



SHORT REPORT

Allergic contact reaction to antiseptics in very young children

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Abstract

Background Contact dermatitis from topical antiseptic use has been reported mostly in adults, but rare cases of chlorhexidine contact dermatitis have also been described in young children.

Objective To evaluate contact allergic dermatitis to antiseptics in young children.

Methods The children mostly referred for a misdiagnose (cellulitis) were patch tested with a selection of the European baseline series, an antiseptics series and the personal topical products used.

Results Fourteen children (8 boys, 6 girls) received a diagnosis of contact dermatitis to antiseptics between May 2010 and December 2017. The mean age at diagnosis was 38 months (8 months to 8 years); three children only had a personal history of atopy. Chlorhexidine gluconate was positive in seven cases, and benzalkonium chloride in eight cases, and in four cases, both allergens were positive.

Conclusion These small case series confirm that both chlorhexidine and benzalkonium chloride are implicated in contact dermatitis from antiseptic use in the paediatric population. We emphasize the initial misdiagnose of these patients, the very young age of the children and the allergenic potential of common antiseptics in non-atopic children. We hypothesize that the systematic use of antiseptics for umbilical cord care could be responsible for the sensitization in newborns.

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Conflicts of Interest

None declared.

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None declared.

Introduction

Antiseptics are widely used for their antibacterial and antiviral properties on healthy and damaged skin and mucous membranes. Commonly used topical antiseptics belong to four different chemical classes: iodine compounds, chlorine compounds, biguanides (chlorhexidine gluconate) and alcohols (ethanol). In Europe, chlorhexidine gluconate is one of the most used biocide,¹ especially in the commercial form Biseptine®, a water solution combining chlorhexidine gluconate 0.25%, benzalkonium chloride 0.025% and benzyl alcohol 4%. Contact dermatitis from antiseptic use, mostly chlorhexidine gluconate, is widely described in the adult population, specifically in medical care workers and in leg ulcer patients.² In children, sensitization to chlorhexidine has been reported mostly in atopic dermatitis patients.³ Only, two cases of chlorhexidine contact dermatitis have been described in non-atopic children under 4 years of age.^{4,5}

Materials and methods

Between May 2010 and December 2017, the patients were referred for patch testing at the Pediatric Dermatology allergy unit because of a strong suspicion of contact dermatitis from antiseptics use. As a standard commercially paediatric patch test series is not available, children were patch tested with an 'in-house' children standard series (selection of allergens of the European baseline series), an antiseptic series including chlorhexidine gluconate and benzalkonium chloride (*Chemotechnique Diagnostics, Malmö, Sweden*) (Table 1) and with the commercial topical products used. Patch tests were applied on the child's back, in plastic tests chambers (IQ Ultra™, Chemotechnique Diagnostics, Belgium) and maintained with an adhesive tape URGODERM (URGO, Chenôve, France). Commercial topical products were tested at the concentration used. Reading was performed at Day 2 and Day 3 according to the

Table 1 'In-house' children standard and antiseptic series

Children standard series	Concentration (% in petrolatum)
Potassium dichromate	0.5
Neomycin sulphate	20.0
Thiuram mix	1.0
Cobalt chloride hexahydrate	1.0
Formaldehyde	1 (% in aqua)
Colophonium	20.0
Peru balsam	25.0
Lanolin alcohol	30.0
Paraben mix	16.0
Para-tertiary-butylphenol formaldehyde	1
Fragrance	8
Methylisothiazolinone + Methylchlorisothiazolinone	0.01 (% in aqua)
2-Mercaptobenzothiazole	0.5
Nickel sulphate hexahydrate	2.5
Tixocortol-21-pivalate	0.1
Thimerosal	0.1
Budesonide	0.01
Hydrocortisone-17-butyrate	1.0
p-phenylenediamine	1.0
Fusidic acid sodium salt	2.0
Cocamidopropyl betaine	1.0 (% in aqua)
Children antiseptic series	
Amerchol L101	50.0
Chlorhexidine digluconate	0.5 (% in aqua)
Propylene glycol	5.0
Stearyl alcohol	30.0
Cetyl alcohol	5.0
Cocamidopropyl betaine	1.0 (% in aqua)
Phenoxyethanol	1.0
Methyldibromo glutaronitrile	0.5
3-Dimethylamino-1-propylamine	1.0 (% in aqua)
Hydrocortisone-17-butyrate	1.0
Fusidic acid sodium salt	2.0
Benzalkonium chloride	0.1 (% in aqua)
Cetearyl alcohol	20.0
Eosin	5.0
Triethanolamine	2.0
Sorbitan sesquioleate	20.0

criteria of the International Contact Dermatitis Research Group (ICDRG).

