Complete Summary

GUIDELINE TITLE

Camphor poisoning: an evidence-based consensus guideline for out-of-hospital management.

BIBLIOGRAPHIC SOURCE(S)

Manoguerra AS, Erdman AR, Wax PM, Nelson LS, Caravati EM, Cobaugh DJ, Chyka PA, Olson KR, Booze LL, Woolf AD, Keyes DC, Christianson G, Scharman EJ, Troutman WG, American Association of Poison Control Centers. Camphor poisoning: an evidence-based practice guideline for out-of-hospital management. Clin Toxicol (Phila) 2006;44(4):357-70. PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Camphor poisoning

Note: This guideline applies to exposure to camphor alone. Co-ingestion of additional substances, such as in commercial products of camphor combined with other ingredients, could require different referral and management recommendations depending on the combined toxicities of the substances

GUIDELINE CATEGORY

Evaluation
Management
Risk Assessment

CLINICAL SPECIALTY

Emergency Medicine
Family Practice
Internal Medicine
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Emergency Medical Technicians/Paramedics
Nurses
Pharmacists
Physicians

GUIDELINE OBJECTIVE(S)

To assist U.S. poison center personnel in the appropriate out-of-hospital triage and initial management of patients with suspected exposures to camphor-containing products by:

- Describing the manner in which an exposure to camphor might be managed
- Identifying the key decision elements in managing cases of camphor exposure
- Providing clear and practical recommendations that reflect the current state of knowledge
- Identifying needs for research

TARGET POPULATION

Adults and children with suspected exposures to camphor-containing products

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Assessment of key decision points for triage:
    - Patient intent
    - Route of exposure and estimated dose of camphor
    - Time since exposure and symptoms

Management

1. Referral to an emergency department
2. Benzodiazepine administration for convulsion control
3. Washing with mild soap and water for topical exposures

4. Immediate irrigation for ocular exposures, with referral for ophthalmologic exam, if symptoms of eye injury are present
5. Removal of patient to a fresh air environment for inhalation exposure, with referral to a healthcare facility based on severity of symptoms
6. Home observation

Note: Gastrointestinal decontamination in the out-of-hospital setting with ipecac syrup and activated charcoal was considered but not recommended

MAJOR OUTCOMES CONSIDERED

- Signs and symptoms of camphor toxicity
- The threshold dose for the development of toxicity

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Literature Search

The National Library of Medicine's PubMed database was searched (to November 2004) using camphor (poisoning) or camphor (toxicity) or camphor (adverse effects) as Medical Subject Heading (MeSH) terms, all limited to humans. PubMed was also searched using camphor as a textword (title, abstract, MeSH term, CAS number) plus either poison* or overdos* or tox* or intox*, limited to humans. This latter process was repeated in International Pharmaceutical Abstracts (1970 to November 2004, excluding abstracts of meeting presentations), Science Citation Index (1977 to November 2004), Database of Abstracts of Reviews of Effects (accessed November 2004), Cochrane Database of Systematic Reviews (accessed November 2004), and Cochrane Central Register of Controlled Trials (accessed November 2004). Reactions (1980 to November 2004), the camphor poisoning management in Poisindex, and the bibliographies of recovered articles were reviewed to identify previously undiscovered articles. Furthermore, North American Congress of Clinical Toxicology abstracts published in the Journal of Toxicology-Clinical Toxicology (1995 to 2004) were reviewed for original human data. The camphor chapter bibliographies in five major toxicology textbooks were reviewed for citations of additional articles with original human data. US poison control centers were invited to submit their current guidelines for the management of camphor exposures. Finally, The Toxic Exposure Surveillance System maintained by the American Association of Poison Control Centers was searched for deaths resulting from camphor poisoning. These cases were abstracted for use by the panel.

Article Selection

The recovered citations were entered into an EndNote library and duplicate entries were eliminated. The abstracts of the remaining articles were reviewed, looking specifically for those that dealt with estimations of mg/kg or ingested doses with or without subsequent signs or symptoms, time to onset of symptoms, and management techniques that might be suitable for out-of-hospital use (e.g., gastrointestinal decontamination). Articles excluded were those that did not meet any of the preceding criteria, did not add new data (e.g., some reviews, editorials), or that exclusively described inpatient-only procedures (e.g., whole bowel irrigation).

