Caring for patients with pain during the COVID-19 pandemic: Consensus recommendations from an international expert panel

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Summary

Chronic pain causes significant suffering, limitation of daily activities and reduced quality of life. Infection from COVID-19 is responsible for an ongoing pandemic that causes severe acute respiratory syndrome, leading to systemic complications and death. Led by the World Health Organization, healthcare systems across the world are engaged in limiting the spread of infection. As a result all elective surgeries, procedures, and patient visits, including pain management services, have been postponed or cancelled. This has impacted the care of chronic pain patients. Most are elderly with multiple comorbidities, which puts them at risk of COVID-19 infection. Important considerations that need to be recognised during this pandemic for chronic pain patients include: ensuring continuity of care and pain medications, especially opioids; use of telemedicine; maintaining biopsychosocial management; use of anti-inflammatory drugs; use of steroids; and prioritising necessary procedural visits. There are no guidelines to inform physicians and healthcare providers engaged in caring for patients with pain during this period of crisis. We assembled an expert panel of pain physicians, psychologists and researchers from North America and Europe to formulate recommendations to guide practice. As the COVID-19 situation continues to evolve rapidly, these recommendations are based on the best available evidence and expert opinion at this present time and may need adapting to local workplace policies.

Introduction

Chronic pain is a prevalent condition worldwide and causes suffering, limitation of daily activities and reduced quality of life [1-3]. According to the United States 2012 National Health Interview Survey, 126.1 million adults reported some pain in the previous 3 months, with 25.3 million adults (11.2%) suffering from daily chronic pain and 14.4 million (6.3%) reporting "a lot" of pain most days or every day [4]. In Europe, almost one in five individuals report having moderate or severe chronic pain, and in the UK the prevalence of moderate to severely disabling chronic pain is estimated to range between 10.4% and 14.3% [5,6]. Most chronic pain conditions occur in the elderly and are musculoskeletal in nature, such as low back, neck and joint pain. These contribute to the largest number of years lived with disability [7, 8]. In the UK, over 50% of the elderly population reported that chronic pain was the most important factor affecting their quality of life [9]. Chronic pain patients often suffer with co-existing comorbidities [5, 6]. In a large cross-sectional database study involving 1,751,841 people, pain was the most common co-existing condition among four common disease states: coronary artery disease; diabetes; cancer; and chronic obstructive pulmonary disease [10]. Adequate management of chronic pain is not only a moral and ethical imperative, but also mitigates against subsequent physical and psychological complications [7, 11,12].

Novel COVID-19 infection can cause severe acute respiratory syndrome (SARS) and death. It is responsible for the ongoing pandemic and on 1 April 2020 there were 883,225 confirmed cases with 44,156 deaths globally (https://coronavirus.jhu.edu/map.html). Healthcare systems across the world have been faced with the challenge of controlling the infection. This has encompassed decisions such as postponing or cancelling all elective surgery procedures and patient visits, including suspension of many pain management services. The care of chronic pain patients has been significantly impacted. Many of these patients have complex needs and urgently require interventions to stave off potentially life-threatening conditions or are facing opioid withdrawal [13, 14].

We performed a literature search that did not identify any document or guidelines for the management of chronic pain patients, either during the current crisis or at the time of previous epidemic or pandemic outbreaks, including SARS-2003. In response to the urgent need, an expert panel consisting of healthcare providers and pain researchers from North America and Europe were brought together to formulate practice

recommendations to help physicians and health providers continue to care for their chronic pain patients [15].

Methods

The first and senior authors (HS, SN) identified and invited physicians and psychologists to participate in the expert panel for framing these recommendations. All panel members were engaged in caring for patients with chronic pain, had experience and training in clinical research, and had previously participated in the formulation of guideline statements and practice recommendations. We conducted a systematic search of the Medline database for terms referring to 'COVID-19' [*Coronavirus Infections/ or *SARS Virus/ or SARS.mp. or *Coronavirus/ or *Severe Acute Respiratory Syndrome/COVID-19] and 'chronic pain/pain' to inform this process. Based on the present pathophysiological understanding of COVID-19 and potential practice implications based on either the 'pathology' or 'nature of chronic pain treatment', the panel developed themes upon which to formulate our practice recommendations. During the review process of this article, one topical review by Eccleson et al. was published online ahead of print on e-health pain management services and has been used to inform this section of our recommendations [16].

