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Acrylic Allergy:

A Problem Related to Adhesives for Sensors and Insulin Infusion Systems

Glucose sensors and insulin infusion systems are devices that allow continuous and dynamic measurement of glucose levels and insulin administration, thus reducing the incidence of hypoglycemia and improving the quality of life and disease control in people with diabetes mellitus. Although they are a convenient and safe option for the treatment of this condition, these devices contain metals, rubber additives, adhesives, and dyes, which may not be entirely harmless to health due to prolonged skin contact with the sensor and the repeated application of adhesives for usage cycles of up to 14 days (1, 2, 3).

Although **contact dermatitis** is a rare condition in the Spanish pediatric population, it has been more frequently described in recent years in children diagnosed with diabetes mellitus who use these devices, with eczema being the most commonly reported dermatological adverse reaction related to it (4).

In these devices, allergens can be present both in the adhesive used and in the device per se, leading to reactions ranging from mild symptoms such as redness or localized itching at the contact area to more severe reactions with the appearance of blisters, yellowish exudate, or generalized reactions (5).

In 2017, coinciding with the market introduction of a new portable glucose monitor, **isobornyl acrylate** (IBOA) was first described by dermatologists from Belgium and Switzerland as the causative allergen in reactions caused by this type of device, followed by other allergens such as different acrylates and methacrylates and colophony (6, 7).

IBOA is a low molecular weight acrylic monomer present in coatings, paints, dyes, plastics, and adhesives. Initially, it was believed that reactions to IBOA were irritative since the standard **epicutaneous test** allergens available on the market yielded negative results. Additionally, it was thought that IBOA did not have the potential to cause allergic sensitization. It is now known that its allergenic effect had been underestimated (6, 8), and it has been identified as the primary allergen in most cases of contact dermatitis caused by glucose sensors and insulin pumps. For this reason, in 2020, it was named Allergen of the Year by the American Contact Dermatitis Society (1, 2). Isobornyl does not cross-react with other **acrylates** and, as mentioned, is not routinely included in the standard battery of allergens for epicutaneous patch tests (9).

It is crucial, not only for the manufacturing companies of these devices but also for public health, to identify the potential allergens present in these devices and to search for possible solutions to prevent initial sensitization and the occurrence of allergic reactions such as contact dermatitis and its complications (1).

We present 13 cases of contact dermatitis associated with portable glucose monitoring devices in our center. The patients had a median age of 13 years (range, 5–17 years) and were referred by the Endocrinology service for presenting eczematous lesions in the area of insertion of the portable insulin infusion system and/or the glucose monitoring device ***(Figure 1)***. »

ACRYLATES ARE WIDELY USED SYNTHETIC PLASTICS AND ARE SIGNIFICANT CAUSATIVE AGENTS OF CONTACT DERMATITIS IN PATIENTS WITH GLUCOSE MONITORS AND INSULIN INFUSION SYSTEMS

