Drugs and Health Products

ARCHIVED - Canadian Adverse Reaction Newsletter - Volume 19 - Issue 1
January 2009

⚠️ This content was archived on June 24 2013.

Archived Content

Information identified as archived on the Web is for reference, research or recordkeeping purposes. It has not been altered or updated after the date of archiving. Web pages that are archived on the Web are not subject to the Government of Canada Web Standards. As per the Communications Policy of the Government of Canada, you can request alternate formats on the "Contact Us" page.

Help on accessing alternative formats, such as Portable Document Format (PDF), Microsoft Word and PowerPoint (PPT) files, can be obtained in the alternate format help section.

Health Products and Food Branch
Marketed Health Products Directorate
Canadian Adverse Reaction Newsletter Editorial Team

In this Issue:

- Local anesthetic infusion with pain pumps and chondrolysis
- Natural health products and adverse reactions: update
- Case presentation: Propolis and renal failure
- Summary of advisories

Scope

This quarterly publication alerts health professionals to potential signals detected through the review of case reports submitted to Health Canada. It is a useful mechanism to stimulate adverse reaction reporting, as well as to disseminate information on suspected adverse reactions to health products occurring in humans before comprehensive risk-benefit evaluations and regulatory decisions are undertaken. The continuous evaluation of health product safety profiles depends on the quality of your reports.

Reporting Adverse Reactions

Canada Vigilance Program
Phone: 1-866-234-2345
Fax: 1-866-678-6789

For more information on how to report an adverse reaction, visit the Reporting Adverse Reactions to Drugs and Other Health Products page.

Caveat: Adverse reactions (ARs) to health products are considered to be suspicions, as a definite causal association often cannot be determined. Spontaneous reports of ARs cannot be used to estimate the incidence of ARs because ARs remain underreported and patient exposure is unknown.

Local anesthetic infusion with postoperative pain pumps and articular
chondrolysis

Postoperative pain pumps are infusion devices designed to continuously deliver controlled amounts of medication.\(^1\)\(^2\) They can be used to infuse local anesthetic solutions directly into operative sites, for pain management following surgical procedures. The device consists of a reservoir containing the local anesthetic solution, which is delivered by gravity or by electric pump through a catheter implanted directly into the surgical wound. Bupivacaine is an anesthetic commonly used with postoperative pain pumps.\(^3\) A combination of bupivacaine and epinephrine is also used, with the epinephrine inducing vasoconstriction and slowing down the absorption of bupivacaine.

As of July 2008, Health Canada received 8 incident reports of articular chondrolysis following shoulder surgery that were suspected of being associated with the use of postoperative pain pumps. The pain pumps were used for about 48 hours after surgery. All of the patients received bupivacaine with epinephrine. Chondrolysis was diagnosed between 1 month and 1 year after the surgeries and the use of the pain pumps.

Chondrolysis is a progressive degeneration of the cartilage for which the cause is not fully understood.\(^3\)\(^5\) Chondrolysis of the shoulder results in narrowing of the joint space, leading to pain and loss of motion; it is a debilitating condition that requires medical attention and possibly surgery.\(^3\)\(^4\) Chondrolysis is listed among the possible adverse incidents in the device labelling of pain pumps.\(^1\)\(^2\)

The device labelling states that the continuous intra-articular infusion of anesthetics, particularly when epinephrine is also used, is not recommended.

The association between postoperative pain pumps and the development of chondrolysis is difficult to identify. Indeed, chondrolysis may appear many months after the use of a pain pump.\(^3\)\(^4\)\(^5\) In addition, confounders such as the concomitant use of health products (e.g., gentian violet, chlorhexidine, bone cement) and radiofrequency devices may be responsible for causing chondrolysis after shoulder surgery.\(^5\)\(^6\)\(^7\)\(^8\)\(^9\)\(^10\)

Health care professionals are encouraged to follow the instructions for use and refrain from using postoperative pain pumps for continuous intra-articular infusion of local anesthetics, particularly with epinephrine, after shoulder surgery.\(^1\)\(^2\) They should report adverse incidents following the use of pain pumps or other medical devices to the Health Products and Food Branch Inspectorate through the Inspectorate Hotline (800 267-9675).

