

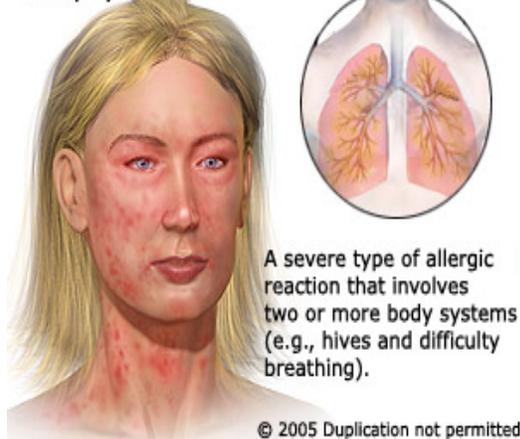
Should Antihistamines be Used to Treat Anaphylaxis?

Anaphylaxis is a serious allergic reaction that is rapid in onset and potentially fatal. Guidelines and experts agree that adrenaline (epinephrine) is the first line treatment for anaphylaxis. Internationally, however, treatment guidelines differ widely, and the widespread use of antihistamines in anaphylaxis, often as first line treatment instead of adrenaline, has led to concern.

International Guidelines are Conflicting on the Use of Antihistamines in Anaphylaxis

Unsurprisingly, a recent comparison of important international guidelines found conflicting advice about antihistamines, reflecting the uncertainty in international clinical practice: a US guideline recommends the use of diphenhydramine as second line treatment in anaphylaxis; evidence for this recommendation is graded as "expert opinion/extrapolated from higher order evidence.

Anaphylaxis



An Australian guideline advises against the use of antihistamines in anaphylaxis (except in special circumstances). The Resuscitation Council of the United Kingdom still recommends chlorphenamine as second line treatment after initial resuscitation, grading evidence to support its use as weak but citing some physiological reasons for its use (refuted below). However all other guidelines, recommend adrenaline as first line treatment for anaphylaxis, based on expert consensus and indirect observational data.

Inside this issue:

- **Should Antihistamines be Used to Treat Anaphylaxis?**
- **Prescribing Opioids to Older Adults.**





Antihistamines are Too Little, Too Late and Potentially Detrimental

Antihistamines are widely recommended in anaphylaxis for their anti-allergenic properties, which comprise the inhibition of mediator release from mast cells and basophils. However, first, antihistamines have no proved clinical effect on the immediate and life threatening symptoms of anaphylaxis. In conventional doses, antihistamines fail to prevent the massive release of histamine observed in anaphylaxis. They are slower in onset than adrenaline and have little effect on blood pressure. They play a negligible role in relieving bronchospasm or gastrointestinal symptoms, relegating them to second tier treatment. As a consequence they may just be useful for relief of mild symptoms, such as allergic reactions limited to the skin or the mucous membranes and flushing, itching, urticaria, and rhinorrhoea. Treatment with both H1-antagonists (antihistamines) and H2-antagonists (such as cimetidine and ranitidine) combined is more effective in alleviating the cutaneous manifestations of anaphylaxis than H1-antagonists alone.

Secondary the risk of potentially fatal cardiac arrhythmias such as QT prolongation and torsade de pointes argues against the administration of older, first generation intravenous H1 antihistamines. The anticholinergic properties of these older drugs may lead to tachycardia and sedation, potentially confusing the picture in anaphylaxis. Newer, less toxic third generation antihistamines are unfortunately only available orally. In fasting adults, these have a delayed onset of 40-60 minutes, greatly reducing their utility in acute anaphylaxis.

Thirdly, a logistical problem of delay exists. In serious cases, the earlier the adrenaline is injected, the more effective it is, but the great interpersonal variability makes the need for early adrenaline administration unforeseeable and unpredictable. An inexperienced physician or lay person might delay the lifesaving adrenaline injection, favouring a presumed innocuous (but ineffective) antihistamine.

What Should we do in the Light of the Uncertainty?

Keep it simple; inject adrenaline first. In anaphylaxis, universal consensus is to give adrenaline intramuscularly. International guidelines recommend 0.01 mg/kg and/or a maximum of 0.3-0.5 mg for adults. Antihistamines should never be given alone or instead of adrenaline in anaphylaxis. First do no harm: because of possible adverse effects and until randomised controlled trials prove a beneficial effect, antihistamines should be considered only after adrenaline administration and with caution. They may be indicated, if at all, mainly to relieve itching, hives, other cutaneous symptoms, and rhinorrhoea.

References

1. Sampson HA, Munoz-Furlong A, Campbell RL, Adkinson Jr NF, Bock SA, Branum A, et al. Second symposium on the definition and management of anaphylaxis: summary report—second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol* 2006;117:391-7.
2. Kemp SF, Lockey RF, Simons FE. World Allergy Organization ad hoc Committee on Epinephrine in Anaphylaxis. *Allergy* 2008;63:1061-70.
3. Alrasbi M, Sheikh A. Comparison of international guidelines for the emergency medical management of anaphylaxis. *Allergy* 2007;62:838-41.
4. Clark S, Bock SA, Gaeta TJ. Multicenter study of emergency department visits for food allergies. *J Allergy Clin Immunol* 2004;113:347-52.

Prescribing Opioids to Older Adults

The use of opioid medications and converting among them in the older adult population can often be challenging. Physiological changes in older adults may affect metabolism and cognitive abilities. Due to renally cleared metabolites, some opioids, such as morphine, should be used with caution among older adults. Others, such as meperidine, should never be used at all. When prescribing or changing opioids, the choice of the correct formulation, appropriate counseling, and close follow-up are essential for optimal pain management and in order to prevent adverse outcomes.