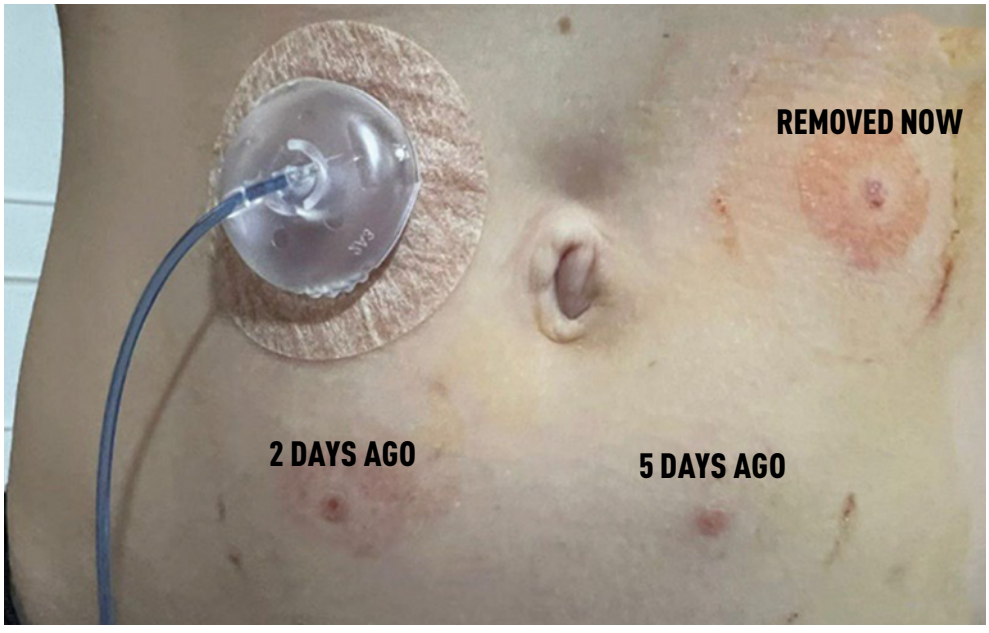


FIGURE 1: Lesions at different progression stages after removal of the cannula.

SENSITIZATION TO ISOBORNYL HAS INCREASED SINCE ITS USE IN THESE SYSTEMS BEGAN. TO IDENTIFY THE RESPONSIBLE SUBSTANCE, IT IS NECESSARY TO CONDUCT AN ALLERGY STUDY USING PATCH TESTS WITH STANDARDIZED ACRYLATE EXTRACTS

TABLE 1. Patients and devices used

	AGE (YEARS)	GENDER	AD	START OF USE	DURATION OF USE UNTIL ECZEMA ONSET (MONTHS)	TIEMPO DE USO HASTA INICIO DEL ECCEMA (MESES)
1	15	F	Yes	Dexcom G6	July 2023	6
2	6	M	Yes	Dexcom G6	May 2023	8
3	8	F	Yes	Dexcom G6	July 2023	5
4	4	F	No	Dexcom G6	February 2023	14
5	13	F	Yes	Dexcom G6	March 2024	10
6	12	F	No	Dexcom G6	June 2023	10
7	16	M	No	Dexcom G6	February 2023	12
8	4	F	No	Dexcom G6	May 2023	7
9	17	F	No	Dexcom G6	October 2023	1
10	7	M	No	Dexcom G6	February 2023	10
11	15	M	No	Medtronic	October 2022	4
12	14	F	No	Freestyle Libre	July 2023	5
13	10	M	No	Freestyle 3	October 2023	3

AD: Atopic Dermatitis; F: Female; M: Male

» Of the 13 patients, 10 were using the Dexcom G6 monitoring device, one the Freestyle3, 1 the Freestyle Libre, and 1 the Medtronic device. All patients were using the YpsoPump insulin pump.

The median time from the start of device use to the onset of eczema lesions was 8 months (range, 1–14). A total of 30.8% of these patients (4/13) had a past medical history of atopic dermatitis ***(Table 1)***.

Patch epicutaneous tests were performed using an acrylate battery (MA-100 Series of (met)acrylate: adhesives, dental, and others, Chemotechnique Diagnostics, Vellinge, Sweden) ***(Table 2)*** and a standard battery (TruTest 36, Martí Tor, Cervelló, Spain), with readings 48-72 and 96 hours after application. Tests with the standard battery have been performed so far in 23.1% (3/13) of the patients. In the rest, the tests are pending after the acrylate battery was first applied, as there was no free skin available to apply them at the same time. One patient also underwent testing with the direct application of adhesives used with the devices.

