edmunds, UK

[3]Nottingham Digestive Diseases Centre and NIHR Biomedical Research Centre, Nottingham University Hospitals NHS Trust and University of Nottingham, Nottingham, UK

Correspondence to: N Levy nicholas.levy@wsh.nhs.uk

The effect of the prescription opioid crisis in North America is well documented.[1] In 2018 some 68 500 Americans died from opioid overdoses, and in 2015 the cost of opioid misuse to the US economy was estimated at $150bn (£110bn; €120bn).[1] The EU now has an estimated 1.3 million high-risk opioid users,[1] and 110 000 people worldwide died from opioid use disorders in 2017—77% more than in 2007.[2]

Opioids were prescribed to roughly 5% of the UK population in 2015.[3] Between 1998 and 2016, opioid prescriptions increased by 34% in England, and the total oral morphine equivalence dose increased by 127% to 431 000 mg/1000 population/year.[4] A recent UK study found that 14.6% of people given opioids for the first time became long term opioid users within a year.[5]

In response to this healthcare crisis, the UK Medicines and Healthcare Products Regulatory Agency (MHRA) has issued recommendations that before prescribing opioids, clinicians must discuss the risks and features of tolerance, dependence, and addiction with patients, and jointly agree a treatment strategy and plan for the end of treatment.[6] These new recommendations have the potential to alter opioid prescribing habits substantially. The UK General Medical Council advises that clinicians should comply with MHRA recommendations along with other guidance, making compliance a professional duty.[7] Appropriate prescribing of opioids should be a priority, focusing where possible on non-pharmacological strategies, including referral to wellbeing services, physiotherapy, exercise, and weight loss programmes, as well as alternative therapies such as mind-body therapy and acupuncture.[8]

Limited use

Clinicians in primary and secondary care will need to work together to ensure that patients receive the correct information in an accessible format before starting a course of opioids, and that a deprescribing plan is agreed to. All stakeholders will need to recognise that opioids are of limited use for chronic pain and that opioids prescribed for non-cancer pain must be considered a "course" of treatment with a definite end date.

Furthermore, the MHRA acknowledges that patients at particular risk will need regular monitoring and support.[6] This puts the onus on clinicians to ensure that repeat prescriptions for opioids are carefully assessed.[9] This applies equally to online consultations. Regular structured prescription reviews should take place[3] and software tools used to identify patients with higher risks—such as people taking high dose opioids or who are prescribed concurrent medicines such as benzodiazepines. Repeat-refill prescriptions have been identified as one of the main drivers for persistent opioid use,[10] and have been raised as an area for action to prevent future deaths in a recent regulation 28 report.[11] Coroners issue regulation 28 reports only in exceptional circumstances,[12] and this report was published after the death from overdose of an old man supplied with 100 tramadol capsules every month on repeat prescription with no review.[11]

The MHRA also highlights the issues of opioid tolerance, dependence, and addiction and recommends slow tapering after prolonged treatment.[6] Providing information on the effect of opioids on the ability to drive safely can help engage patients in discussions about their opioid prescriptions. In addition, interdisciplinary chronic pain rehabilitation programmes have been shown to be effective in promoting opioid weaning after long term use.[13] However, simple deprescribing is unlikely to be successful for patients with an opioid use disorder, who often have complex psychological needs. They may benefit from enrolment in opioid agonist treatment programmes.[14] These will need to be expanded, with implications for resources in primary and secondary care.

The MHRA also reminds clinicians that transdermal fentanyl patches are contraindicated in patients who have not previously received opioids[6] as they are associated with persistent opioid use.[10] This advice should be expanded and applied to all modified release opioid preparations, including modified release oxycodone, especially in surgical patients.[9]

Wider approach

Although the MHRA recommendations will need to be adhered to within the UK, they are equally applicable globally, especially as drug companies are now aggressively marketing their products in low and middle income countries.[15] An important omission in the

recommendations is opioid diversion, which is major cause of harm. Around half of adults who misuse opioids obtain them from friends and family.[16] Furthermore, mortality in children and young people from unintentional opioid overdose continues to rise, with the increase in availability of opioids within the community.[17] Thus, it is essential that patients understand how to store medicines securely and dispose of unused doses safely.[9]

A wider and more coordinated approach is necessary to tackle opioid use and misuse. Opioid stewardship programmes are needed, which include "coordinated interventions designed to improve, monitor, and evaluate the use of opioids to support and protect human health."[18] The MHRA recommendations should be regarded as an important advance in opioid stewardship.

Competing interests: We have read and understood BMJ policy on declaration of interests and declare DNL has received speakers' honorariums from Fresenius Kabi for unrelated work in the past three years.