The treatment of pain in the older adult population can present significant challenges. Older adults may have a number of chronic conditions. Some of these may affect which drugs they can use, and others may require medications that may put these patients at a higher risk for drug-drug interactions. Age-related changes in physiology, such as renal function, may limit which drugs can be prescribed. Cognitive, language, and hearing obstacles are important considerations as well.

Commonly Used Opioids and their side effects for older adults

Morphine morphine is six times more potent than oral codeine. Its metabolites are excreted renally. Many older adults have comorbid illnesses such as diabetes, hypertension, and congestive heart failure predispose them to kidney disease. In addition, creatinine clearance decreases with age, even among healthy individuals. Therefore, a normal creatinine value may not guarantee that morphine metabolites will not accumulate, particularly at higher dosages. For this reason, morphine should be used with caution in the older adult population.

Codeine weak opioid is indicated for mild pain and may be used to step down from a stronger opioid in instances when a patient's pain is decreasing over time. weak opioid, it has no analgesic effect on its own, but is a prodrug, converted to morphine by the liver. Due to genetic differences, some people lack the ability to make this conversion due to low CYP2D6 enzyme levels; for them, an equianalgesic dose of another opioid should be considered if codeine appears to have no effect.

Oxycodone is twice as potent as morphine. Less than 15% of an oxycodone dose is excreted in the kidneys, making it an excellent drug for older adults. It also has a moderate side effect profile. It is available only orally; thus, patients who may require alternate routes throughout their course of treatment may benefit from another choice of drug.

Hydromorphone Five times stronger than morphine, hydromorphone also has renally cleared metabolites; however, owing to its higher potency, a much smaller dose can be used for an equianalgesic effect. This makes it a more suitable choice for patients with renal impairment. One advantage of hydromorphone is that it is available both orally and parenterally, allowing for use via either route without the need for converting between drugs.

Fentanyl Transdermal fentanyl may be used for patients who do not tolerate the orally available opioids or who cannot swallow sustained-release formulations. Patches are available in multiples of 12.5 µg/h, but the recommended starting dose is usually 25 µg, the equivalent of a minimum equivalent daily dose of 50 mg of oral morphine. Because it can take up to 48 hours to attain full effects from the patch and another 48 to completely clear the drug upon discontinuation, fentanyl patches should only be prescribed to patients with stable opioid requirements. A conservative starting dose should be used, and there should be close monitoring for the first few days. Patients will still require a conventional as-need

with caution in the older adult population.

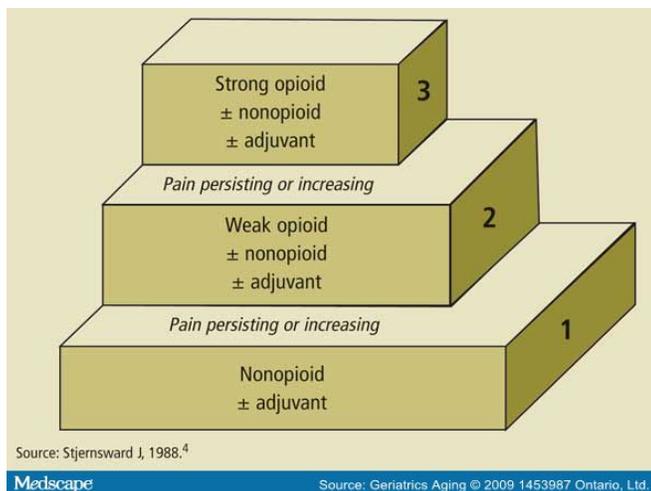
Patients will still require a conventional as-need

needed breakthrough drug. Hydromorphone and oxycodone are the best choices.

Meperidine There have been numerous warnings about the use of meperidine, for older adults, both the American Pain Society and the Institute for Safe Medication Practice do not recommend meperidine's use as an analgesic for chronic pain in this population. Its toxic metabolite, normeperidine, has an extremely long half-life and accumulates rapidly in patients with impaired renal function. In older adults with reduced creatinine clearance, this poses an even greater danger. Normeperidine has neuroexcitatory properties and can lower the threshold for seizures. Early evidence had provided an indication for meperidine in pancreatitis and biliary colic because of animal models which showed decreased sphincter of Oddi pressures compared with other opioids. However, human trials have since shown that meperidine is not superior to other opioids in avoiding smooth muscle spasm in biliary colic.

References

1. O'Mahony D, Gallagher PF. Inappropriate prescribing in the older population: need for new criteria. *Age Ageing* 2008;37:138-41.
2. Shi S, Mörike K, Klot U. The clinical implications of ageing for rational drug therapy. *Eur J Clin Pharmacol* 2008;6:183-99.



The World Health Organization's "Analgesic Ladder"

Advisory Board:

Dr. Ezz El-Denshary

Professor of Pharmacology & Toxicology
 College of Pharmacy- MUST and
 Faculty of Pharmacy, Cairo University

Dr. Naglaa Assaf

Lecturer of Pharmacology & Toxicology
 College of Pharmacy, MUST University.

Editorial Board:

Dr. Samar M. Saleh

Drug Information Pharmacists, DIC, MUST
 Drug Information Center (DIC), College of
 Pharmacy- MUST

Dr. Doaa Hamdan

Drug Information Pharmacists, DIC, MUST
 Drug Information Center (DIC) ,College of
 Pharmacy- MUST

Dr. Noha Gamal

Demonstrator at pharmacognosy department,
 Drug Information Pharmacists, DIC, MUST
 Drug Information Center (DIC) ,College of
 Pharmacy- MUST.

College Dean:

Prof. Dr. Mohamed F. El-Miligi

Address : M.U.S.T, 6 October City -
 Almutamayez district.
 Fax / Phone: 02/38377643
 Ext : 4 404
 E-mail: banhawii@yahoo.com

مركز معلومات الدواء



Drug Information Center