Fannie St-Gelais, PhD, Health Canada

---

Natural health products and adverse reactions: update

Many Canadians use natural health products (NHPs) on a regular basis\(^1\). either alone or in combination with other health products. However, NHPs may be associated with potential health risks, including adverse reactions (ARs) and interactions with drugs, other NHPs or food. The January 2004 issue of the *Canadian Adverse Reaction Newsletter* discussed safety concerns suspected of being associated with the use of echinacea, ginkgo and St. John's wort. The concerns were based on reports of ARs received by Health Canada from Jan. 1, 1998, to June 30, 2003\(^2\). Table 1 provides an update on ARs reported for these NHPs since that publication.

Table 1: Summary of reports of adverse reactions (ARs) suspected of being associated with echinacea, ginkgo and St. John's wort received by Health Canada from July 1, 2003, to May 31, 2008\(^3\)

<table>
<thead>
<tr>
<th>Product</th>
<th>No. of reports of ARs</th>
<th>Previously reported safety concerns(^4)</th>
<th>Other reported ARs(^5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echinacea</td>
<td>21</td>
<td>Allergic reactions (3 reports)</td>
<td>Agitation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Diarrhea</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Discoloured faeces</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dyspnea</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fecal incontinence</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Insomnia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Proctalgia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pyrexia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Vertigo</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Vomiting</td>
</tr>
<tr>
<td>Ginkgo</td>
<td>24</td>
<td>Bleeding (1 report)</td>
<td>Dizziness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Increased blood pressure</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Palpitations</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Syncope</td>
</tr>
<tr>
<td>St. John's wort</td>
<td>11</td>
<td>Drug interactions (2 reports)</td>
<td>Hepatitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Increased hepatic enzyme levels</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Photosensitivity(^6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rash</td>
</tr>
</tbody>
</table>

\(^*\) These data cannot be used to determine the incidence of adverse reactions (ARs) because ARs are underreported and neither patient exposure nor the amount of time the health product was on the market has been taken into consideration.

\(^1\) This is not an exhaustive list of reported ARs. Several reaction terms may be listed per AR report. Reaction terms are listed according to the *World Health Organization Adverse Reaction Terminology* (WHOART) or the *Medical Dictionary for Regulatory Activities* (MedDRA).

\(^2\) Allergic reactions are mentioned in the *Echinacea purpurea* monograph\(^3\).

\(^3\) This report described nose bleeds. The ginkgo biloba monograph warns against using ginkgo in combination with other health products that affect blood coagulation (e.g., blood thinners, clotting factor replacements, acetylsalicylic acid, ibuprofen, fish oils, vitamin E), because such use may increase the risk of spontaneous bleeding\(^4\).

\(^4\) Drug interactions involved levonorgestrel-ethinyl estradiol (oral contraceptive) in one case and ibuprofen in the second case.

\(^5\) The St. John's wort monograph contains a warning to avoid prolonged exposure to sunlight, ultraviolet light or ultraviolet therapy\(^5\).

In addition, safety concerns suspected of being associated with valerian have been reported. Valerian may be used as a sleep aid or sedative\(^6\). From Jan. 1, 1990, to May 31, 2008, Health Canada received 31 reports of ARs suspected of being associated with valerian-containing products; 15 of the reports described psychiatric ARs, such as visual hallucination, nightmares and abnormal thinking. There have also been reports in the literature of visual hallucinations,\(^2\) delirium\(^5\) and cardiac...
complications following cessation of valerian use. Other reports received by Health Canada describing ARs suspected of being associated with valerian-containing products include gastrointestinal disturbances (e.g., vomiting, diarrhea, nausea), allergic reactions, increased hepatic enzyme levels and cardiac complications (e.g., bradycardia, arrhythmia).

