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Prescription Opioid Misuse by Adolescents: A Review of the Literature and Recommendations for Prevention

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The previous issue of *Pediatric Pharmacotherapy* focused on optimizing pain management after outpatient surgery through analgesic choice, improved access, and targeted parent education about pain assessment and medication use. This companion article addresses another concern related to pediatric analgesic use, the rising rate of misuse of prescription opioids in adolescents. There is now a growing body of literature on this problem, with multiple studies summarizing the extent of this problem and its relationship to shifts in prescribing patterns, as well as recommendations for reducing the potential for misuse.

Prevalence

Adolescents may misuse prescription opioids obtained from medications belonging to family or friends, purchase them illegally, or develop dependence on their own medically-indicated opioids. According to recent studies, approximately 7-20% of adolescents have taken a prescription opioid for nonmedical uses.[1-3] The percentage rises to 20-50% for young adults between 18 and 25 years of age. Rates of prescription opioid misuse among young adults appear to be similar across levels of educational attainment (13.2% in those without a high school diploma and 11.3% in those attending college), as well as racial or ethnic groups. While not consistent among studies of adolescents, several authors have reported a higher rate of prescription opioid misuse in females and an increased risk for use during high school.[2,3] An analysis of the Oklahoma Youth Risk Behavior Study found that females were 1.5 times as likely as males to have misused a prescription opioid and students in 12th grade were 1.7 times more likely than 9th grade students to report opioid misuse.[2]

Prescription opioid misuse has been linked to a number of adverse consequences for adolescents and young adults, including engagement in high risk behaviors, progression to intravenous substance abuse, and unintentional overdose.[1-4] In 2016, Tadros and colleagues published an evaluation of emergency department visits by children and adolescents for prescription opioid overdose.[5] Of the 21,928 pediatric visits documented in the Nationwide Emergency Department Sample (NEDS) database between 2006 and 2012, 24% of the recorded overdoses were associated with intentional opioid misuse. A third of the patients requiring hospitalization were in the intentional misuse category, with a mean cost of $14,235 per patient. A total of 39 patients required mechanical ventilation, but there were only 11 deaths.

Opioid Prescribing in Adolescents

The frequency at which controlled substances are prescribed for adolescents and young adults in the United States has increased significantly over the past two decades, with rates doubling in the last decade alone.[6-8] This increase has been seen in a variety of both hospital and ambulatory care settings and for a wide range of conditions. It has been estimated that 20-50% of adolescents evaluated for headaches, back pain, or joint pain receive a prescription for an opioid. In 2014, DeVries and coworkers conducted an observational cohort analysis of claims data from the HealthCore Integrated Research Environment during 2007 and 2008.[9] Of the 8,373 adolescents with headache, 46% received an opioid prescription despite current treatment guidelines recommending against their use. Forty-eight percent received one opioid prescription at follow-up, while 22.5% received two opioid

prescriptions and 29% received three or more. Twenty-five percent of patients given opioid prescriptions had migraine headaches. During follow-up, 28% of the patients given opioids had at least one visit to the emergency department for recurrent headache, compared to only 14% of those not given opioids ($p < 0.01$).

A second study published in 2014 evaluated opioid prescribing in pediatric emergency departments using data from the 2001-2010 National Hospital Ambulatory Medical Care Survey.[10] Opioid use in patients with pain-related visits rose from 11.2% in 2001 to 14.5% in 2010 ($p = 0.015$). Hydrocodone was the most frequently prescribed opioid. There was no equivalent increase in the use of nonopioid analgesics and no increase in schedule III, IV, or V agents.

Opioid Prescribing and Subsequent Misuse

While the growth in opioid prescribing in adults has been found to be a factor in subsequent opioid misuse in multiple studies, there has been relatively little research on the relationship between medically-indicated prescription opioid use and later opioid misuse in adolescents. Groenewald and colleagues at the University of Washington assessed pediatric opioid prescribing trends in the Medical Expenditure Panel Surveys conducted by the National Center for Health Statistics and the Agency for Healthcare Research and Quality between 1996 and 2012.[11] While the percentage of children and adolescents prescribed opioids each year in the United States has remained relative stable over the past decade (2.02% in children 6-11 years of age and 4.61% in adolescents 12-17 years of age), the frequency of those children and adolescents who receive 5 or more opioid prescriptions per year has increased. Predictors of opioid prescribing included older patient age, being white non-Hispanic, and having private or public insurance.