Results

Fourteen children, eight boys and six girls, with a mean age of 38 months (8 months to 8 years) were included; three children had a history of atopy, one had atopic dermatitis and food allergies to shrimp and hazelnut, and the two others had asthma. Of 14 children, nine were initially misdiagnosed by their general practitioner (GP) or paediatricians for bacterial cellulitis, mostly

located to the face, treated with antiseptics and topical or systemic antibiotics. The right diagnosis of contact dermatitis was later made by the dermatologist (Fig. 1).

Among those 14 patch tested children, Biseptine[®], the leading commercial antiseptic topical product, was tested in 11 children and was positive in 10 cases. Seven children had a positive patch test for chlorhexidine gluconate, eight for benzalkonium chloride and four were positive to both allergens (Fig. 2 and Table 2). Two patients, negative for chlorhexidine gluconate and benzalkonium chloride, were positive to Biseptine[®]. Five children presented, in addition, positive reactions to allergens of the standard series such as Fragrance Mix1, balsam of Peru, nickel sulphate, potassium dichromate or rarely paraphenylenediamine or mercaptobenzothiazole; these additional standard tests were not relevant for the actual diagnosis (Table 2).

Discussion

Most of the children were referred at the Pediatric Emergency Unit by their paediatrician or GP for a misdiagnosis of cellulitis, but the absence of systemic symptoms, fever and lymphadenopathy, helped the paediatric dermatologists to make the correct diagnosis.⁶

Contact dermatitis to antiseptics in the adult population is well documented, with a sensitization rate estimated to 2% in healthcare workers^{7,8} and up to 20% in patients treated for leg ulcers.² In the paediatric population, limited data concern only atopic children. Mailhol *et al.*³ showed in 2009 that 2.7% of atopic children <16 years old were allergic to chlorhexidine. Only,

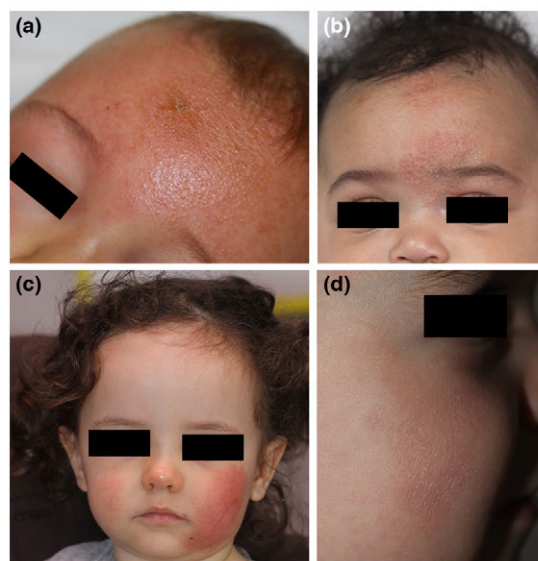


Figure 1 Contact dermatitis to antiseptics misdiagnosing a bacterial dermatitis. (a) patient number 5. (b) patient number 9. (c) patient number 8. (d) patient number 6.

