Short title: Chlorhexidine hypersensitivity BP

1. Purpose

The purpose of *PG60(POM) Guideline on the perioperative management of patients with suspected or proven hypersensitivity to chlorhexidine* is to prevent recurrent inadvertent exposure and subsequent hypersensitivity reaction in these patients.

The ANZCA Anaesthetic Allergy Subcommittee was convened in 2012 and works closely with the Australian and New Zealand Anaesthetic Allergy Group (ANZAAG). The subcommittee identified that as chlorhexidine was a very common hidden agent in the theatre environment and it has an increasing frequency of induced anaphylaxis, it warranted a policy in its own right. PG60(POM) has been developed as a 'Guideline' with the long term goal of wide application and endorsement by relevant government bodies, medical colleges and professional associations.

2. Justification

Chlorhexidine (1:6-Di-4'-ChlorophenyldiguanidohexaneChlorhexidine (1:6-Di-4'-Chlorophenyldiguanidohexane) is a broad spectrum antiseptic that is extensively used in healthcare environments. Its many applications in healthcare include well recognised inclusions in antiseptic solutions and gels for the disinfection of skin, but it is also in a large number of other products that may not be as well recognised. Chlorhexidine may be present in lubricants for indwelling urinary catheter insertion, impregnated into central venous catheters, dressings, surgical drapes and other medical devices. It is also widely available in the community in many presentations such as antiseptic hand rubs, mouthwashes, toothpastes and throat lozenges.

Recognition of the efficacy of chlorhexidine has seen its use dramatically increase within hospital environments and in the community in recent years. This has resulted in a problematic situation for those allergic to it. Ready identification of all products containing chlorhexidine is difficult with non-uniform standards of labelling. Frequent changes of products used by, and available to the practitioner, makes the task of avoiding the allergen during the patient's hospital stay particularly difficult. Utility of lists of chlorhexidine containing products are limited by the need for frequent updates to ensure inclusion of all products incorporating chlorhexidine.

In recent times there have been increasing reports of hypersensitivity to chlorhexidine, usually immediate type hypersensitivity (or anaphylaxis). When patients present to a healthcare facility with a history of confirmed or suspected hypersensitivity to chlorhexidine, there are no published guidelines detailing mechanisms to prevent exposure of these patients to chlorhexidine products during their healthcare encounter.

3. Review of the issues concerned

3.1 Increasing recognition of chlorhexidine as an allergen

Chlorhexidine was first developed for use in 1954 by Imperial Chemical Industries (ICI), Manchester, United Kingdom. The first report of cutaneous hypersensitivity was from Calnan in London in 1962[1]. Further reports of anaphylaxis to chlorhexidine originated from Japan, by Okano[2] in 1983 and Nishioka[3] in 1984.

The true incidence of anaphylaxis to chlorhexidine is not known and is almost impossible to calculate. Reasons for this include the absence of mandatory reporting of reactions and the inability to accurately ascertain the total number of exposures to chlorhexidine in all its forms. An additional confounder is that chlorhexidine anaphylaxis is thought to be under-recognised[4].

Helping to conspire against identification as an allergen, chlorhexidine anaphylaxis is typically delayed when absorption occurs across skin or mucosa[5], compared to the majority of perioperative antigens where anaphylaxis manifests within a few minutes of intravenous administration.

While it appears that the incidence of anaphylaxis to chlorhexidine is low (due to the increasing denominator episodes of exposure), the numbers of patients experiencing adverse reactions appear to be increasing[6]. Many case reports and case series of chlorhexidine anaphylaxis are described in the literature[7-50].

A governmental warning was issued in Japan in 1984, prohibiting the use of chlorhexidine on mucosal membranes[8]. Warnings specific to hypersensitivity reactions from chlorhexidine impregnated central devices, such as central venous access devices (CVADs), have also been issued by the Food and Drug Administration[51] in the United States of America and by the Therapeutic Goods Administration in Australia in 2012[52].

Data from New Zealand Centres for Adverse Reaction Monitoring (CARM) shows 69 cases of anaphylaxis had been reported in New Zealand since 2000[53]. The largest published case series is from Auckland where 26 cases of chlorhexidine hypersensitivity were diagnosed between 1998 and 2008[7].

