

Clinical Toxicology and Its Relevance to Asthma and Atopy



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KEYWORDS

- Asthma • Bronchoconstriction • Opiate • Mast cell • Degranulation • Heroin
- Insufflation

KEY POINTS

- Both licit and illicit opiates have effects on the immune and neurologic components of asthma inflammation and clinical disease.
- How these effects summate determines the clinical output of this complex interplay, with either worsening or improvement of asthma.
- Laboratory toxicology/drug monitoring of patients can provide clinicians with objective information to facilitate appropriate prescribing and management determinations.

There are notable increases in the use of prescription pain relievers, substance use disorder treatment admission rates, and prevalence of asthma. The overall US prevalence of asthma increased from 7% of the general population in 2001 to 8% in 2010.¹ Select population demographics may have a greater prevalence in that the Black non-Hispanic population approaches 10% and the Puerto Rican subset of the Hispanic demographic has been reported at 16.5% in 2004.¹ The sales of prescription pain relievers in 2010 were 4 times those in 1999, and the substance use disorder treatment admission rate in 2009 was 6 times the 1999 rate.² The overdose death rate in 2008 was about 4 times the 1999 rate.² Fortunately, asthma death rates have leveled off in recent years.¹ However, increased asthma mortality rates are higher in women, Black persons, and adults.¹ The prevalence of asthma is greater for women (9.2%), than men (7.0%).¹ Women are more likely to have chronic pain, be prescribed prescription pain relievers, be given higher doses, and use them for longer periods than men.³ Further, women may become dependent on prescription pain relievers more quickly than men.³ Recent data from the Centers for Disease Control and

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Prevention have shown the greatest increase in epidemic of prescription drug overdoses from 2013 to 2014 occurred among non-Hispanic Black (8.2%), versus non-Hispanic White (8.0%) women and no change (0%) among Hispanics.³ Taken together, both asthma and prescription pain reliever abuse are increasing and may disproportionately affect non-Hispanic Black women.

Drug overdose is the leading cause of accidental death in the United States, with 47,055 such deaths in 2014, with 18,893 overdose deaths related to prescription pain relievers.^{4,5} There is a yin-yang interaction regarding the use of opiate analgesics with asthma pathophysiology and clinical course, which may be contributing to the current epidemic of opiate analgesic deaths.

In a recent review of hospitalizations among inner-city adults,⁶ of 11,397 patients admitted in Chicago or Cleveland from 2005 to 2008, 3% were dependent on inhalational heroin. Heroin-dependent patients were 3 times more likely to be admitted for respiratory problems, compared with nondependent patients. This relationship was more striking for those with asthma exacerbations (odds ratio of 7.0).⁶ Of 23 inner-city patients admitted to an inner-city intensive care unit with asthma exacerbations,⁷ 56% describe asthma exacerbations associated with heroin insufflation. A 1996 review of fatal asthma in the same inner-city setting found that about a third of cases were confounded by substance abuse or alcohol,⁸ which was roughly the same proportion as those dying from homicide. Asthmatic patients whose asthma death is confounded by opiate use are more likely to be older, have no immediate respiratory complaints before the event, and to be found dead.⁹ Inhalation of heroin with cocaine has been linked to measurable airway hyperreactivity, which persists after the cessation of this substance abuse,¹⁰ and, therefore, might contribute to ongoing bronchospasm and asthma activity.

These reports of the effects of illicit opiate use on asthma clinical disease activity are not complemented by studies of the effect of licit opiate use on asthma, which is an understudied area. In 2014 more people died of drug overdoses the United States than any previous year on record.⁴ Approximately two-thirds of these involved opioids. These opioid deaths involve 2 trends: an increase in heroin use as well as a 15-year increase in deaths from prescription opiates, including fentanyl and tramadol. There is an increased availability of illicit fentanyl.¹¹ Although rare, licit fentanyl has been reported to cause asthma^{12,13} and cough.¹⁴

The pediatric population warrants additional consideration. Asthma prevalence is greater in children in general than adults (8.6% for those younger than 18 years compared with 7.4% in adults) and is greater in select populations: 13.4% in the Black non-Hispanic populations and 23.5% in the Puerto Rican subset of the Hispanic population.¹ Differences in physician gender and perception may bias referral to a pulmonologist compared with maintenance in a primary care setting as well as opioid prescribing habits for pediatric asthma and pain management.¹⁵ Further, in a study of patients' opioid misuse, providers were more likely to assess African American patients, younger patients, and patients with a history of illicit drug use as likely to have misused prescribed opioids. However, this perception was not correct; only the patients who had a history of illicit drug use reported opioid misuse.¹⁶

In addition, in the pediatric population (12–17 years old), the prescribing rates for prescription opioids among adolescents and young adults nearly doubled from 1994 to 2007. In 2014, an estimated 28,000 adolescents had used heroin in the past year, and an estimated 16,000 were current heroin users. Most adolescents who misuse prescription pain relievers are given to them for free by a friend or relative; individuals often share their unused pain relievers, unaware of the dangers of nonmedical opioid use.¹⁷ Thus, the relationship of opioid use and asthma in the pediatric population may exacerbate the risks over and above the adult population.

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