Considerations and recommendations

General considerations for patients with chronic pain and COVID-19 infection

Chronic pain, the immune response, opioid therapy and COVID-19

Pain and the immune system have a close relationship. Chronic pain exerts complex effects on the immune system, including immunosuppression in some individuals [17]. Immune cells and their products have a role in both inflammatory and neuropathic pain [18]. Significant immune system changes occur in patients with COVID-19 [19], with a higher risk of mortality observed in the elderly alongside individuals who have hypertension; diabetes; coronary artery disease; and chronic lung disease [20]. Although the mortality risk in cancer patients is unclear, early reports suggest a higher risk [21]. The association of comorbidities, old age and chronic pain increases the risk of immune suppression and subsequent COVID-19 infection. Opioids can have serious adverse effects including endocrine changes and the potential to suppress the immune system [22-24], however some suggest there could be beneficial effects [25]. Opioids can interfere with the innate and acquired immune response, act on the hypothalamic-pituitary-adrenal axis and the autonomic nervous system [23, 25, 26]. Higher doses and longer duration of therapy are associated with greater endocrine

abnormalities [26]. Individual opioids differ in their effect on the immune system [27, 28], however morphine and fentanyl have been observed to be the most immunosuppressive [23, 29]. Based on available data, buprenorphine appears to be the safest to use in immunocompromised or elderly patients susceptible to infection [24]. The clinical relevance of these observations for individual opioids is unclear; however, observational studies indicate the potential for an increase in incidence and severity of infections in patients on opioids [30, 31]. It is therefore appropriate to consider that chronic pain patients on opioids could potentially be more susceptible to COVID-19 and other secondary infections. Furthermore, the potential for respiratory depression is higher in patients using fentanyl patches, as fever enhances absorption [32, 33].

Steroids in chronic pain and COVID-19

Chronic pain patients may take oral steroids or receive steroid injections for a wide variety of musculoskeletal conditions [34]. Patients who receive steroids have the potential for secondary adrenal insufficiency and an altered immune response [35], along with several other adverse effects including myopathy and osteoporosis [36]. Among available steroids, the depot form of methylprednisolone is most frequently used for chronic pain. Secondary adrenal insufficiency with 80 mg methylprednisolone can last up to 4 weeks, however for a small proportion it could be up to 2 months [37]. Also, a recent trial evaluating epidural steroid injections noted that the duration of immune suppression could be less when using dexamethasone and betamethasone [38]. In a large retrospective study, the injection of corticosteroids into joints was shown to be associated with a higher risk of influenza [39]. Although the pathophysiology of COVID-19 infection suggests an exaggerated immune response, steroid use in COVID-19 patients is only recommended in those with refractory shock and this is based on low quality evidence [40]. During the 2003 SARS pandemic, arthralgias involving large joints were commonly observed during the recovery phase and many patients were treated with steroid therapy [41]. Those patients receiving higher doses and for longer treatment durations were more likely to develop osteonecrosis [42]. In view of these considerations, we feel that any new therapy that may influence the COVID-19 disease course should be discussed with the treating infectious disease physician. It should also be recognised that steroids are routinely used in many procedures despite an absence of evidence supporting the practice [43, 44]. The Faculty of Pain Medicine of the Royal College of Anaesthetists' position statement urges caution on the safety of steroids injected during the current COVID-19 pandemic [45].