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level of Evidence	Description of Study Design
1a	Systematic review (with homogeneity) of randomized clinical trials
1b	Individual randomized clinical trials (with narrow confidence interval)
1c	All or none (all patients died before the drug became available, but some now survive on it; or when some patients died before the drug became available, but none now die on it.)
2a	Systematic review (with homogeneity) of cohort studies
2b	Individual cohort study (including low quality randomized clinical trial)
2c	"Outcomes" research
3a	Systemic review (with homogeneity) of case-control studies
3b	Individual case-control study
4	Case series, single case reports (and poor quality cohort and case control studies)
5	Expert opinion without explicit critical appraisal or based on physiology or bench research
6	Abstracts

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data Extraction

All articles that were retrieved from the search were reviewed by a single abstractor. Each article was assigned a level of evidence score from 1 to 6 using a rating scheme based on that of the Centre for Evidence-based Medicine at Oxford University (see the "Rating Scheme for the Strength of the Evidence" field). Single case reports were classified along with case series as level 4. The complete paper was then reviewed for original human data regarding the toxic effects of camphor or original human data directly relevant to the out-of-hospital management of patients with camphor poisoning. Relevant data (e.g., dose of camphor, resultant effects, time to onset of effects, therapeutic interventions or decontamination measures given, efficacy or results of any interventions, and overall patient outcome) were compiled into a table and a brief summary description of each article was written. This full evidence table is available at http://www.aapcc.org/DiscGuidelines/Guidelines%20Tables/Camphor%20evidence%20table.pdf. The completed table of all abstracted articles was then forwarded to the panel members for review and consideration in developing the guideline. Every attempt was made to locate significant foreign language articles and have their crucial information extracted, translated, and tabulated. Copies of all of the articles were made available for reading by the panel members on a secure American Association of Poison Control Centers (AAPCC) website.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The American Association of Poison Control Centers (AAPCC), the American Academy of Clinical Toxicology (AACT), and the American College of Medical Toxicology (ACMT) appointed members of their organizations to serve as panel members. To serve on the expert consensus panel, an individual had to have an exceptional record in clinical care and scientific research in toxicology, board certification as a clinical or medical toxicologist, significant U.S. poison center experience, and be an opinion leader with broad esteem. Two specialists in poison information were included as full panel members to provide the viewpoint of the end-users of the guideline.

Guideline Writing and Review

A guideline draft was prepared by the primary author. The draft was submitted to the expert consensus panel for comment. Using a modified Delphi process, comments from the expert consensus panel members were collected, copied into a table of comments, and submitted to the primary author for response. The primary author responded to each comment in the table and, when appropriate, the guideline draft was modified to incorporate changes suggested by the panel. The revised guideline draft was again reviewed by the panel and, if there was no strong objection by any panelist to any of the changes made by the primary author, the draft was prepared for the external review process.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The rating scheme for the strength of the recommendation (A-D, Z) is directly tied to the level of evidence supporting the recommendation.

Grade of Recommendation	Level of Evidence
A	1a
	1b
	1c
B	2a
	2b
	2c
	3a
	3b
C	4
D	5
Z	6

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

External review of the second draft was conducted by distributing it electronically to Association of Poison Control Centers (AAPCC), American Academy of Clinical Toxicology, and American College of Medical Toxicology members and the secondary review panel. The secondary review panel consisted of representatives from the federal government, public health, emergency services, pediatrics, pharmacy practice, and consumer organizations (see Appendix 3 in the original guideline document). Comments were submitted via a discussion thread on the AAPCC web site or privately through email communication to AAPCC staff. All submitted comments were stripped of any information that would identify their sources, copied into a table of comments, and reviewed by the expert consensus panel and the primary author. The primary author responded to each comment in the table and his responses and subsequent changes in the guideline were reviewed and accepted by the panel. Following a meeting of the expert consensus panel, the final revision of the guideline was prepared.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the weight of the evidence (A-D, Z) and classes of recommendations (1a-6) can be found at the end of the "Major Recommendations" field.

1. Patients with stated or suspected self-harm or who are the recipients of malicious administration of a camphor-containing product should be referred to an emergency department immediately. This activity should be guided by local poison center procedures. In general, this should occur regardless of the amount ingested **(Grade D)**.
2. Patients who have ingested more than 30 mg/kg of a camphor-containing product or who are exhibiting symptoms of moderate to severe toxicity (e.g., convulsions, lethargy, ataxia, severe nausea and vomiting) by any route of exposure should be referred to an emergency department for observation and treatment **(Grade D)**.
3. Patients exhibiting convulsions following a camphor exposure should be transported to an emergency department by pre-hospital emergency medical care providers **(Grade D)**. A benzodiazepine should be used to control convulsions **(Grade C)**.
4. Patients who have been exposed to a camphor product and who remain asymptomatic after 4 hours can be safely observed at home **(Grade C)**.
5. The induction of emesis with ipecac syrup should not be performed in patients who have ingested camphor products **(Grade C)**.
6. Activated charcoal administration should not be used for the ingestion of camphor products. However, it could be considered if there are other ingredients in the product that are effectively adsorbed by activated charcoal or if other substances have been coingested. **(Grade C)**.
7. For asymptomatic patients with topical exposures to camphor products, the skin should be thoroughly washed with soap and water and the patient can be observed at home for development of symptoms **(Grade C)**.
8. For patients with topical splash exposures of camphor to the eye(s), the eye(s) should be irrigated in accordance with usual poison center procedures and that referral take place based on the presence and severity of symptoms **(Grade D)**.
9. Patients with camphor inhalation exposures should be moved to a fresh air environment and referred for medical care based on the presence and severity of symptoms. It is unlikely that symptoms will progress once the patient is removed from the exposure environment **(Grade D)**.