References

1. Ayoo K, Mikhaeil J, Huang A, Wasowicz M. The opioid crisis in North America: facts and future lessons for Europe. *Anaesthesiol Intensive Ther* 2020;52:139-47. doi: 10.5114/ait.2020.94756
2. G. B. D. Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018;392:1736-88. doi: 10.1016/S0140-6736(18)32203-7
3. Cartagena Farias J, Porter L, McManus S, Strang J, Hickman M, Reed K, et al. Prescribing patterns in dependence forming medicines. London: NatCen Social Research 2017. Available from: http://phrc.lshtm.ac.uk/papers/PHRC_014_Final_Report.pdf (Accessed on 04/12/2020).
4. Curtis HJ, Croker R, Walker AJ, Richards GC, Quinlan J, Goldacre B. Opioid prescribing trends and geographical variation in England, 1998-2018: a retrospective database study. *Lancet Psychiatry* 2019;6:140-50. doi: 10.1016/S2215-0366(18)30471-1
5. Jani M, Yimer BB, Sheppard T, Lunt M, Dixon, WG. Time trends and prescribing patterns of opioid drugs in UK primary care patients with non-cancer pain: A retrospective cohort study. *PLoSMed* 2020;17:e1003270. doi: 10.1371/journal.pmed.1003270
6. Medicines and Healthcare products Regulatory Agency. *Drug Safety Update* 2020; 14(2):1-14. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/920770/Sept-2020-DSU-PDF.pdf (Accessed on 04/12/2020).
7. General Medical Council. Good practice in prescribing and managing medicines and devices 2013. Available from: https://www.gmc-uk.org/-/media/documents/prescribing-guidance_pdf-59055247.pdf?la=en&hash=958C4EED51E3D145EA8798A1AFD85887D3A577B2 (Accessed on 04/12/2020).
8. Mao J. Challenges of managing chronic pain. *BMJ* 2017;356:j741. doi: 10.1136/bmj.j741

9. Levy N, Quinlan J, El-Boghdadly K, Fawcett WJ, Agarwal V, Bastable RB, et al. An international multidisciplinary consensus statement on the prevention of opioid-related harm in adult surgical patients. *Anaesthesia* 2020 [Epub ahead of print]. doi: 10.1111/anae.15262
10. Shah A, Hayes CJ, Martin BC. Characteristics of initial prescription episodes and likelihood of long-term opioid use - United States, 2006-2015. *MMWR Morb Mortal Wkly Rep* 2017;66:265-69. doi: 10.15585/mmwr.mm6610a1
11. Sullivan G. Regulation 28 Report to Prevent Future Deaths 2020. Available from: https://www.judiciary.uk/wp-content/uploads/2020/07/Peter-Cole-2020-0123.pdf. (Accessed on 04/12/2020).
12. Courts and Tribunals Judiciary. Reports to Prevent Future Deaths. Available from: https://www.judiciary.uk/related-offices-and-bodies/office-chief-coroner/https-www-judiciary-uk-subject-community-health-care-and-emergency-services-related-deaths/. (Accessed on 04/12/2020).
13. Huffman KL, Rush TE, Fan Y, Sweis GW, Vij B, Covington EC, et al. Sustained improvements in pain, mood, function and opioid use post interdisciplinary pain rehabilitation in patients weaned from high and low dose chronic opioid therapy. *Pain* 2017;158:1380-94. doi: 10.1097/j.pain.0000000000000907
14. Pearce LA, Min JE, Piske M, Zhou H, Homayra F, Slaunwhite A, et al. Opioid agonist treatment and risk of mortality during opioid overdose public health emergency: population based retrospective cohort study. *BMJ* 2020;368:m772. doi: 10.1136/bmj.m772
15. Furlan AD, Harvey AM, Chadha R. Warning from Canada: Latin America, South Africa and India may face an opioid epidemic in the coming years. *J Glob Health* 2020;10:010324. doi: 10.7189/jogh.10.010324
16. Lipari RN, Hughes A. How people obtain the prescription pain relievers they misuse 2017 Available from: https://www.samhsa.gov/data/sites/default/files/report_2686/ShortReport-2686.html. (Accessed on 04/12/2020).
17. Gaither JR, Shabanova V, Leventhal JM. US national trends in pediatric deaths from prescription and illicit opioids, 1999-2016. *JAMA Netw Open* 2018;1:e186558. doi: 10.1001/jamanetworkopen.2018.6558
18. Sandbrink F, Uppal R. The time for opioid stewardship is now. *Jt Comm J Qual Patient Saf* 2019;45:1-2. doi: 10.1016/j.jcjq.2018.10.004