All 13 patients tested positive for IBOA (No. 16) from the acrylate battery at both 48 and 96 hours ***(Table 3)***. In 38.5% (5/13) of the patients, tests were also positive for other acrylates (1, 4-Butanediol dimethacrylate, Tetrahydrofurfuryl methacrylate, Ethyl acrylate, 2, 2-bis (4-(2-Methacryl-oxyethoxy) phenyl) propane (BIS-EMA), 1, 4-Butanediol diacrylate, Di (ethylene glycol) diacrylate, Triethylene glycol diacrylate, and Butyl acrylate). As an example of the results, ***Figure 2*** shows the acrylate tests for patient #10 and patient #12. In 66.7% (2/3) of the patients, tests with the standard battery were positive. In patient #8, for colophony, and in patient #13, for Cl+-Me-Isothiazolinone in the readings performed at 72 hours. »

TABLA 2. Listado de antígenos de la batería MA-100 Series de (met)acrilato

ART. NO	NAME	CONCENTRATION
1	Methyl methacrylate	2,0% pet
2	BUTYL METHACRYLATE	2,0% pet
3	2-Hydroxyethyl methacrylate	2,0% pet
4	Hydroxypropyl methacrylate	2,0% pet
5	Ethylene glycol dimethacrylate	2,0% pet
6	Triethylene glycol dimethacrylate	2,0% pet
7	1,4-Butanediol dimethacrylate	2,0% pet
8	Urethane dimethacrylate	2,0% pet
9	Bisphenol A dimethacrylate (BIS-MA)	2,0% pet
10	Bisphenol A glycerolate dimethacrylate (BIS-GMA)	2,0% pet
11	1,6-Hexanediol diacrylate	0,1% pet
12	Tetrahydrofurfuryl methacrylate	2,0% pet
13	Tetraethylene glycol dimethacrylate	2,0% pet
14	DIMETHYLAMINOETHYL METHACRYLATE	0,2% pet
15	ETHYL CYANOACRYLATE	10,0% pet
16	ISOBORNYL ACRYLATE	0,1% pet
17	Ethyl acrylate	0,1% pet
18	2-Hydroxyethyl acrylate	0,1% pet
19	ETHYL METHACRYLATE	2,0% pet
20	2,2-bis(4-(2-Methacryl-oxyethoxy) phenyl)propane (BIS-EMA)	2,0% pet
21	1,4-Butanediol diacrylate	0,1% pet
22	Di(ethylene glycol) diacrylate	0,1% pet
23	Tri(propylene glycol) diacrylate	0,1% pet
24	Trimethylolpropane triacrylate	0,1% pet
25	Triethylene glycol diacrylate	0,1% pet
26	N,N-Methylene-bisacrylamide	1,0% pet
27	Butyl acrylate	0,1% pet

TABLA 3. Pruebas epicutáneas con baterías estándar y de acrilatos.

	DEVICE	TRUTEST 36	ACRYLATE SERIES MA-100
1	Dexcom G6	Pending	48h: nº16 ++ 96h: nº16 +++
2	Dexcom G6	Pending	48h: nº16 ++ 96h: nº16 +++
3	Dexcom G6	Pending	48h: nº16 ++++, nº24 + 96h: nº16 ++
4	Dexcom G6	Pending	48h: nº16 ++ 96h: nº16 +++, nº20 +
5	Dexcom G6	Pending	Pending
6	Dexcom G6	Pending	48h: nº16 ++ 96h: nº16 ++
7	Dexcom G6	48h and 72 h: Negative	48h: nº7 ++, nº12 ++, nº16 ++ 96h: nº7 +, nº12 + y nº16 +
8*	Dexcom G6	48h: Negative 72h: nº7 ++	48h: nº16 ++ 96h: nº16 +++
9	Dexcom G6	Pending	48h: nº 16 ++ 96h: nº 16 +
10	Dexcom G6	Pending	48h: nº16 ++ 96h: nº16 ++
11**	Medtronic	Pending	48h: nº16 ++, nº17 ++ 96h: nº16 ++, nº17 ++.
12	Freestyle Libre	Pending	48h: nº 7, 12, 13, 16, 21, 22, 25: ++ Nº 17, 18 y 27 + 96h: nº 12, 16, 22 y 25 ++, nº21 y 27 +
13	Freestyle 3	48h: nº17++ y nº2 + 72h: nº17 +	48h: nº16 ++ 96h: nº16 ++

