

FDA Public Health Notice

Potential Hypersensitivity Reactions To Chlorhexidine-Impregnated Medical Devices

(You are encouraged to copy and distribute this notice)

March 11, 1998

Dear Health Care Professional:

FDA is informing you about the potential for serious hypersensitivity reactions to chlorhexidine-impregnated medical devices. Because these types of reactions are not well known to device users, and because the full extent of the problem is not yet clear, we are providing you with the information we have to date and encouraging you to report such hypersensitivity reactions to us as they occur. This will help us better evaluate the potential public health hazard these products might pose, and to decide on what action, if any, should be taken.

History of Chlorhexidine Use

Chlorhexidine containing compounds have been used as topical disinfectants since the middle 1970's. An effective antimicrobial agent, chlorhexidine subsequently found use in many antiseptic skin creams, mouth rinses, and disinfectants used to prepare the skin for surgical procedures. Additionally, chlorhexidine may be incorporated in cosmetic products, where it reportedly functions as a cosmetic biocide. In the early 1990's, FDA cleared three types of medical devices that incorporate chlorhexidine in the composition of the device: intravenous catheters, topical antimicrobial skin dressings, and implanted antimicrobial surgical mesh.

Evidence of Hypersensitivity Reactions

Although the antimicrobial properties of chlorhexidine are well known, it is not as well known that chlorhexidine has been associated with hypersensitivity reactions. Anaphylactoid and other types of reactions have been reported with chlorhexidine used topically, intra-urethrally, as a lubricant on urinary catheters, and with chlorhexidine-impregnated catheters. These incidents have occurred in Japan,¹⁻³ Switzerland,⁴ the United Kingdom,⁵ Australia,⁶ Malaysia,⁷ and the United States.^{8,9}

1. Immediate systemic hypersensitivity reactions to chlorhexidine gels/lubricants used during urological procedures

Hypersensitivity reactions associated with chlorhexidine gels/lubricants used during urological procedures have been reported in several countries. (None have been reported thus far in the U.S.) In one case, a 61 year-old man in the Netherlands exhibited a severe allergic reaction associated with a chlorhexidine gel used for an intra-urethral preparation.¹⁰ In another incident in Nedlands, Australia, a 52 year-old man had an anaphylactic reaction to a chlorhexidine lubricant on a urinary catheter While undergoing a temporal lobectomy.¹¹ Six cases of severe allergic reactions to chlorhexidine gel used with urinary catheters have also been reported in Melbourne, Australia.¹²

2. Immediate systemic hypersensitivity reactions to central venous catheters

From communication with the Japanese government, FDA became aware that 13 Japanese patients experienced anaphylactoid type adverse events while using central venous catheters impregnated with

chlorhexidine. Tachycardia, hypotension and complaints of chest pain were reported. One patient subsequently died, although the exact cause of death is unknown. It is not clear why these reactions occurred in Japanese individuals but not in others; possible explanations include an increased exposure to chlorhexidine-containing products resulting in heightened sensitivity, a genetic predisposition to react to this chemical, or some other factor. Sale of these central venous catheters in Japan began in 1996. The adverse events occurred between June 25, 1996, and June 24, 1997. The World Health Organization issued a notice stating that the manufacturer of the central venous catheters voluntarily withdrew the product from the market in Japan on August 19, 1997.¹³ Approximately 117,000 catheters were sold. To date, FDA has not received any reports of immediate systemic hypersensitivity reactions related to central venous catheters for patients in the United States. (Of the 3 million sold worldwide since 1990, 2.5 million were in the U.S.)

3. Other types of reactions

In addition to the immediate systemic hypersensitivity reactions reported with the use of topical chlorhexidine, chlorhexidine gel/lubricant and chlorhexidine-impregnated catheters, other types of reactions have been documented. In one U.S. study, six of 10 neonates weighing under 1000 grams showed local hypersensitivity reactions to chlorhexidine gluconate-impregnated patches used to secure central venous catheters.¹⁴ Severe contact dermatitis in seven neonates with this type of dressing was also reported in another U.S. study.¹⁵ Two cases of occupational asthma in nurses were reported from chlorhexidine and alcohol aerosols,¹⁶ and bradycardia was reported in a neonate associated with a chlorhexidine spray used on the mother's breasts.¹⁷

Recommendations

- If a patient exhibits an unexplained hypersensitivity reaction, check whether chlorhexidine was used or was impregnated in a medical device that was used.
- If you suspect a patient may have (or has had) a hypersensitivity reaction to a drug or medical device that contains a chlorhexidine compound, monitor the reaction carefully, provide immediate respiratory and/or cardiovascular support as needed, and discontinue the use of the drug or medical device as expeditiously as possible.
- As outlined below, please report to us any chlorhexidine hypersensitivity reactions you may discover. This will help us delineate the problem and may help avoid serious reactions in the future.

Reporting Adverse Events to FDA

The Safe Medical Devices Act of 1990 (SMDA) requires hospitals and other user facilities to report adverse events (deaths, serious illnesses and injuries) associated with the use of medical devices. Included in this requirement are hypersensitivity reactions such as those discussed in this Notice. For this type of mandatory reporting, you should follow the procedure established by the hospital with which you are affiliated. Questions about mandatory reporting can be addressed by contacting the Division of Surveillance Systems, Reporting Systems Branch by telephone at (301) 594-2735 or FAX at (301) 827-0038. Written reports will go into FDA's MDR database.

Beyond the requirements of the law, we encourage reporting any adverse reactions associated with chlorhexidine-impregnated medical devices. Even if a report is not mandatory, it may provide important information about why these adverse events are occurring. Please submit voluntary reports directly to

MedWatch, the FDA's voluntary reporting program. Submit these reports to MedWatch: by telephone at (800) FDA-1088, by FAX at (800) FDA-0178, or by mail to:

MedWatch
Food and Drug Administration
HFA-2
5600 Fishers Lane
Rockville, MD 20857-9787

In general, when reporting adverse events, we encourage the inclusion of background information to help in the evaluation of such events. This information might include a patient's general condition, concurrent medications, interventions to resolve the adverse event, and patient's previous exposure to the device.

Getting More Information

If you have any questions about the content of this Public Health Notice, please contact Deborah Yoder, RN, Office of Surveillance and Biometrics, Division of Postmarket Surveillance, HFZ-520, 1350 Piccard Drive, Rockville, Maryland, 20850, FAX (301) 594-1967 or e-mail dyb@cdrh.fda.gov.

You can print additional copies of this notice from the CDRH homepage at www.fda.gov/cdrh/safety.html. If you do not have access to internet and would like additional copies, call (301) 594-3060, FAX (301) 594-2968 or e-mail Marian Zellner mtz@cdrh.fda.gov. If you are interested in receiving future FDA Safety Alerts, Public Health Advisories, and other FDA postmarket safety notifications by e-mail when they are released, subscribe to our list server. To subscribe, visit the page: <http://list.nih.gov/cgi-bin/wa?SUBED1=dev-alert&A=1>

Sincerely yours,

Bruce Burlington, M.D.
Director
Center for Devices and Radiological Health

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