Psychological, physical, and social functions in chronic pain and COVID-19

The pain neuromatrix model integrates multiple inputs inclusive of: genetically informed synaptic architecture; sensory and/or afferent processing; cognitive; affective; motivational; immunoendocrine; and autonomic nervous system [46]. Chronic pain patients have higher prevalence of anxiety, depression, catastrophising, and suicidal ideation [47]. This may worsen during a period of crisis. Chronic pain patients also experience: social isolation; stigma; loss of personal identity; and financial stress. These all negatively impact on psychological health, social circumstances, and ongoing pain, which are likely further exacerbated during a pandemic. It is imperative these issues are addressed during a pandemic and this is best achieved by using a biopsychosocial model of pain management.

Therapeutic considerations and recommendations for chronic pain during the COVID-19 pandemic

A summary of therapeutic considerations and recommendations for chronic pain management during the COVID-19 pandemic is displayed in Table 1.

In-person visits

In-person visits during a pandemic expose patients and others to the risk of infection, hence all elective surgeries and procedures should be postponed or cancelled. Furthermore, conserving resources is important as health systems already strained by diminished production capacity, travel and shipping restrictions, must be prepared for further casualties. Whenever possible, telemedicine should be considered. However there are certain clinical scenarios that necessitate in-person visits, including procedures. Categorising pain procedures as elective, urgent and emergent is, in many cases, subjective. The American College of Surgeons provides some direction, noting that both medical and logistical contexts must be considered on a case-by-case basis [48]. We provide examples of urgent and semi-urgent pain procedures later in these recommendations. It is important that, for planned visits, patients and personnel are screened for symptoms of COVID-19. Individuals with a high risk of having COVID-19 should potentially undergo diagnostic testing prior to in-person visits, if available as per local testing protocols, or be seen after symptoms subside. This needs to be undertaken, recognising the limited sensitivity of detecting infection from the presently available tests and the feasibility that a patient may have become infected after a previous negative test. Once the community spread of infection becomes significant, all cases may be presumed to be COVID-19 positive.

Clinical settings must adhere to physical distancing recommendations and other regulations as noted by the local health authorities.

Telemedicine

Telehealth and telemedicine are related terms that define telecommunication and the electronic exchange of information through a variety of platforms. This includes such services as telehealth visits, virtual encounters, and e-visits. Randomised controlled trials have demonstrated high levels of: patient satisfaction; comfort; convenience; and acceptance for telehealth services including for patients requiring post procedural follow-up and with chronic disease states [49, 50]. There is an enormous potential for cost reduction and time savings with telehealth services [50]. In any pandemic, it is important that physicians continue to provide medical services in a safe and effective way and telehealth can help meet these needs. Preliminary data exists regarding the effectiveness for psychotherapies delivered on internet-based platforms such as smartphone apps and whilst these may be beneficial during public health crises, there are recognised limitations such as a lack of culturally tailored information and testing in individuals with persistent pain [51]. For telemedicine, technology should be selected that is easy to use and maintains the confidentiality of personal health information. Healthcare providers must be aware of the licensure requirements in their area of practice and recognise that many of the waivers and alterations in regulations that have occurred during the COVID-19 pandemic will be reversed once the pandemic resolves. Therefore continuously monitoring these changes ensures practice remains compliant with privacy and data protection legislation. During the COVID-19 pandemic the US and the UK, under special billing provisions, have reduced or eliminated pre-existing barriers to telehealth including the requirement to use a Health Insurance Portability and Accountability Act compliant platform [52]. Similarly, in Canada, the provincial Ministries of Health have relaxed the regulations around the use of telemedicine. An example from the UK is the adoption of Microsoft Teams by NHS digital for roll-out to NHS staff in England and Wales to facilitate working from home and streamlining communication between patients and medical professionals. Microsoft Teams is currently being integrated by NHS digital into its security platform and was made available to all NHS email users from 20 March 2020 [53]. Whilst outside the scope of these recommendations, the review by Eccleston et al. outlines more details regarding considerations for rapid integration of remotely supported pain management services [16].

