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Children’s Cancer Pain in a World of the Opioid Epidemic: Challenges and Opportunities

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Abstract

The opioid crisis in the United States has grown at an alarming rate. Children with cancer are at high risk for pain and opioids are a first-line treatment in this population. Accordingly, there is an urgent need to optimize pain management in children with cancer without contributing to the opioid crisis. This report details opportunities for this optimization, including clinical practice guidelines, comprehensive approaches to pain management, mobile health, and telemedicine. It is vital to balance appropriate use of analgesics with efforts to prevent misuse in order to reduce unnecessary suffering and minimize unintended harms.

The Problem: Opioid Epidemic

The opioid crisis in the United States (U.S.) has grown at an alarming rate, with a 200% increase in opioid-related overdose deaths since 2000.¹ The roots of the opioid epidemic in the U.S. are multifactorial and largely stem from the routine use of opioid medications to treat acute pain starting in the 1980's. This was followed by a shift in the treatment of chronic pain in the 1990's from cognitive-behavioral therapy as the primary intervention to opioids.^{2,3} The shift to managing chronic pain with opioids primarily reflects a significant increase in rates of disabling chronic pain, patient expectations for a "quick fix," and a medical system that changed reimbursement strategies to prioritize the use of simplistic treatment approaches for complex health problems.^{2,4} Moreover, a campaign initiated by the American Pain Society in the 1990's to include pain as the "fifth vital sign" subsequently led to the adoption of routine measurement of pain severity in health settings using a numeric rating scale as well as opioid administration based upon patient pain scores.⁵ Accordingly, the U.S. is in the midst of an epidemic of opioid misuse, addiction, and overdose.⁴

The opioid epidemic extends to the pediatric population, with evidence indicating that deaths from drug overdose in adolescents more than doubled from 1999 to 2007 and have continued to rise, with the majority of deaths due to opioid-related drug overdoses.⁶ Most adolescents who abuse opioids began with a prescription opioid⁷ and many transitions that occur during adolescence, including neurobiological, behavioral, and psychological changes can leave adolescents vulnerable to both chronic pain and drug use.^{8,9} Thus, adolescents are a particularly vulnerable population in the context of the opioid epidemic.

There have been many policy changes and trends over the past decade in an effort to combat the opioid crisis. These include guidelines for providers who prescribe opioids, prescription-drug

monitoring programs, and investment into prevention and treatment programs.⁷ In addition, the National Institutes of Health (NIH) launched a new scientific initiative to fund research to help combat the opioid crisis, focusing on prevention and intervention efforts to reduce mortality, identification of novel interventions to treat opioid addiction, and identification of safe non-addictive alternatives to the management of chronic pain.¹⁰ However, the overwhelming majority of these programs are focused on adult populations.

The Problem: Pain in Children with Cancer

Every year over 12,000 children will be diagnosed with cancer in the United States¹¹ and the majority of these children will experience pain, which is one of the most distressing symptoms reported in this population.¹² In fact, after diagnosis with leukemia, the most common childhood cancer diagnosis, 100% of children reported pain over the course of the first year.¹³ Pain can be related to the underlying disease; however, for most children the pain they experience is iatrogenic, or caused by the treatment itself.^{14,15} Parents have identified pain as the “most problematic” symptom children experience during cancer treatment¹⁶ and children have described pain as the most distressing and frightening aspect of their cancer experience.^{17,18} Unfortunately, evidence suggests that cancer pain and symptoms are seriously under treated in most children, particularly in the home setting.^{13,19–23} Pain is not just an issue at diagnosis and during treatment for cancer. Survivors of cancer are also at high risk for the experience of chronic pain given the effects of treatments, which include surgery, radiation, and cytotoxic medications.²⁴

With changes to the delivery of healthcare that have occurred, the majority of children now receive cancer treatment on an outpatient basis.²⁵ This phenomenon is not limited to oncology. In fact, the majority of healthcare has transitioned to an ambulatory setting, which has increased patient and family satisfaction,^{26,27} but has also shifted healthcare provider responsibility for pain

and symptom management to parents and caregivers. Research by our group and others has shown that parents significantly under treat children's pain in the home setting,²⁸ despite raising pain as a major problem during children's cancer treatment.¹⁶ One parent-related factor that has been identified in the literature as a potential barrier to children's pain management at home is parent attitudes regarding analgesic use for children. For example, parents who endorse concerns about side effects of analgesics and/or report poor understanding of pain management provide less analgesic medication for cancer-related pain that children experience in the home setting.²⁹ Unfortunately, these misconceptions are prevalent in parents of children with cancer.³⁰

