Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

COVID-19 Articles Fast Tracked Articles

Availability of Internationally Controlled Essential Medicines in the COVID-19 Pandemic

Katherine Pettus, PhD, James F. Cleary, MB, BS, FAChPM, Liliana de Lima, MHA, Ebtesam Ahmed, PharmD, and Lukas Radbruch, MD

International Association for Hospice and Palliative Care (K.P., L.d.L.), Houston, Texas; Walther Center for Global Palliative Care (J.F.C.), Indiana University, Indianapolis, Indiana; St. John's University (E.A.), New York, New York, USA; and University Hospital (L.D.), Bonn, Germany

Abstract

Section 2 of the 2019 World Health Organization Model List of Essential Medicines includes opioid analgesics formulations commonly used for the control of pain and respiratory distress, as well as sedative and anxiolytic substances such as midazolam and diazepam. These medicines, essential to palliative care, are regulated under the international drug control conventions overseen by United Nations specialized agencies and treaty bodies and under national drug control laws. Those national laws and regulations directly affect bedside availability of Internationally Controlled Essential Medicines (ICEMs). The complex interaction between national regulatory systems and global supply chains (now impacted by COVID-19 pandemic) directly affects bedside availability of ICEMs and patient care. Despite decades of global civil society advocacy in the United Nations system, ICEMs have remained chronically unavailable, inaccessible, and unaffordable in low- and-middle-income countries, and there are recent reports of shortages in high-income countries as well. The most prevalent symptoms in COVID-19 are breathlessness, cough, drowsiness, anxiety, agitation, and delirium. Frequently used medicines include opioids such as morphine or fentanyl and midazolam, all of them listed as ICEMs. This paper describes the issues related to the lack of availability and limited access to ICEMs during the COVID-19 pandemic in both intensive and palliative care patients in countries of all income levels and makes recommendations for improving access. J Pain Symptom Manage 2020;60:e48–e51. © *2020 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.*

Key Words

Essential medicines, palliative care, morphine, COVID-19, breathlessness

Key Message

Global shortages and stockouts of internationally controlled essential medicines for palliative and critical care in the context of the COVID-19 pandemic call for coordinated strategic interventions to improve access and relieve preventable suffering.

Introduction

Section 2 of the 2019 World Health Organization (WHO) Model List of Essential Medicines includes opioid analgesics formulations commonly used for the control of pain and respiratory distress, as well as sedative and anxiolytic substances such as midazolam and diazepam.[1] As these essential palliative care medicines are regulated under the international drug control conventions overseen by United Nations (UN) specialized agencies and treaty bodies[2] and under national drug control laws, we refer to them as Internationally Controlled Essential Medicines (ICEMs).

The complex interaction between regulatory systems and global supply chains, as well as limited training, affects availability of ICEMs and patient care. The Lancet Commission on Pain and Palliative Care reported that of the total number of tons of morphine-equivalent opioids distributed in the world per year, only 0.1 metric tons is distributed to low-

Address correspondence to: Katherine Pettus, PhD, IAHPC Advocacy Officer, 5535 Memorial Drive, Houston, TX 77007, USA. E-mail: Kpettus@iahpc.com

Accepted for publication: April 30, 2020.

0885-3924/$ - see front matter
https://doi.org/10.1016/j.jpainsymman.2020.04.153

income countries, reflecting a huge abyss is access to relief and resulting in massive, avoidable suffering.[3] While several authors, multilateral agencies, and academia have used other different methods to estimate the actual need versus the reported consumption, these all demonstrate similar inequities in availability and access.[4,5] All these methods have been used for statistical purposes only and not as measures of therapeutic appropriateness.

Despite decades of global civil society advocacy in the UN system, ICEMs have remained chronically unavailable, inaccessible, and unaffordable in low- and middle-income countries. This is in spite of the fact that the WHO and other UN treaty bodies recognize palliative care and pain relief as elements of the right to health.[6] Shortages in high-income countries have recently been reported as well, owing to the increase in demand as a result of the COVID-19 pandemic.[7]

The authors, along with representative of other palliative care organizations and academia, have long advocated for the principle of "balance," which represents the dual obligation of governments to establish a system of control that ensures the adequate availability of controlled substances for medical and scientific purposes, while simultaneously preventing their nonmedical use, diversion and trafficking, two primary goals of the international control system.[8]

This paper describes the issues related to the lack of availability and limited access to ICEMs during the COVID-19 pandemic in both intensive and palliative care patients in countries of all income levels and makes recommendations for improving access.