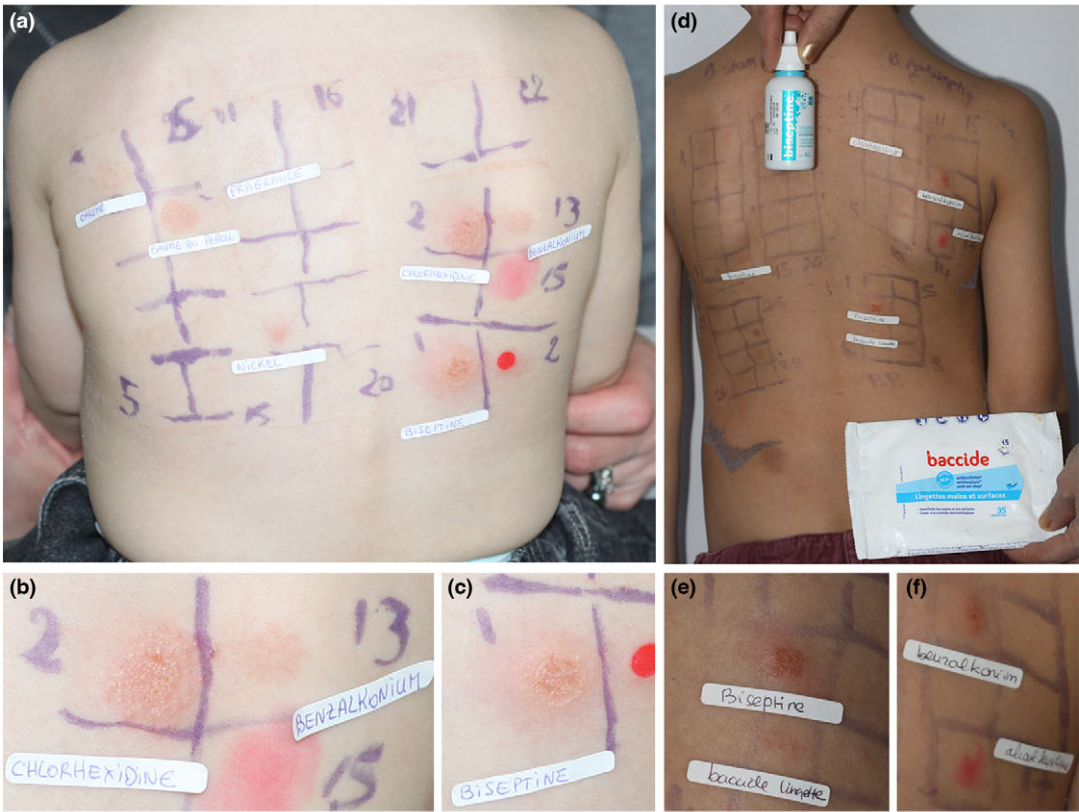


Figure 2 Examples of positive patch tests. (a), (b), (c) patient number 6. (d), (e), (f) patient number 14.

Table 2 Results of patch tests performed (14 children)

Results of patch tests performed (n = 14)	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Chlorhexidine gluconate	–	+	+	–	NT	++	++	–	+	–	++	–	+	–
Benzalkonium chloride	–	++	–	+	NT	+	++	++	–	–	–	+	+	++
Biseptine®	++	++	NT	+	+	++	NT	NT	++	++	++	+	–	++
Others positive patch tests	MP FM1			MBT		MP FM1 Ni Cr				MP FM1 Cr		Ni MBT	Ni neomycin	

Cr, potassium dichromate; FM1, fragrance mix 1; MBT, mercaptobenzothiazole; MP, myroxylon pereirae; Ni, nickel sulphate; NT, non-tested; –, negative patch test result; +, positive patch test result.

two cases of contact dermatitis to chlorhexidine in non-atopic children have been reported. The first case was published in 2008 in a multihospitalized 4-year-old child with a positive patch test to chlorhexidine.⁴ We published the second case in 2010 in a 23-month-old child with a positive patch test to chlorhexidine and to biseptine.⁵ With this small series, we confirm the possibility of a very early sensitization to antiseptics in non-atopic children with a mean age of 38 months at diagnosis.

Firstly, we emphasize the major implication of chlorhexidine gluconate in allergic contact dermatitis of young children. Secondly, we demonstrate the role of benzalkonium chloride. Benzalkonium chloride is an allergen of growing importance in the adult population⁹ and was added consequently to the standard adult series in 2008. Until now, no contact dermatitis to benzalkonium chloride has been reported in children, whereas benzalkonium chloride is an important irritant. Our results, including

only true-positive allergic patch test reactions, suggest that benzalkonium chloride is also a sensitizer in the young population and should be added to the children antiseptics series.

Two children had positive patch tests to the commercial topical Biseptine[®], whereas they were negative both to chlorhexidine gluconate and benzalkonium chloride. Biseptine[®] contains three compounds: chlorhexidine gluconate, benzalkonium chloride and benzyl alcohol. In our 'in-house' antiseptics children series designed in 2010 (Table 1), we did not add benzyl alcohol. We hypothesize that these two children were allergic to benzyl alcohol. As a consequence, we decided to test benzyl alcohol systematically in our new antiseptics children series since 2017, but no positive test has been recorded so far. The possibility of false-negative reactions could also be discussed because of the lack of late readings (Day 7), but late reading is not currently recommended for these allergens.

A large study demonstrated in industrialized countries that a systematic use of antiseptics is not necessary to decrease septic risk in neonates in contrast to not industrialized countries.^{10–12} This prompted us to review the neonatal care data in our patients, and for six children of our series, we identified a long delay of umbilical cord healing. We suggest that the systematic use of antiseptics, such as Biseptine[®], could be a mode of percutaneous sensitization in some children. Water and soap for umbilical cord care seem sufficient to prevent septic risk in industrialized countries.

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