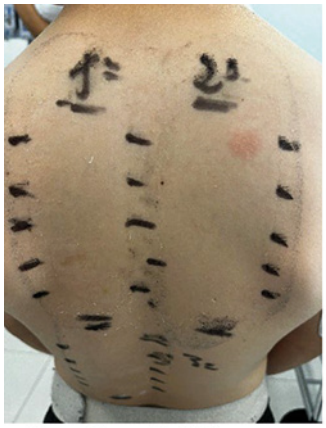
*In patient #8, 2 pieces of tape used in sensors were also tested: 1 used in Medtronic sensor (negative) and the other in Mylife sensor (positive, with erythema and small vesicles).

**In patient #11, previous tests were conducted in 2022 with Freestyle Libre and Dexcom G6 sensors, both positive.

» A total of 23.1% (3/13) of the patients had previously used other devices and also presented eczema lesions. Patient #8 had used Medtronic, patient #13 had used Freestyle Libre and Freestyle 2, and patient #11 had used Freestyle and Glucomen day CGM. The remaining patients had maintained the same device since the beginning, receiving treatment with topical corticosteroids or with hydrocolloid dressings as a barrier isolating agent. Despite this, they continued to present eczema lesions, although milder.

DISCUSSION

Throughout history, contact dermatitis caused by acrylates and methacrylates has been described in relation to occupational exposure, dental products, acrylic nails, and wound dressings. Generally, contact dermatitis reactions from the use of glucose monitoring devices were rarely reported; however, in the past 10 years, the number of diagnosed and published cases has increased. In most patients, lesions have been described in the contact area with the adhesive of devices from various brands available on the market (Freestyle Libre from Abbot, Mi- »



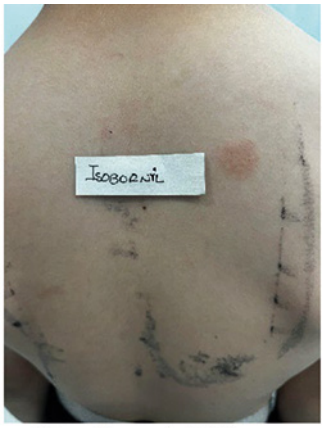
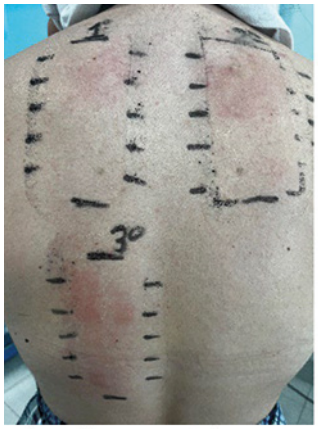


FIGURE 2. A: Patient #10. Reading at 48 and 96 hours. Positive for IBOA.



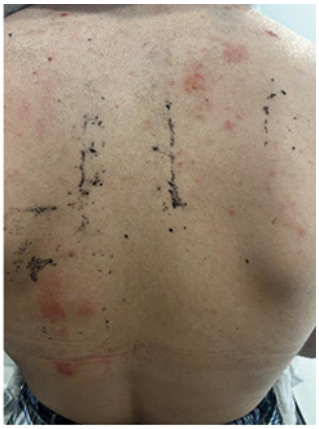


FIGURE 2. B: Patient #12. Reading at 48 and 96 hours. Positive tests for IBOA (upper right lesion) and other acrylates (see Table 3).

» nimed from Medtronic, Dexcom G6 from Dexcom, and Omnipod from Insulet Corporation). Within the complex mixture of acrylates used in these devices, isobornyl acrylate (IBOA) has been identified as the most frequent causal allergen (1).