Systems Level Availability Issues

Palliative care providers in low- and middle-income countries facing the pandemic with already low stocks and fragile importation, production, and supply chains, as well as unduly restrictive regulations controlling access, have contacted the authors with concerns about projected increases in demand for morphine and other ICEMs (Z. Ali, personal communication, April 15, 2020; S.Rana, personal communication, April 24, 2020).

The International Narcotics Control Board (INCB) is the UN Organization charged with monitoring the implementation of the drug control conventions, including global trade in ICEMs. For several years, even before the COVID-19 pandemic, the INCB has reported that the availability of these medicines is low to inadequate[9] and, in response to the pandemic, recently published a press release calling on governments to take the necessary steps to ensure continued access to controlled medicines for pain relief and palliative care and for mental health and neurological conditions by fast-tracking shipments of controlled medicines to health systems and supporting appropriate training of health care providers.[10]

The European Union (EU) Executive Steering Group on Shortages of Medicines Caused by Major Events, which provides strategic leadership for urgent and coordinated action on shortages within the EU in this pandemic, has set up with the pharmaceutical industry a system to fast-track interaction on shortages between industry and the EU Executive Steering Group.[11]

Provider Level Availability Issues

The most prevalent symptoms in COVID-19 are breathlessness, cough, drowsiness, anxiety, agitation, and delirium. Frequently used medicines to treat some of these symptoms include opioids such as morphine, fentanyl, and midazolam. Recently reported data indicate that the median-maximum dose/24 hours for patients with confirmed COVID-19 referred to hospital palliative care are morphine, 10−30 mg; fentanyl, 100−200 mcg; alfentanil, 500−1000 mcg; and midazolam, 10−20 mg.[12] Symptom control for rising cohorts of COVID-19 and other palliative care patients in countries with low or no access to ICEMs will be seriously compromised. Major hospitals in the U.S. and nine university hospitals in Europe have recently reported dangerous shortages of ICEMs and have requested governments to increase procurement (Reuters, personal communication, 2020, https://www.reuters.com/article/us-health-coronavirus-usa-opioids-exclus-idUSKBN21K2ZJ).[13] Several U.S. medical associations sent an urgent letter to the Drug Enforcement Administration reporting that the increase in the number of patients requiring ventilation has resulted in an increase in the demand for several opioids, some of which were already in shortage before the COVID-19 outbreak.[14] They request that supply be rapidly increased to ensure that hospitals can access the medications they need to treat COVID-19 patients. In addition, public health experts and physicians recently asked the governors of U.S. states that still practice the death penalty to release their stockpiled drugs to prioritize the needs and lives of patients.[15] And in the U.K., the National Health Service is reportedly working to increase stocks while at the same time facing many challenges.[16]

Recommendations

1. As palliative care practitioners and global advocates with experience and knowledge about countries with low and inadequate access to

ICEMs, we urge representatives of palliative care associations in all countries currently coping with, or preparing for this or for future pandemics, to contact their health ministries and national Competent Authorities to ensure that they are aware of the INCB recommendations mentioned in its press release cited previously. These include ensuring the maintenance of sufficient buffer stocks and using simplified control procedures for the export, transportation, and provision of ICEMs.

2. We urge palliative care associations to consider recommending their national competent authorities to utilize pooled procurement mechanisms such as the Pan American Health Organization Strategic Fund, the Pharmaceutical Procurement Service in the Organization of Eastern Caribbean States, the Gulf Corporation Council, and UNICEF and to resupply and build buffer stocks, as the markets will take advantage of increased demand to raise prices.
3. The Lancet Commission on Pain and Palliative Care developed and costed an Essential Package that is the minimum a health system, however resource-constrained, should make universally accessible. The Essential Package includes medications for safe and effective palliative care and pain relief for both adults and children largely based on the WHO Model List. Its medicines and equipment, including morphine and diazepam, can all be safely prescribed or administered in a primary care setting where health professionals have received basic training in palliative care.
4. As many frontline health workers will be unfamiliar with the use of opioids and benzodiazepines in the context of the pandemic, we recommend accelerated clinician training, including online, for COVID-19–related symptom control. Training specialist nurses to prescribe and deliver opioids to palliative care patients in all home care settings (as in Uganda and Rwanda) aligns with WHO calls to invest in nurses in this International Year of the Nurse and Midwife.

Conclusion

The Human Rights Council, the World Health Assembly, and some regional treaty bodies recognize palliative care and pain relief as elements of the right to health.[11] Governments have a minimum core obligation to protect this right with immediate effect, even in the face of a disastrous humanitarian emergency such as the COVID-19 pandemic. Global health experts describe lack of access to essential palliative care medicines as a critical public health issue, and opioids, in particular morphine, as essential for the relief of severe health-related suffering. The additional COVID-19 burden of health-related suffering only underscores the government obligation to take a balanced approach to the regulation of internationally controlled substances, and to make strategic interventions, in partnership with clinical associations, to ensure the availability, accessibility, and affordability of essential medicines for primary, intensive, and palliative care.