Angela Tonary, PhD; Stephanie Jack, MSc; David Cunningham, MD, FRCP; Karen Pilon, RN, Health Canada

**Key points for health care practitioners**

- Ask patients about their use of natural health products (NHPs) as part of their medical record
- Product monographs for NHPs are available on the Health Canada Web site.
- NHPs that have been issued a product licence by Health Canada can be found in the [Licensed Natural Health Products Database](http://www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/carn-bcei_v19n1-eng.php#cp).

---

**Case Presentation**

Recent Canadian cases are selected based on their seriousness, frequency of occurrence or the fact that the reactions are unexpected. Case presentations are considered suspicions and are presented to stimulate reporting of similar suspected adverse reactions.

**Propolis: suspected association with renal failure**

Propolis is a natural resinous product collected by bees that is used in the construction of hives. It is available in Canada as a single ingredient or in combination in many natural health products (NHPs). Propolis is used for the relief of various conditions, including bacterial, fungal and viral infections, inflammation and, topically, for skin and mouth lesions. In the April 2005 issue of the [Canadian Adverse Reaction Newsletter](http://www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/carn-bcei_v19n1-eng.php#cp), an article described adverse reactions (ARs) such as allergic reactions and skin or mucous membrane irritation suspected of being associated with bee products.

Health Canada received a report of a 3-year-old boy with a known history of gluten enteropathy in whom acute renal failure developed while he was taking propolis. The gluten enteropathy was stable with dietary restriction. The child received the homeopathic product containing propolis 2-3 times per week as needed as prophylaxis for infection. The exact form and dose of propolis used was not reported. The child was also taking other NHPs in a sporadic fashion; however, information on the dosage and frequency of exposure to these other products is unknown. After approximately 4 months of use of propolis, the boy's serum creatinine level increased to 84 µmol/L (normal < 53 µmol/L for children < 5 years old). Propolis was stopped, and his creatinine level returned to normal. No information was provided on the child's clinical status or need for hospital care. The cessation of propolis was the only reported form of treatment.

---

A case of acute renal failure requiring hemodialysis following the use of propolis was previously reported in the literature. This case involved 2 exposure periods resulting in positive dechallenge and rechallenge in a 59-year-old man with a history of cholangiocarcinoma who had self-mediated with a Brazilian variety of propolis.


Canadian Adverse Reaction Newsletter: distribution changes

The January 2009 issue of the Canadian Adverse Reaction Newsletter (CARN) is the last issue to be published in the Canadian Medical Association Journal (CMAJ). CARN will continue to be available on the MedEffect™ Canada Web site and by subscribing to MedEffect™ e-Notice. Print versions are available to interested individuals upon request. In addition, in October 2008, highlights of CARN were faxed to hospitals and medical clinics. Summaries of CARN can also be found in various health professional journals.

- To receive CARN free by email, subscribe to Health Canada's MedEffect™ e-Notice.
- To receive print versions of future issues of CARN, contact the CARN Editorial Team
- Electronic versions of the latest issue and previously published issues of CARN are available on the MedEffect™ Canada Web site.

The CARN editorial team would like to take this opportunity to thank CMAJ for the services it has provided over the years.

Quarterly Summary of health professional and consumer advisories (posted on Health Canada’s Web site: Aug. 2 - Nov. 12, 2008)