In 2015, Miech and colleagues evaluated the relationship between medically-indicated opioid use and later opioid misuse in adolescents using data obtained from the ongoing Monitoring the Future survey.[12] This annual survey includes students in the 12th grade at approximately 130 high schools. Students are randomly selected to complete the survey, with a subset randomly selected to participate in annual follow-up surveys. The authors selected a sample of 6,220 students who completed the survey between 1990 and 2012 and had follow-up surveys until age 23 for their analysis.

Medically-indicated opioid use prior to the 12th grade was independently associated with a 33% increase in the risk for future opioid misuse after high school (relative risk 1.33, $p < 0.05$). Of note, the association was concentrated in those young adults who had little to no history of drug abuse and a strong disapproval of illegal drug use at baseline assessment. Sixty-nine percent of the respondents who indicated misusing opioids on follow-up surveys stated the reason was to feel good, get high, or relieve tension; relatively few respondents were using opioids as an analgesic. This misuse appeared to be relatively infrequent, with most respondents stating that they took a non-medically indicated opioid fewer than six times in the last year. The authors suggest that the increased risk for future opioid use in adolescents with little or no previous history of drug abuse may reflect the impact of a pleasurable relief of pain and a feeling of safety with the use of a medically-indicated opioid as their first experience. They recommend that clinic-based education and abuse prevention efforts should include all adolescents, including those who might not appear to be at risk for prescription opioid abuse.

Opioid Misuse after Surgery

The risk for development of dependence from medically-indicated opioids and resulting prescription opioid abuse was highlighted in a recent case in the *Journal of Opioid Management*.[13] An 18-year-old girl with idiopathic scoliosis underwent surgery to correct complications from a prior spinal surgery at 14 years of age. Her initial surgery had left the patient with chronic pain which was treated with prescription opioids (tramadol and acetaminophen, Ultracet™) and escitalopram. Over time, the patient began to escalate her doses to manage her pain and reduce anxiety. Pain management during her surgical revision included patient-controlled analgesia with hydromorphone and methadone 5 mg every 8 hours. On postoperative day 3, she was transitioned to oral hydromorphone as needed, with a methadone taper, naproxen, and gabapentin.

A pre-discharge psychiatric evaluation revealed concerns that she might receive inadequate pain management. In addition, two of her friends had fatally overdosed on prescription opioids and alprazolam. On her first follow-up visit, her long-standing lumbar pain was better controlled, but she continued to complain of discomfort and insisted on receiving a prescription for Ultracet™. After further discussion, she disclosed long-standing abuse of Ultracet™ and symptoms of severe physiologic and psychological dependence when attempting to stop. She initially rejected recommendations for

rehabilitation services, but one year later enrolled in a community outpatient adolescent-centered dependency treatment program and had remained pain free and abstinent from prescription opioid use for more than 2 years at the time the case report was published.

Opioid Misuse in Patients with Chronic Pain

In 2014, Ehrentruat and colleagues analyzed the development of opioid misuse behaviors in adolescents and young adults receiving treatment at the St. Jude Children's Research Hospital.[13] The authors conducted structured chart reviews in 398 adolescents and young adults (12 to 33 years of age) seen over a 17-month period. Opioids were prescribed to 94 patients (23.6%). Of those patients, 11.7% had documentation describing aberrant opioid-associated behavior (AOB) such as demanding more medication, stating that medication has been lost, hoarding medication, requesting opioids from multiple prescribers, attempting to obtain opioids from emergency departments or nonmedical sources, referring to the drug by its brand or street name, using the medication for purposes other than pain relief (relaxation, euphoric effects), unauthorized dose increases, concurrent use of alcohol or other drugs, or worsening function.

Ninety percent of the patients had at least one psychosocial risk factor for AOB, such as a history of substance abuse or psychiatric comorbidities in the patient or a family member. There was no correlation between documented AOB and the presence of any of the risk factors, although this may have been the result of the small sample size. The associations between AOB and gender or age were also not statistically significant. There was, however, a significant association between the concurrent use of multiple opioids and AOB ($p = 0.003$). Based on their findings, the authors suggest that prescribers consider the patient's psychosocial risk factors prior to prescribing opioids and attempt to minimize the use of multiple agents whenever possible.