Disclosures and Acknowledgments

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. World Health Organization Model List of Essential Medicines, 21st List, 2019. Geneva: World Health Organization, 2019. Licence: CC BY-NC-SA 3.0 IGO. Available from https://apps.who.int/iris/bitstream/handle/10665/325771/WHO-MVP-EMP-IAU-2019.06-eng.pdf?ua=1. Accessed April 29, 2020.

2. United Nations Office on Drugs and Crime. Single convention on narcotic drugs New York: United Nations. Available from https://www.unodc.org/pdf/convention_1961_en.pdf 1961. Accessed April 29, 2020.

3. Knaul FM, Farmer PE, Krakauer EL, et al. Alleviating the access abyss in palliative care and pain relief—an imperative of universal health coverage: the Lancet Commission report. Lancet 2018;391:1391–1454.

4. Foley KM, Wagner JL, Joranson DE, Gelband H. Pain control for people with cancer and AIDS. In: Jamison DT, Breman JG, Measham AR, et al, eds. Disease Control Priorities in Developing Countries, 2nd edn Washington, DC: The International Bank for Reconstruction and Development, The World Bank; New York, NY: Oxford University Press, 2006.

5. Scholten WK, Christensen AE, Olesen AE, Drewes AM. Quantifying the adequacy of opioid analgesic consumption globally: an updated method and early findings. Am J Public Health 2019;109:52–57.

6. Lohman D, Schleifer R, Amon JJ. Access to pain treatment as a human right. BMC Med 2010;8:8.

7. France 24. Medicine shortage looms over coronavirus-hit Europe. Available from https://www.france24.com/en/20200407-medicine-shortage-looms-over-coronavirus-hit-europe. Accessed April 29, 2020.

8. Pettus K, De Lima L, Maurer M, Husain A, Connor S, Torode J. Ensuring and restoring balance on access to controlled substances for medical and scientific purposes: joint statement from palliative care organizations. J Pain Palliat Care Pharmacother 2018;32:124–128.

9. International Narcotics Control Board (INCB): Availability of Internationally Controlled Drugs: Ensuring Adequate Access for Medical and Scientific Purposes. New York, NY: United Nations, 2016.

10. INCB Press Release. The International Narcotics Control Board calls on governments to ensure continued access to controlled medicines for pain relief and palliative care and for mental health and neurological conditions during the COVID-19 pandemic. 2020. Available from https://www.incb.org/incb/en/news/press-releases/2020/incb-calls-on-governments-to-ensure-continued-access-to-controlled-medicines-during-the-covid-19-pandemic.html. Accessed April 24, 2020.

11. European Medicines Agency. Press Release. EU authorities agree new measures to support availability of medicines used in the COVID-19 pandemic. 2020. Available from https://www.ema.europa.eu/en/news/eu-authorities-agree-new-measures-support-availability-medicines-used-covid-19-pandemic. Accessed April 29, 2020.

12. Lovell N, Maddocks M, Etkind SN, et al. Characteristics, symptom management and outcomes of 101 patients with COVID-19 referred for hospital palliative care. J Pain Symptom Manage. 2020. Available from https://www.jpsmjournal.com/article/S0885-3924(20)30211-6/fulltext. Accessed April 29, 2020.

13. European University Hospital Alliance. University hospitals urgently call for more European collaboration to prevent drug shortages. 2020. Available from http://www.euhalliance.eu/2020/03/31/university-hospitals-urgently-call-for-more-european-collaboration-to-prevent-drug-shortages/. Accessed April 29, 2020.

14. American Society of Health System Pharmacists. RE: request to immediately increase allocation of controlled substances to combat COVID-19. 2020. Available from https://www.ashp.org/-/media/assets/advocacy-issues/docs/GRD-DEA-Letter-CII. Accessed April 20, 2020.

15. Business Insider. Doctors are asking states to use their lethal-injection drugs to treat patients with COVID-19, instead. 2020. Available from https://www.businessinsider.com/doctors-ask-to-use-death-penalty-drugs-for-covid-19-2020-4. Accessed April 15, 2020.

16. British Broadcasting Service. Coronavirus: 'Local shortages' of intensive care drugs. 2020. Available from https://www.bbc.com/news/health-52150861. Accessed April 12, 2020.