<table>
<thead>
<tr>
<th>Date</th>
<th>Product</th>
<th>Subject</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nov 10</td>
<td>Foreign products</td>
<td>Foreign product alerts</td>
</tr>
<tr>
<td>Nov 7</td>
<td>Argatroban</td>
<td>Recall of 2 lots</td>
</tr>
<tr>
<td>Oct 28</td>
<td>Eros Fire</td>
<td>Warning not to use Eros Fire or any unauthorized products</td>
</tr>
<tr>
<td>Oct 28</td>
<td>Vitamin C supplements</td>
<td>Warning not to use two vitamin C supplements</td>
</tr>
<tr>
<td>Oct 23</td>
<td>Venlafaxine</td>
<td>Information regarding overdosage of Venlafaxine Extended-Release</td>
</tr>
<tr>
<td>Oct 17</td>
<td>Foreign products</td>
<td>Foreign product alerts</td>
</tr>
<tr>
<td>Oct 6 &amp; 8</td>
<td>Codeine</td>
<td>Information on the use of codeine products, especially by nursing mothers</td>
</tr>
<tr>
<td>Sept 19</td>
<td>Foreign products</td>
<td>Foreign product alerts</td>
</tr>
<tr>
<td>Sept 3</td>
<td>Unauthorized products</td>
<td>Unauthorized health products found on the Canadian market</td>
</tr>
<tr>
<td>Sept 2</td>
<td>Ligating clips</td>
<td>Recall: Teleflex Weck Brand Ligating Clips</td>
</tr>
<tr>
<td>Aug 22</td>
<td>Foreign products</td>
<td>Foreign product alerts</td>
</tr>
<tr>
<td>Aug 21</td>
<td>Life Choice products</td>
<td>Advisory not to use Life Choice Ephedrine and Kava Kava</td>
</tr>
<tr>
<td>Aug 21</td>
<td>Viraicet</td>
<td>Viraicet can be used again in nonpregnant HIV-infected adults and children</td>
</tr>
<tr>
<td>Aug 18</td>
<td>Foreign products</td>
<td>Foreign product alerts</td>
</tr>
<tr>
<td>Aug 14</td>
<td>Acidophilus products</td>
<td>Additional &quot;non-dairy&quot; products posing milk allergy risk</td>
</tr>
<tr>
<td>Aug 11</td>
<td>Foreign products</td>
<td>Foreign product alerts</td>
</tr>
<tr>
<td>Aug 11 &amp; 6</td>
<td>Torisel</td>
<td>Hypersensitivity/infusion reactions</td>
</tr>
<tr>
<td>Aug 8</td>
<td>Acidophilus products</td>
<td>Milk allergy risk identified in &quot;non-dairy&quot; products</td>
</tr>
<tr>
<td>Aug 6</td>
<td>Unauthorized products</td>
<td>Advisory not to use Rize 2 The Occasion Capsules</td>
</tr>
<tr>
<td>Aug 1</td>
<td>Accusol 35</td>
<td>Risk of precipitate formation with Accusol 35 hemodialysis solutions</td>
</tr>
<tr>
<td>July 31</td>
<td>Desmopressin</td>
<td>Nasal spray formulations: risk of hyponatremia and water intoxication</td>
</tr>
<tr>
<td>July 31</td>
<td>Defibrillators</td>
<td>Recall: LifePak CR Plus and LifePak Express defibrillators</td>
</tr>
</tbody>
</table>
Date Modified: 2008-12-30

Date Modified: 06/06/14 11:43

To receive the Newsletter and health product advisories free by e-mail, subscribe to MedEffect™ e-Notice.

Canadian Adverse Reaction Newsletter

Health Canada
Marketed Health Products Directorate
Address Locator 0701C
Ottawa ON K1A 0K9
Telephone: 613-954-6522
Fax: 613-952-7738

Editorial Staff
Ann Sztuke-Fournier, BPharm (Editor-in-Chief)
Ilhemme Djelouah, BScPhm, DIS, AFSA, Medical Biology (University of Paris V)
Gilbert Roy, BPharm
Jared Cousins, BSP
Christiane Scott, BPharm, MBA
Marielle McMorran, BSc, BSc(Pharm)

Suggestions?
Your comments are important to us. Let us know what you think.

Reporting Adverse Reactions
Canada Vigilance Program
Telephone: 1-866-234-2345
Fax: 1-866-678-6789

Copyright
© 2009 Her Majesty the Queen in Right of Canada. This publication may be reproduced without permission provided the source is fully acknowledged. The use of this publication for advertising purposes is prohibited. Health Canada does not assume liability for the accuracy or authenticity of the information submitted in case reports.

Due to time constraints relating to the production of this publication, information published may not reflect the most current information.
ISSN 1499-9447; Cat no H42-4/1-19-1E

Aussi disponible en français.

Caveat: Adverse reactions (ARs) to health products are considered to be suspicions, as a definite causal association often cannot be determined. Spontaneous reports of ARs cannot be used to estimate the incidence of ARs because ARs remain underreported and patient exposure is unknown.