In the May-June 2016 issue of the *Journal of Opioid Management*, these authors published an excellent summary of the risk factors for opioid misuse in adolescents and young adults.[14] While the authors focus on the oncology population, they include information of value to healthcare providers caring for patients with disease or treatment-related pain. The article addresses clinical considerations that were identified in their earlier research, such as the need for evaluation of psychosocial risk factors, as well as the use of strategies to reduce such as prescription monitoring programs and ongoing patient and family education regarding both the benefits and risks of treatment.

Strategies to Prevent or Reduce Opioid Misuse

A number of new strategies and programs have been introduced to stem the growing rate of prescription opioid misuse. Prescription drug monitoring programs (PDMPs) are now available in 37 states and 11 more states have programs in development.[15] These electronic databases collect information on controlled substances dispensed anywhere in the state. The benefits of a PDMP can aid in reducing prescription drug abuse, addiction and diversion by identifying abuse or diversion, facilitating identification of patients needing assistance with potential addiction, and informing healthcare providers of trends in drug abuse, and providing data to educate the public about prescription drug addiction.

In March 2016, the Centers for Disease Control and Prevention (CDC) published an extensive guideline for prescribing opioids in chronic pain.[16] The guideline, the work of a core panel of experts throughout the United States, includes recommendations for when to initiate opioids, opioid selection and dosing, as well as methods for assessing risk and addressing harms. While targeted at adult patients, the recommendations are applicable to adolescents as well. Key recommendations include the need to establish clear treatment goals with the patient and realistic goals for pain and function, the use of immediate release opioids for initiation of therapy, and the use of the lowest effective dose and prescribing no greater quantity than necessary for the expected duration of pain. The guideline also includes recommendations for managing patients with pain lasting more than 3 months and patients with known risk factors for misuse.

Following publication of the CDC guideline, Dr. Vivek H. Murthy, Surgeon General of the United States issued a call to action for healthcare providers to join in preventing opioid misuse. In an open letter, Dr. Murthy urged healthcare providers to commit to safe prescribing practices by signing the Turn the Tide pledge at www.TurnTheTiderx.org. The website also serves as a resource guide for both clinicians and patients.

On August 31st, the Food and Drug Administration (FDA) announced that a new black box warning would be added to opioid and benzodiazepine products to highlight the risks of concomitant use of these drugs and the need to carefully consider the benefit to risk ratio of

using these drugs together.[18] The number of patients receiving prescriptions for both drugs rose by 41% over the past decade. It has recently been estimated that one in three deaths from unintentional opioid overdose also involved a benzodiazepine. In addition to the boxed warning, manufacturers will be required to add information on avoiding the use of these drugs together in the patient medication guide. The announcement by the FDA followed a petition from health directors in 16 states and 12 major US cities that was filed in February 2016.

Attempts to curb prescribing have not been limited to the CDC and FDA. Last month, Aetna announced that it will begin to "actively encourage change" in opioid prescribing patterns.[19] The insurer has instituted a program to analyze its claim database to identify physicians whose opioid prescribing patterns are outside the norm. Those practicing in areas in which high-dose therapy was expected, such as oncologists, were excluded. In an introductory letter sent to 931 physicians across the United States, Aetna told recipients that they were "identified as falling within the top 1 percent of opioid prescribers in your specialty." Physicians included in the analysis were responsible for more than 8.6 million opioid prescriptions. None were suspected of fraud or abuse, but were more likely than average physicians to provide a larger number of refills, with a mean of 4.5 versus 0.3 refills per prescription. Another approach to minimizing refills is being piloted by BlueCross BlueShield of Massachusetts. This insurer now requires prior authorization for all narcotic refills.

Summary

Prescription opioid misuse has increased dramatically in US adolescents within the past two decades. The growth in opioid prescribing, for adolescents as well as in adults, has been correlated with this increase. A number of healthcare organizations, governmental and private foundations are working to reduce this abuse. Individual providers are encouraged to review the appropriateness of opioid prescribing in their own practice and to join in efforts to reverse the rise in prescription opioid misuse in adolescents and young adults.

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