



Question: A patient presents with an allergy to an opioid, can an alternative opioid be prescribed?

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Summary

There is very little evidence available to guide the choice of opioid in a patient with a history of an anaphylactic allergic reaction to a particular opioid analgesic. Alternative analgesics should be considered.

Allergic and anaphylactic reactions to the opioid analgesics are rare and ill-defined.¹ Opioids cause endogenous histamine release to varying degrees, and histamine causes a number of allergy like symptoms.¹ The presence of cross sensitivity is questionable and the risk is extremely low if it does exist.¹ If an alternative opioid is to be considered, the information outlined below should be taken into consideration. The use of an opioid with different chemical and structural properties may be considered. However, patients who exhibit true allergy to an opioid analgesic should be monitored extremely carefully if another opioid is to be used.

Information

As with any exogenous chemicals, opioid analgesics would be expected to cause allergic or anaphylactic reactions.¹ However, a review of the literature indicates that they occur rarely, indeed, reports which do exist often point to confounding variables and none describe cross sensitivity.¹ True anaphylactic reactions are extremely rare.^{2,3,4}

Virtually all opioid analgesics, but particularly the naturally occurring and semi-synthetic

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compounds, cause histamine release as a pharmacologic effect,¹ which may be responsible in part for reactions such as urticarial, pruritus, hypotension and flushing.⁵ These reactions to the release of histamine are not allergic or anaphylactic in nature.¹ Contact dermatitis and systemic hypersensitivity have also been reported.^{2,5}

There a number of different types of allergic reaction (e.g. immediate, cytotoxic, immune complex and delayed) but the common feature is that all such reactions are mediated by the immune system.⁴ In contrast, the vast majority of opioid side effects are not immune related.⁴

Opioid analgesics are contraindicated in patients with known hypersensitivity to the particular drug.²

Categories of Opioid Analgesics

Opioid analgesics have been categorised using at least 4 different schemes. Knowledge of categories is of value when dealing with cases of intolerance to particular opioids.³ To some extent, these schemes address the potential for cross sensitivity.¹

1. Naturally occurring vs semi-synthetic vs synthetic compounds¹

The naturally occurring and semi-synthetic compounds appear to be the most potent histamine releasers and therefore might be the most likely to elicit or aggravate asthmatic attacks.¹

2. Presence or absence of a 6-hydroxyl group on the basic morphine structure¹

This has been suggested as the cause of a pseudoscarlatina reaction in 4 patients when they were exposed to compounds with this moiety.¹

3. Basic Chemical Structure¹

The basic chemical structure of the opioid based on the related structural group, morphine, pethidine or a unique structure.

4. Chemical Class⁶

Commonly used opioids can be divided into three chemical classes⁶

Table 1 Categories of Opioid Analgesics^{1,6}

Opioid Analgesic	Source of Chemical	Morphine-Related Structure with 6-Hydroxyl Group	Related Structural Group	Chemical Class
Alfentanil	Synthetic	-	Pethidine	Phenylpiperidines
Buprenorphine	Semi-synthetic	No	Morphine	Phenanthrenes
Codeine	Natural	Yes	Morphine	Phenanthrenes
Fentanyl	Synthetic	-	Pethidine	Phenylpiperidines
Hydromorphone	Semi-synthetic	No	Morphine	Phenanthrenes
Methadone	Synthetic	-	Unique	Diphenylheptanes
Morphine	Natural	Yes	Morphine	Phenanthrenes
Oxycodone	Semi-synthetic	No	Morphine	Phenanthrenes
Pethidine	Synthetic	-	Pethidine	Phenylpiperidines
Tramadol	Synthetic	-	Unique	Phenanthrenes

Management

Alternative analgesics such as paracetamol or NSAIDs should be considered.¹

Based upon theoretical considerations, a patient who continues to need an opioid after demonstrating a true allergy to morphine or a semi-synthetic opioid a trial of a synthetic opioid may be considered.³ Patients should be monitored carefully if an agent from another class is substituted.¹ Co-administration of an anti-histamine or glucocorticoid may be considered.³

Barnett (2001) recommends that methadone can be used in cases of true morphine allergy (although relatively uncommon) and is useful for opioid rotation.⁷

References

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