Biopsychosocial management of pain

It is imperative for patients with pain to have access to trained psychologists, physical therapists and social workers to address the psychological and physical impact of their pain and other co-morbidities. Social distancing precautions in response to this pandemic pose unique challenges for multidisciplinary care. However advances in telemedicine outlined above, including interactive audio-video platforms, provide an opportunity to comprehensively assess patients and deliver virtual biopsychosocial and physical care that can be supplemented with in-person consultations at a later stage. Multidisciplinary pain self-management programs and strategies for self-management of pain can and are being delivered online [54]. Individual studies report excellent outcomes [55] and a systematic review of internet interventions for chronic pain found that those based on cognitive behavioural therapy can be efficacious [56]. Examples of interventions that can be delivered effectively over the internet for patients with chronic pain include: managing stress; addressing sleep disturbances; teaching mindfulness practices; cognitive strategies; pacing activities; social support programs; simple physical exercises; and observing a healthy lifestyle.

Opioid prescriptions

Guidelines on opioid prescribing already exist to help minimise the harm from their application in chronic pain management [57, 58]. Broadly these considerations include: the need to d**e**termine when to initiate or continue opioids for chronic pain; appropriate opioid selection, dosage, duration, follow-up and discontinuation; and assessment of risks and harms of opioid use. Ideally, changes to opioid prescriptions should be made only after in-person careful evaluation of ongoing treatment, which includes a history and physical examination. However during the current COVID-19 health emergency, physicians may not be able to adhere to such a practice. In view of this, many countries have made changes to their policy on controlled substances. Such temporary allowances include enabling pharmacists to: extend prescriptions for a limited period of time; act on a verbal order by a physician for refill of controlled substances; deliver prescriptions of controlled substances to patient's homes or other locations of self-isolation; and permitting registered practitioners to prescribe opioids without an in-person medical evaluation as long as some necessary conditions are met [59, 60]. Although controlled substances may be provided without a direct in-person medical evaluation, it is still recommended that opioid safe prescribing procedures be performed including: assessing for adequate response; adverse events; aberrant behaviours; function; and quality of life

improvements [61]. Pill counts can still be performed and informed consent obtained via video communication. Patients should continue to be educated on the risks and benefits of opioids, naloxone should be prescribed when appropriate and the review of medical history and medications that impact opioid prescribing should be continued. We must be cognisant that psychological stress may exacerbate pain leading to greater opioid requirements and that patients may use medically-prescribed opioids for non pain related conditions such as: anxiety; depression; and insomnia despite evidence that in the long-term they can worsen these conditions [62]. Therefore any significant, sustained increase in opioid dose requires an in-person evaluation.

Anti-inflammatory drugs use for chronic pain

A substantial number of chronic pain patients use non-steroidal anti-inflammatory drugs (NSAIDS) for their pain control [63]. Non-steroidal anti-inflammatory drugs exert their analgesic effect primarily through peripheral inhibition of prostaglandin synthesis by acting on the cyclo-oxygenase enzyme, although other peripheral and central mechanisms of analgesic action exist. There are two structurally distinct forms of the cyclo-oxygenase enzyme (COX-1 and COX-2) [64]. COX-1 is constitutively expressed in normal cells, while COX-2 is induced in inflammatory cells. One of the mechanisms underlying antihypertensive actions of angiotensin converting enzyme (ACE) inhibitors involves the kinin-prostaglandin system [65]. An observation by the current French health minister had initially prompted some physicians to advise against the use of Ibuprofen or other NSAIDS, based on the assumption that its use may increase the severity of COVID-19 disease [66]. This was based on the assumption that NSAIDS could increase the levels of ACE. However this has not been substantiated by other any reports and multiple regulatory bodies have since refuted this assertion [67-69]. However NSAIDS may mask early symptoms of the disease such as fever and myalgias.

