Combating chlorhexidine allergy in perioperative setting

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ABSTRACT

Chlorhexidine is labelled as hidden allergen as the health care professionals (HCPs) are unaware of the wide range of products containing chlorhexidine. Adverse events from chlorhexidine allergy can be reduced by appropriate perioperative management especially heeding on positive history during preoperative assessment, awareness regarding this hidden allergen, and educating HCPs on possible chlorhexidine-containing products. The regulatory agencies all over the world have issued recommendations regarding safety and risk of hypersensitivity reactions with chlorhexidine-containing products. The onus lies on HCPs to disseminate this knowledge to the stakeholders. We present a brief update to combat chlorhexidine allergy in perioperative setting.

INTRODUCTION

Chlorhexidine, an antiseptic with antibacterial, some antiviral, and antifungal activity is a synthetic bisbiguanide, binding well with cutaneous proteins accounting for its prolonged antiseptic effects.[1] It is widely used in health care setting worldwide and has become ubiquitous in the perioperative setting. It is found in surgical skin preparation solutions, skin wipes, lubricant gels for urethral catheterisation, vaginal and rectal examination. It has also been impregnated into central venous catheters (CVCs) and other medical devices in wound dressings, throat gargles/mouthwashes, toothpastes, contact lens solutions and cosmetics.[2] Malaysia alone has 47 products containing chlorhexidine registered with the Drug Control Authority (DCA) in various dosage forms, such as creams, lotions, gels, scrubs, solutions, mouthwashes and lozenges.[3]

Due to its widespread use, the incidence of allergic reactions is on the rise though the true prevalence of chlorhexidine allergy remains unknown. It has been labelled as the "hidden allergen" in health care setting.[4]

Adverse reactions to chlorhexidine range from mild cutaneous reactions to anaphylaxis and involve both immediate and non-immediate hypersensitivity. The most common allergic reactions, T cell-mediated, type IV hypersensitivity reactions, described are delayed. Contact dermatitis is the most frequent manifestation after topical use. Immediate IgE-mediated and type I hypersensitivity reactions have also been reported though less frequently. The symptoms range from urticaria to anaphylaxis with cardiorespiratory arrest and death.[2,4]

The National Pharmaceutical Regulatory Agency (NPRA), Ministry of Health, Malaysia, reported 55 adverse events and 29 reports suspected to be related to chlorhexidine-containing products, majority of which involved rash, pruritis and skin irritation and four cases developed anaphylaxis/anaphylactic shock. The NPRA has issued a safety directive concerning chlorhexidine that all local package inserts and labels of products containing chlorhexidine be updated with information on risk of hypersensitivity reactions.[3] Various other international regulatory bodies have issued warnings for chlorhexidine-containing products and devices.[5]

The anesthesiologists widely use chlorhexidine in the perioperative setting for the skin preparation for central and peripheral blocks and venous canulation, central venous lines impregnated with chlorhexidine and local anesthetic and lubricant jelly. The international guidelines recommend that chlorhexidine in alcohol should be used for skin antisepsis before performing central neuraxial blockade (CNB) and peripheral nerve blocks.[6]

In the largest UK study of anaesthetic hypersensitivity reactions, the 6th National Audit Project (NAP6), chlorhexidine accounted for 9% of cases and third most prevalent cause of anaphylaxis after antibiotics and neuromuscular-blocking agents, the overall estimated incidence being 0.78 per 100,000 exposures. One case of chlorhexidine-induced anaphylaxis was fatal. Three cases were potentially avoidable by heeding a relevant history.[7] The routes of exposure of chlorhexidine included skin preparation for peripheral cannulation, neuraxial block or surgery, coated CVC and urethral gel. Majority of cases had two to three routes of exposure. None had exposure via skin preparation for peripheral venous cannulation only.[7]

Life-threatening anaphylaxis is commonly associated with mucosal and parenteral exposure and less often through intact skin.[6,8,9] Severe anaphylactic reactions are usually preceded by milder non-specific reactions, often dismissed by patients as well as doctors.[9,10]

We present ways to prevent chlorhexidine-induced morbidity and mortality during perioperative management.[6,7,9]

PREOPERATIVE MANAGEMENT

A detailed history pertaining to allergy status during preoperative assessment is essential. History of localised reactions post-exposure may indicate possibility of severe

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systemic reactions on subsequent exposures. Studies have shown that most patients diagnosed with chlorhexidine allergy had already reported a possible chlorhexidine allergy that could have been confirmed prior to the adverse event. Thus, perioperative morbidity and mortality can be reduced by thorough history taking and evaluation.[7]

The specific history should include allergy-type symptoms during previous medical or dental procedures or when using hygiene products at home or at work especially history of itch, rash or redness following preoperative antiseptic body wash, cannulation or venesection. If the previous reaction is not investigated, patient should be referred to allergy clinic for further investigation.

Preoperative assessment for chlorhexidine allergy are not yet standardised. Testing includes skin prick test, intradermal tests and blood tests for allergen-specific IgE and basophil activation performed within 6 months of exposure due to a decrease in IgE levels subsequently with time. Due to unclear reasons, patients with chlorhexidine allergy show positive allergy tests to neuromuscular blocking agents, latex, opioids and beta-lactam antibiotics.[7]

A high index of suspicion with a positive history of allergy is vital. Prevention is better than cure. The allergens should be avoided with the use of readily available alternatives. For instance, using povidone-iodine for skin preparation and alcohol-based swabs for venepuncture.

For CNB, 0.5% chlorhexidine solution in alcohol is preferred to 2% chlorhexidine solution due to the lack of convincing evidence of the antimicrobial superiority of 2% solution and clear evidence of its neurotoxicity. Meticulous measures should be taken to prevent chlorhexidine from reaching cerebrospinal fluid. Chlorhexidine should be kept away from drugs and not be poured into containers on or near the same surface as CNB equipment. The operator should check for contamination of his gloves and equipment. The solution should be allowed to dry before skin puncture.[6]

INTRAOPERATIVE MANAGEMENT

During the intraoperative period, continuous vigilant monitoring of the patient can detect early signs, and timely management can prevent untoward consequences. The clinical features include hypotension, tachycardia, non-urticarial and urticarial rash, desaturation, bronchospasm, unwell feeling, angioedema, nausea/vomiting, bradycardia, laryngeal edema and cardiac arrest. Management includes discontinuation of exposure with standard resuscitative measures and anaphylaxis management. Resuscitation drugs such as adrenaline, hydrocortisone and antihistamines have been reported in cases with successful treatment.[9]

POSTOPERATIVE MANAGEMENT

Postoperatively, the patient should be kept under observation and thoroughly investigated for possible allergens. During hospital stay, "allergy alert" sign should be attached to the front door and charts of the patient. Any patient with possible warning features should be referred to allergy clinic for further investigation.

The patient should be issued a wristband or pocket card as an allergy alert upon discharge. They should be educated on allergy and possible allergens together with the family members. List of easily available alternatives should be provided.

We suggest educating HCPs about this hidden allergen and creating awareness among HCPs and public on chlorhexidine allergy.

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