Parents are tasked with managing chronic pain in patients with cancer, but are not educated in symptom assessment or use of pharmacological and non-pharmacological interventions. In fact, there are very few documented interventions focused on parents and caregivers of patients with cancer.³¹ With regard to pharmacologic strategies, related literature indicates that parents report using 'trial and error' to administer analgesics to children following surgery.³² Considering the myriad tasks related to pharmacologic pain management, including determining what medication may be appropriate, when and how to administer the medication, the appropriate dose to use, determining whether the medication is effective, and monitoring side effects,³³ a 'trial and error' approach is particularly concerning. Finally, there are a number of effective non-pharmacological strategies used in pain management, including distraction, mindfulness, or other complementary approaches. However, these strategies are not often introduced to parents,³¹ and when they are, they appear to be administered haphazardly and with varying degrees of success.³⁴

Unfortunately, data regarding opioid use and adherence in patients with cancer is extremely limited because cancer patients are excluded from almost all guidelines, treatment protocols, and legislation (both at the state and federal level) focused on the use of opioids. In fact, the Centers

for Disease Control and Prevention (CDC) released guidelines for opioid prescribing for chronic pain in 2016 that specifically did not include cancer patients due to concerns regarding the complexity of cancer-related pain as well as beliefs that opioid misuse was not an issue in patients with cancer.²⁴ Moreover, the World Health Organization and other national guidelines have supported the use of opioids in the cancer population.^{35,36} The support for opioid use in cancer patients is likely the result of both a perception of the lack of abuse concern and clinical need for opioid use in the treatment of cancer-related pain. Opioids are often considered to be first-line analgesics in the oncology setting due to concerns that the use of over-the-counter pain medications, including acetaminophen and non-steroidal anti-inflammatory medications, may mask important clinical symptoms such as fever, which can indicate a medical emergency.³⁷ In fact, the overwhelming majority of children with cancer referred for neuropathic pain in the outpatient setting were using opioids as either a single agent or in combination with other analgesics.³⁸ Finally, little is known about patterns of opioid use and misuse in the oncology setting because patients with cancer are also excluded from clinical trials that focus on chronic pain and analgesic use.

The Challenge: Optimizing Cancer Pain Management for Children in the Context of the Opioid Crisis

The question arises, then, how can we optimize the management of pain in children with cancer without contributing to the opioid crisis? Given that children with cancer are at high risk for the experience of recurrent pain, both during treatment and throughout survivorship, and that parents are responsible for the majority of children's cancer pain management, it is imperative to equip parents and caregivers with evidence-based strategies to more appropriately manage pain. These strategies should allow for symptom management at home without placing children,

particularly adolescents, at risk for opioid misuse. Unfortunately, there is a dearth of research regarding a best practice model in this context.

Clinical Practice Guidelines

As noted above, current guidelines for opioid prescribing for chronic pain exclude cancer patients. Additionally, such guidelines fail to include integrative approaches to pain management, such as complementary and alternative medicine (CAM). In addition, cancer-specific guidelines, such as those by the American Society of Clinical Oncologists (ASCO) and the National Comprehensive Cancer Network (NCCN) focus solely on adults and survivors.^{36,39} The lack of guidelines for pediatric patients with cancer should be a call to clinicians, investigators, and professional associations to come together to develop clear guidelines for management of cancer pain in children and adolescents. Opioid stewardship programs that involve a collaborative effort of multidisciplinary stakeholders have shown promise in optimizing pain management.⁴⁰ One healthcare provider often not included in the management of cancer-related pain is the clinical pharmacist. Pharmacists can play a vital role in optimizing pain management and improving medication safety through customizing analgesic medications to the needs of the patient and clinical context and providing necessary patient education.⁴¹

The Need for a Comprehensive Approach to Pain Management

A multidisciplinary approach to pain management is needed, particularly in light of the opioid crisis. That is, pain management should include a broad repertoire of pharmacologic and non-pharmacologic strategies. Regarding the latter, the incorporation of integrative medicine (IM) modalities with conventional strategies is a means of comprehensive, multidisciplinary treatment.⁴² IM strategies include evidence-based strategies for pain such as guided imagery, biofeedback, and acupuncture. Although reports suggest the use of these strategies by pediatric

oncology patients is high,⁴³ efficacy data for some IM strategies is lacking and long-term effectiveness has not been well established, particularly in the pediatric population.⁴⁴ This suggests a need for rigorous evaluation of the safety and effectiveness of IM interventions, particularly in the context of pain management for pediatric cancer patients.