Definitions

Grades of Recommendation and Levels of Evidence

Grade of Recommendation	Level of Evidence	Description of Study Design
A	1a	Systematic review (with homogeneity) of randomized clinical trials
	1b	Individual randomized clinical trials (with narrow confidence interval)
	1c	All or none (all patients died before the drug became available, but some now survive on it; or when some patients died before the drug became available, but none now die on it.)

Grade of Recommendation	Level of Evidence	Description of Study Design
B	2a	Systematic review (with homogeneity) of cohort studies
	2b	Individual cohort study (including low quality randomized clinical trial)
	2c	"Outcomes" research
	3a	Systemic review (with homogeneity) of case-control studies
	3b	Individual case-control study
C	4	Case series, single case reports (and poor quality cohort and case control studies)
D	5	Expert opinion without explicit critical appraisal or based on physiology or bench research
Z	6	Abstracts

CLINICAL ALGORITHM(S)

An algorithm is provided in Appendix 4 of the original guideline document for the triage of camphor ingestions.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate out-of-hospital triage and initial management of patients with suspected exposures to camphor-containing products

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guideline is based on an assessment of current scientific and clinical information. The expert consensus panel recognizes that specific patient care decisions may be at variance with this guideline and are the prerogative of the patient and the health professionals providing care, considering all of the

circumstances involved. This guideline does not substitute for clinical judgment.
- This guideline has been developed for the conditions prevalent in the U.S. While the toxicity of camphor is not expected to vary in a clinically significant manner in other nations, the available forms of camphor and the out-of-hospital conditions could be much different. This guideline should not be extrapolated to other settings unless it has been determined that the conditions assumed in this guideline are present.

Limitations of the Published Data

While there were some published data suggesting a general toxic threshold dose range for camphor, the data suffered from a number of limitations, including the following.

1. Understandably, there were no prospective studies that specifically investigated the toxic dose threshold for camphor.
2. The published data existing for camphor are almost entirely case reports and suffer from all of the usual problems attributed to case report data including incomplete patient information and unconfirmed exposure to the toxin.
3. The bulk of the literature on camphor was published prior to 1970. Many of the case reports are from the early part of the 20th century and do not provide the same level of information that is considered standard for case reports published in the recent literature.
4. Only a small number of articles contained any toxic threshold or dose-effect information.
5. Even when such information was presented in an article, there were often questions regarding the accuracy of the dose estimate due to inherent uncertainties in the history, differences in camphor content between products, and sometimes uncertainty with the report itself (e.g., confusion between the total product ingested or total camphor ingested, use of ambiguous or outdated language).
6. Dose-effect information was often confounded by the presence of co-exposures, differences in decontamination or treatment measures, and concurrent medical conditions that could have altered the clinical presentation or outcome.
7. It was difficult, if not impossible, to account for inter-individual differences in age, weight, underlying health condition, or other factors that might affect camphor's toxicokinetics and toxicodynamics.
8. Among larger case series, many of the patients remained asymptomatic; doses and/or effects were typically reported as ranges, percentages, or means for the cases so that individual doses resulting in specific effects could not be determined.
9. In the few available prospective trials of therapeutic use of camphor, camphor was generally administered in small doses or by routes that are not expected to occur in the setting of a poisoning.
10. The basic premise upon which the recommendations are based is that all camphor products have similar bioavailability characteristics irrespective of the formulation and that the amount of camphor in a product is the primary determinant in the potential for toxicity. This is an assumption for which there are no data, for or against, in the literature. This might not be a valid

assumption and formulation could be a factor in observed differences in toxicity.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Manoguerra AS, Erdman AR, Wax PM, Nelson LS, Caravati EM, Cobaugh DJ, Chyka PA, Olson KR, Booze LL, Woolf AD, Keyes DC, Christianson G, Scharman EJ, Troutman WG, American Association of Poison Control Centers. Camphor poisoning: an evidence-based practice guideline for out-of-hospital management. Clin Toxicol (Phila) 2006;44(4):357-70. PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Feb 16

GUIDELINE DEVELOPER(S)

American Association of Poison Control Centers - Professional Association

SOURCE(S) OF FUNDING

Health Resources and Services Administration, U.S. Department of Health and Human Services

GUIDELINE COMMITTEE

Not stated

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

There are no potential conflicts of interest reported by the expert consensus panel or project staff regarding this guideline.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American Association of Poison Control Centers.

Print copies: Available from the American Association of Poison Control Centers, 3201 New Mexico Avenue NW, Suite 330, Washington, DC 20016

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on November 29, 2006. The information was verified by the guideline developer on December 13, 2006.

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