Procedural precautions and considerations

For patients needing procedures, all considerations and recommendations mentioned above for in-patient visits are applicable. Several guidelines from various medical organisations have emphasised the importance of personal protective equipment (PPE) [15]. One must be also aware of local policies on precautions and equipment. Additional aspects related to procedural precautions that should be highlighted include the recommendation that all procedures should be carried out by an experienced person. These procedures do not lead to aerosol generation and therefore personal protective equipment that adheres to geographical

recommendations for contact and droplet precautions is generally considered sufficient. Additional protection for consideration may be made on a case-to-case basis depending upon local availability. Furthermore any equipment such as the ultrasound machine and intrathecal (ITP) equipment or programmer, should be protected from contamination using an appropriate cover. In addition it is important to ensure that the needed medications (for example ITP refill) and equipment are ready and transported in a fully covered plastic bag, with the bag and its medications handled with sterile gloves in a clean area.

Examples of scenarios that represent "urgent" pain patient procedures during the COVID-19 pandemic include ITP refills or malfunction and neuromodulation infection or malfunction. ITP refills necessitate close proximity (< 1 metre) between the operator and patient. For patients on intrathecal baclofen, an abrupt reduction in gamma-aminobutyric acid agonist activity in the central nervous system following abrupt cessation of baclofen infusion can lead to a catastrophic intrathecal baclofen withdrawal syndrome [70]. This usually evolves over 1 to 3 days but may become fulminant if not recognised and treated promptly. The best management strategy is resuming the intrathecal infusion as soon as possible. Other supportive measures including high-dose benzodiazepine intravenous infusion or baclofen may be lifesaving before intrathecal baclofen therapy can be resumed, though acute withdrawal may still occur with high-dose oral baclofen [71]. Although clonidine is not currently approved as intrathecal therapy [72], it is often used in clinical practice and the Polyanalgesic Consensus Conference panel recommendations for intrathecal drug delivery assign a grade B evidence for its use in neuropathic and nociceptive pain [73]. Intrathecal clonidine withdrawal can result in hypertensive crisis and cardiomyopathy [74]. It should be noted that there are no reported withdrawal symptoms when intrathecal ziconotide as a sole therapy was discontinued [73]. In general for all patients at high risk of intrathecal drug withdrawal should be identified and educated pre-emptively. Pain physicians should be familiar with the emergency treatment of intrathecal medication withdrawal symptoms and may need to consider higher drug concentrations for the period of the pandemic in order to reduce ITP refill visits. Although the use of some highly concentrated intrathecal medications can be associated with granuloma formation (inflammatory mass) at the tip of the catheter, this usually occurs with long-term infusions and needs to be weighed against the risk of infection acquired as a result of repeated hospital and practice visits. For more details about the recommended doses and concentrations for different intrathecal medications, practitioners are encouraged to refer to the Polyanalgesic Consensus Conference recommendations [73].

Neuromodulator systems used to treat chronic pain often include an implanted power generator connected to a stimulating "lead" in the dorsal epidural or in the perineural space. Being elective procedures, new trials or implants must be avoided during pandemics. In patients who have recently undergone an implant procedure, any procedure-related complications should initially be evaluated over telemedicine. In cases of unwanted paraesthesias, patients can be asked to switch off the stimulation using the external remote controller and consider managing their pain with medications alongside other biopsychosocial strategies. However certain issues may require in-person evaluation and management and the need for these must be considered on a case-by-case basis, with shared decision-making. Examples of issues necessitating an in-person evaluation may include: suspected infection of the implanted power generator or lead; unintended loss or change of programming resulting in severe unmanageable pain; and the need for an MRI for an unrelated indication such as risk of stroke or brain injury. Depending on whether the infection is superficial or deep, device explant may be warranted and should be performed as soon as possible [73]. Although not urgent, some situations may warrant a careful evaluation of individual risks and benefits so that a patient may be considered for an in-patient visit. These circumstances meet the criteria of semi-urgent" pain patient visits or procedures during the COVID-19 pandemic. Decision making on such occasions should be based on factors such as: the acuteness of the condition; potential for significant morbidity without intervention; the need for additional resources (such as monitoring for ketamine infusions); the likelihood of benefit; and the potential for the patient to use emergency services. Overall, the goals must be to avoid: deterioration of function; reliance on opioids; or emergency service visits that increase risk of exposure. Such procedural scenarios may include, but not limited to, the following: intractable cancer pain; acute herpes zoster or subacute, intractable post-herpetic neuralgia; acute herniated disc and/or worsening lumbar radiculopathy; intractable trigeminal neuralgia; early complex regional pain syndrome; acute cluster headaches and other intractable headache conditions; and other intractable medically resistant pain syndromes.