Upon analyzing these devices, it has been described that IBOA is not present in the adhesive patch but in the glue used to join the upper and lower parts of the sensor. The antigen moves by drag to other parts of the sensor, eventually being detected in the plastic part that contacts the patient's skin. However, there are described cases of patients with very positive epicutaneous tests for IBOA who test negative for the adhesive and the plastic support material of the device. This suggests that the concentration of IBOA in these components must be minimal (5, 9). Despite IBOA being the most common responsible antigen, it should be considered that the adhesive per se may cause contact dermatitis due to other acrylates and methacrylates (10).

The incidence of contact dermatitis in users of these devices can reach up to 79% in some series, requiring device replacement due to poor tolerance in most cases. Eczema lesions may appear weeks or months after the initial contact, generating sensitization that will accompany the patient throughout their life, with similar eczema reactions after each new exposure (2,7). In a series of 6 cases aged 6-13 years, the onset of dermatitis after first device use ranged from 1-24 months (5), a period that includes the latency observed in our series.

Among the risk factors for contact dermatitis, in addition to the antigen dose and exposed area, the time and duration of exposure are crucial. This fact has been confirmed in patients who could not tolerate monitoring devices requiring up to 14-day applications but tolerated insulin pumps, which required shorter exposure times (6). Also, the presence of epidermal barrier alterations and chronic skin inflammation should be considered as risk factors or facilitators. Therefore, patients with atopic dermatitis or chronic eczema may have a higher risk of developing contact dermatitis from some components of these devices. In our case, up to 30% of patients had a history of atopic dermatitis.

When performing epicutaneous tests, it is important to note that there is no cross-reactivity between IBOA and other acrylates, as their chemical structures are different; however, sensitization to various acrylates may occur concomitantly (4,10). In our series, 100% of patients had a positive test for isobornyl acrylate at both 48 and 96 hours, a higher frequency than reported in other studies. Positive tests for other acrylates were also found in 38% of the cases.

New versions of some of these devices free of IBOA have been created; however, reactions continue to be reported after their use in some patients, although with good tolerance in those who were allergic to IBOA. In the analysis of the new device, a new substance called butylhydroxytoluene (BHT) was found as a potential causal agent. This substance has been previously described as responsible for contact dermatitis from cosmetics and drugs, although only at high concentrations (6).

Treatment strategies for patients with contact dermatitis from glucose sensors and insulin infusion systems include the application of emollients or skin dressings, as well as topical corticosteroids or calcineurin inhibitors locally, although there is concern that these may interfere with the proper functioning of the sensor and device. It has also been described that the use of dressings like Compeed, Stomahesive (Convatec), or hydrocolloid dressings may help prevent allergens from the device from penetrating the skin without affecting the sensor's performance. However, in most cases, eczema lesions are not entirely prevented, often remaining mild. D

CONCLUSIONS

Acrylates are synthetic plastics widely used and are important causal agents of contact dermatitis. Sensitization to isobornyl acrylate has increased since its introduction in glucose sensors and insulin infusion systems. To identify the responsible substance, it is necessary to perform epicutaneous tests with standardized acrylate extracts. Epicutaneous tests conducted only with the adhesive of the device are associated with false negatives.

At the time of diagnosis, it should be considered that some of the epicutaneous test batteries available (standard, adhesive and plastic, or acrylate batteries) do not include isobornyl or methacrylates among their allergens. Therefore, to ensure proper investigation of each case, test batteries that include these compounds should be developed.

The treatment of contact dermatitis caused by antigens from components of devices that cannot be removed involves creating skin barriers to limit contact.

Doctors should be aware of the possibility of allergic skin reactions when using these monitors and devices, as well as the need to refer to Allergy specialists for further study.

Lastly, the presence of some of these substances is not included among the components listed on the packaging of these devices. This limits the identification of the causal agent(s) and, on the other hand, complicates the selection of alternative materials once a diagnosis is made. Health authorities must ensure the continuous monitoring of substances used in the manufacturing of these devices, their proper identification, as well as the detection of new allergens to enhance surveillance of new cases.

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