There is no centralised database in Australia for reporting chlorhexidine allergy. However, multiple testing centres affiliated with the Australian and New Zealand Anaesthetic Allergy Group are noting an increase in cases of chlorhexidine anaphylaxis diagnosed. One individual testing centre in Sydney, Australia has a case series of 29 cases of confirmed chlorhexidine anaphylaxis tested between 2007 and January 2015. At this centre chlorhexidine has risen to become the third most common allergen identified to cause perioperative anaphylaxis, after neuromuscular blockers and antibiotics [54].

A finding of additional concern is that multiple patients in this series had more than one episode of anaphylaxis caused by chlorhexidine as a result of failure to identify chlorhexidine as an antigen, or failure to recognise the presence of chlorhexidine in products found in the hospital environment. The findings highlight the need for chlorhexidine-free management guidelines to protect these patients from iatrogenic injury.

3.2 Difficulty in identifying products containing chlorhexidine

Chlorhexidine is increasingly incorporated in antiseptic handrub solutions, gels, pastes, dressings and devices (including central venous catheters and drapes). As such, it is often seen as a hidden or “occult” antigen in the clinical environment. Furthermore, products purchased in hospitals for each application change in accordance with purchasing contracts and evolution of clinical guidelines, particularly infection control recommendations.

The inconsistent labelling of products that contain chlorhexidine also presents a barrier to successful avoidance of these products in allergic patients. There is no universal symbol to ensure it is simple to identify that a product contains chlorhexidine, such as there is for latex. Print outlining product composition is often small and not placed in a prominent or uniform position.

Registers of such products are not an easy solution, but are an important step in ensuring the safe management of chlorhexidine hypersensitive patients. They need to be individually prepared according to the clinical guidelines and purchasing practices in each hospital and frequently updated by each institution.

It is particularly important to understand that whilst a register of chlorhexidine containing products may help identify such products, absence of a product on the register is no guarantee that the product is chlorhexidine-free. A health worker should check every product they use on each occasion of use in patients who have a history to suggest chlorhexidine hypersensitivity to prevent exposure. This is time consuming and laborious but necessary to prevent inadvertent chlorhexidine exposure in allergic individuals.

3.3 Difficulty avoiding contact with chlorhexidine products once identified

During a hospital stay, an individual patient may transition through many departments of a hospital, such as emergency departments, operating theatres, intensive care units, general wards, and radiology. A system of labelling the patient and their immediate environment is necessary to achieve continuity of the knowledge of their allergy status as they progress through the system.

It is often worthwhile to develop a plan, ideally in the pre-admission setting, for anticipated medical procedures that may occur during the patient's hospital stay. This plan can include perceived risks and alternative antiseptics/approaches to procedures. It is essential that non-chlorhexidine alternatives are maintained as standard stock in all clinical environments within hospitals to ensure safe care for these patients.

The patient should be educated regarding their chlorhexidine hypersensitivity and advised to notify each new staff member wherever possible.

Simple measures should be taken to isolate the patient from common forms of chlorhexidine exposure. For example, they should be housed in single rooms wherever possible, with all chlorhexidine products removed from the immediate environment and replaced with chlorhexidine-free alternatives.

4. Summary

Chlorhexidine is an excellent antiseptic agent that may occasionally cause anaphylaxis. Though anaphylactic reactions to chlorhexidine are uncommon, it is an increasingly prevalent allergen in the perioperative setting.

Exposure to chlorhexidine in the clinical environment is routine. Avoidance of recurrent anaphylactic reactions should begin with the identification and substitution of all products containing chlorhexidine. Careful planning and implementation is required to prevent inadvertent exposure to chlorhexidine in the sensitised patient as they move throughout the hospital system.

Related ANZCA documents

PG60(POM) Guideline on the perioperative management of patients with suspected or proven hypersensitivity to chlorhexidine

PG28(A) Guideline on infection control in anaesthesia

Document Development Group

The ANZCA Safety and Quality Committee acted as the document development group and delegated the task to the Anaesthetic Allergy Subcommittee as the expert panel.

Expert panel

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