References

1. Kienbaum P, Thürauf N, Michel MC, Scherbaum N, Gastpar M, Peters J: Profound increase in epinephrine concentration in plasma and cardiovascular stimulation after μ-opioid receptor blockade in opioid-addicted patients during barbiturate-induced anesthesia for acute detoxification. ANESTHESIOLOGY 1998; 88:1154–61

2. Riordan CE, Kleber HD: Rapid opiate detoxification with clonidine and naltrexone. Lancet 1980; 1(8177):1079–80

3. Loimer N, Schmid R, Lenz K, Presslich O, Grünberger J: Acute blocking of naloxone precipitated opiate withdrawal symptoms by methohexitone. Br J Psychiatry 1990; 157:748–52

4. Legarda JJ, Gossop M: A 24-h inpatient detoxification treatment for heroin addicts: A preliminary investigation. Drug Alcohol Depend 1994; 35:91–3

Possible Mechanism(s) of Opioid-induced Coughing

To the Editor:—Doctors Bennett[1] and Yemen[2] recently exchanged letters addressing the issue of opioid-induced coughing. Doctor Yemen, in particular, expressed his curiosity as to the mechanism whereby opioids, known more as cough suppressants, could stimulate coughing. Dr. Yemen speculated that opioid-induced coughing might be related to opioid actions recently documented to occur at the level of the vocal cords.[3] I would like to bring to attention information not mentioned in their letters that is relevant to the question asked.

It is known that the antitussive actions of opioids are central in origin. However, fentanyl, and sufentanil and alfentanil, elicit a brief cough in up to 50% of patients when injected by intravenous bolus.[4] Opioid-induced coughing is elicited within seconds of drug injection. A pulmonary chemoreflex, mediated by C-fiber receptors (also known as J receptors), is thought to underlie this phenomenon.[4] Opioid receptors have been shown in smooth muscles of the trachea and bronchi and in alveolar walls, but not in the small airways.[5] Alveolar wall opioid receptors may be associated with J receptors.

The cough reflex after opioid injection is not likely to be vagally mediated because atropine pretreatment does not affect it.[6] Opioids may also elicit cough by stimulating irritant receptors in tracheal smooth muscle. Interestingly, pretreatment with inhaled β-adrenergic agonists significantly reduces the incidence of cough associated with intravenous opioid injection.[6]

In my experience, any opioid of the fentanyl series can elicit this usually brief cough response. Opioid-induced coughing is frequently more noticeable in patients who smoke. I have not witnessed an opioid-induced cough reflex that was not self-limited. As an aside, the elicitation of the cough reflex after opioid administration seems to be temporally related to circulation time and may serve as a clinical clue to "vein-to-brain" time, or cardiac output.

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References

1. Bennett JA: Small doses of sufentanil will produce violent coughing in young children (reply to letter). ANESTHESIOLOGY 1998; 89:272

2. Yemen TA: Small doses of sufentanil will produce violent coughing in young children (letter). ANESTHESIOLOGY 1998; 89:271

3. Bennett J, Abrams J, Van Riper D, Horrow J: Difficult or impossible ventilation after sufentanil induction of anesthesia is caused primarily by vocal cord closure. ANESTHESIOLOGY 1997; 87:1070

4. Bohrer H, Fleischer F, Werning P: Tussive effect of a fentanyl bolus administered through a central venous catheter. Anaesthesia 1990; 45:18

5. Cabot P, Cramond T, Smith M: Quantitative autoradiography of peripheral opioid binding sites in rat lung. Eur J Pharmacol 1996; 310:47

6. Liu P, Hsing C, Chu Y: Terbutaline inhalation suppresses fentanyl induced coughing. Can J Anaesthesiol 1996; 43:1216