Moreover, given the increasing responsibility of parents and caregivers in the role of pain management, efforts targeting appropriate pain assessment are needed. Despite pain as a major concern for children and parents, pain assessment throughout cancer treatment is not performed systematically.⁴⁵ Moreover it has been documented that parents of children with cancer report misconceptions about how children express pain, including beliefs that children will always report when they are in pain and children who are playing or otherwise engaged cannot be in pain.³⁰ Further, there are no validated parental assessments of children's pain severity in the oncology setting. Thus, efforts are needed to adequately equip parents in understanding proper assessment of children's cancer-related pain as well as development of validated parent-report measures of children's pain in the oncology setting.

mHealth

Mobile devices have become ubiquitous in the U.S. and nearly 80% of Americans own smartphones.⁴⁶ Patients and caregivers routinely search for health-related information using their mobile devices and mobile apps are particularly engaging for pediatric patients living in the current technology rich environment.^{47,48} Accordingly, globally, there has been an explosion in mobile health (mHealth) – the use of mobile devices to assess, monitor, and impact health outcomes. Although the field of mHealth is not without its challenges,⁴⁹ it does provide a potential avenue to deliver pain management to populations more broadly.

In fact, in recent years, investigators have harnessed mHealth technology to attempt to bridge gaps in pain management in pediatric oncology. Our own group has developed Pain Buddy, an animated, interactive web-based pain and symptom assessment and management program for children and adolescents aged 8-18 years undergoing treatment for cancer. Pain Buddy is comprised of a validated pain and symptom assessment component, an electronic communication component that provides symptom data to healthcare providers in real time, and cognitive and behavioral skills training for children (e.g., guided imagery, mindfulness, diaphragmatic breathing) for pain management.⁵⁰ Pain Buddy has been shown to be well accepted and feasible to use by patients and healthcare providers⁵⁰ and is currently undergoing efficacy testing. Pain Squad is another app that is used on smartphones for children and adolescents with cancer that assesses pain severity and characteristics and strategies used to manage pain.⁵¹ Pain Squad+ is a newer iteration of the program that focuses on self-management of cancer-related pain in adolescents that uses algorithms to provide adolescents with both pharmacological and non-pharmacological pain management strategies.⁵² Pain Squad+ has improved pain-related outcomes for children and adolescents with cancer.^{53,54} Despite evidence supporting the efficacy and acceptability of these apps, broader dissemination efforts have been limited; thus, efforts focused on implementation of such programs is necessary in order to have a substantive impact on pediatric cancer-related pain. Moreover, in the adult arena, there are many commercially available applications targeting healthcare in patients with cancer (e.g., <https://www.mobihealthnews.com/content/mobile-app-launches-better-connect-cancer-patients-appropriate-care-clinical-trials>; <https://www.cancer.net/navigating-cancer-care/managing-your-care/mobile-applications>). Efforts to develop similar resources for the pediatric population *and*

include a focus on pain management may be an avenue to bridge the gap in cancer pain management.

Telemedicine

Telemedicine has been defined as “technology-enabled health and care management and delivery systems that extend capacity and access.”⁵⁵ More recently, the benefits of telemedicine have been recognized by the healthcare community and have been increasingly used to enhance the accessibility of tertiary care for children, particularly in rural and underserved areas.^{56,57} In the adult arena, telemedicine has been shown to be effective for management of multiple cancer-related symptoms, including pain.⁵⁸ In pediatric oncology, telemedicine has been utilized to improve access to care and has been effective in improving cancer-related outcomes.⁵⁹ Telepharmacy, a more specific application of telemedicine, involves pharmacist-related services such as medication management, chronic disease management, care transition, pharmacogenomics, and remote dispensing and ambulatory care. In the ambulatory setting, telepharmacy interventions have improved disease outcomes, patient self-management, and treatment adherence; however, such interventions have not been assessed in pediatric oncology patients.⁶⁰ Utilizing advanced technologies with better decision support and real-time reporting capabilities, healthcare providers can effectively manage a patient’s symptoms in a timely manner. For pediatric patients with cancer, telemedicine may provide a cost-effective approach to optimize pain management in the home setting.

Summary

The opioid epidemic is a national health concern that is not specific to the adult population. Misuse of opioids extends to the pediatric setting and has particular importance with regard to pediatric oncology, where pain is prevalent and opioids are often the first-line analgesic used to

manage cancer-related pain. Despite the high rates of pain in pediatric oncology patients and potential benefits of opioid use, there is little clinical and policy guidance on opioid use in this setting. Further, the shift in pain management to the home setting has complicated appropriate opioid use as parents and caregivers often are not well equipped to assess and manage child pain. To make progress in this area, multidisciplinary researchers, healthcare providers, and policy makers need to pave the way in optimizing pain management. Fruitful advancement can come from creating clinical practice guidelines, testing and implementing integrative approaches to care, developing systematic pain measurement methods for parents and caregivers to use, and providing parents and caregivers with best practices in the area of pain management. Capitalizing on mHealth, Telemedicine, and Telepharmacy could be useful to achieve these goals and allow for the appropriate use of opioids to treat cancer-related pain in pediatric patients and increase their quality of life. A vital aspect of this effort is that fear of opioids not lead to the significant under treatment of children's cancer pain. Rather, it is critical to develop evidence-based protocols for management of cancer-related pain in children that reduces unnecessary suffering and minimizes unintended harms.

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