Conclusion

Chronic pain causes significant suffering, leading to a reduced quality of life. During the COVID-19 pandemic there is a risk of chronic pain patients failing to receive important treatment due to reallocation of resources and reduction in services, to both limit the spread of infection and to deal with saving lives of those infected.

Chronic pain patients may also be at increased risk of COVID-19 due to multiple factors. Important considerations for healthcare professionals caring for those with chronic pain are to: ensure continuity of care and pain medications; utilisation of telemedicine; maintaining biopsychosocial management approach; evaluation and safe conduct of urgent and semi-urgent procedures to avoid morbidity in chronic pain patients; and the need to modify ongoing therapies to decrease COVID-19 risk. These recommendations have been developed to aid healthcare professionals and we acknowledge these are not guidelines. However with COVID-19 being a rapidly evolving situation they represent summaries of the best available evidence and expert opinion at this present time and may need adapting to local workplace policies.

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Table 1: Summary of therapeutic considerations and recommendations for chronic pain management during the COVID-19 pandemic

In-patient visits

- Any elective in-person patient visits or meetings should be suspended.
- No elective pain procedures should be performed, excepting specific semi-urgent procedures.

Use of telemedicine

- Use telemedicine as the first approach and exclusively in most cases.
- Ensure adherence to the subscribed needs of telemedicine required by individual state or country of practice.

Biopsychosocial management of pain

- Telemedicine platforms are available to engage in multidisciplinary interactions.
- Whenever possible, online self-management programmes that integrate components of exercise, sleep hygiene, pacing and healthy lifestyle should be considered.
- Multi-disciplinary therapies could be helpful in overcoming increased opioids needs and / or procedures during the pandemic.

Prescribing opioids

- Use telemedicine to evaluate, initiate, and continue opioid prescriptions.
- Ensure all patients receive their appropriate prescription of opioids to avoid withdrawal.
- Naloxone education and prescription for high-risk patients.
- Inform patients of the risks and impact of long-term opioid therapy on the immune system.
- Communicate with other healthcare providers in the patients' circle-of-care including family physicians, pharmacists and nurses.

Principles for using NSAIDS

- We recommend all patients prescribed or who use non-steroidal anti-inflammatory drugs on a regular basis to continue their use, whilst monitoring for adverse effects.
- We recommend educating patients on non-steroidal anti-inflammatory drugs that any mild fever or new myalgia should be promptly reported.

Intrathecal drug delivery systems

- Avoid insertion of any new ITP except for highly selected cancer pain cases where the benefit is

considered to outweigh the risk. Consider proceeding straight to an implant, without a trial, for appropriate candidates.

- In COVID-19 suspected or symptomatic patients, consider the possibility of delaying the refill if the low reservoir alarm date allows a time frame until the patient has served a recommended self-isolation period.
- Following a thorough discussion with the patient, consider: the risk benefit balance of discontinuing ITP therapy in high risk patients on ziconotide therapy where no withdrawal effects have been reported; and the risk benefit ratio of using higher drug concentrations for the period of the pandemic in order to reduce ITP refill related visits.

Neurostimulator issues

- Avoid any new trials or implants.
- Use telemedicine as much as possible to resolve patient concerns. An audiovisual interview makes it easier to evaluate or troubleshoot most issues.

Principles for semi-urgent visits/procedures

- Comprehensive evaluation required and the need to help patients make informed decisions.
- Use telemedicine to evaluate the patient, triage the urgency, and make suitable arrangements for treatment. This will minimise delay and prevent unnecessary visits.

Figure 1: Chronic pain patient care during the COVID-19 pandemic

Figure 1: Flow chart summarizing chronic pain patient care during the COVID-19 pandemic