

Allergic contact dermatitis to IBOA in FreeStyle Libre: Experience from a tertiary care Portuguese hospital

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Diabetes mellitus (DM) is a chronic condition, the prevalence of which is increasing in Europe.¹ Continuous glucose monitoring systems, such as FreeStyle Libre (Abbott Diabetes Care, UK) have improved DM management.² This device is applied to the skin through an adhesive and remains in place for up to 14 days, dynamically measuring interstitial glucose levels.³ Several cutaneous side effects have been recognized since its introduction, such as infections, hematomas, and irritant or allergic contact dermatitis (ACD).^{4,5} Regarding ACD, the most commonly identified culprit allergen is isobornyl acrylate (IBOA; CAS no. 5888-33-5). This study describes cases of contact dermatitis caused by glucose sensors in a tertiary care Portuguese hospital.

METHODS

Overall, 10 patients with cutaneous reactions to the glucose sensor FreeStyle Libre were included in the study, along with 20 controls. All patients with cutaneous reactions were using first-generation Freestyle Libre, the only reimbursed glucose monitoring device available in Portugal. Patients were tested with the Portuguese baseline series, an acrylates and plastic and glues series (Chemotechnique Diagnostics, Vellinge, Sweden), and with IBOA, purchased from Sigma-Aldrich and diluted 0.1% pet. Patch tests were applied on the upper back with IQ Ultra test chambers from Chemotechnique Diagnostics, remaining under occlusion for 2 days. Readings were performed on day (D) 2 and D4, according to ESCD criteria.⁶



FIGURE 1 ACD to FreeStyle Libre—clinical picture. ACD usually presents as a papulosquamous reaction in the area of contact with the allergen

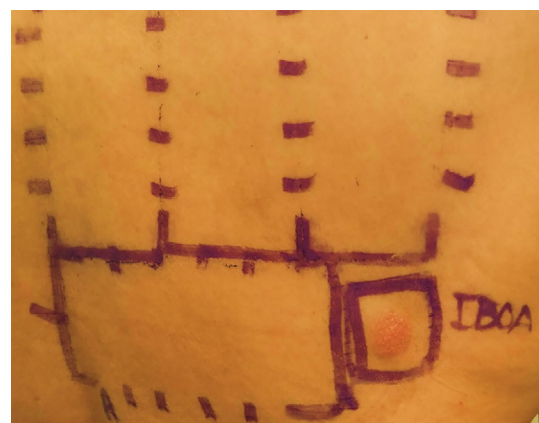


FIGURE 2 ACD to FreeStyle Libre—patch test results. Strong reaction to IBOA, characterized by erythema, infiltration, and vesicles

TABLE 1 Patient characteristics and patch tests results

Patient number	Gender	Age (years)	Type of DM	Duration of disease (years)	Positivities in patch tests		History of atopy	Time between onset of sensor use and development of symptoms (months)	Sensor usage was stopped?
					IBOA	Other			
1	M	19	1	11	++	—	No	20	No
2	F	62	1	2	+++	Myroxylon pereirae, Hydroperoxides of Linalool Fragrance mix I	Yes (family history)	16	Yes, with impact in quality of life and DM control
3	F	43	1	17	++	—	Yes (family history)	6	No
4	F	23	1	20	—	—	Yes (family history)	0	Yes, with impact in quality of life
5	F	23	1	12	++	Sesquiterpene lactone mix, MCI/MI, Hydroperoxides of linalool N-Octylisothiazolinone	Yes (family history)	12	Yes, with impact in quality of life
6	F	28	1	17	++	Fragrance mix I	Yes (personal history)	6	Yes, with impact in quality of life
7	F	41	1	11	++	—	No	3	No
8	F	63	1	11	++	—	No	4	No
9	M	59	1	39	++	—	No	1	No
10	M	65	2	10	—	—	Yes (personal and family history)	2	Yes, with impact in quality of life

Abbreviation: MCI/MI, methylchloroisothiazolinone/methylisothiazolinone.

RESULTS

Of the 10 patients included in the study, 7 were female and 3 were male, with a mean age of 42.6 years. Nine patients had type 1 DM, and one patient had type 2 DM. Two patients had a past personal history of atopy; five had a family history. The mean duration of DM before starting to use the sensor was 15 years. Time between the beginning of sensor use and the onset of cutaneous symptoms was, on average, 7 months. Redness and itching were the most common symptoms, reported by all the patients (Figure 1). Some patients reported a burning sensation, desquamation, hemorrhage, or local pain.

Positive patch test reactions to IBOA were observed in 8 of 10 patients, 7 with ++ and one with a +++ positive reaction (Figure 2). The acrylates and plastic and glues series was negative in all patients. Regarding the Portuguese baseline series, positive reactions were observed in three patients, as depicted in Table 1. The two patients who did not react to IBOA also turned out to be negative on all patch tests. All the 20 controls tested negative for IBOA.

Dermatitis prompted the cessation of the use of the sensor in five patients. The other five continued to use the sensor, in most cases using barrier products such as Sekura or Cavilon spray. All patients who stopped using the sensor reported a significant worsening of their quality of life. In one case, cessation of sensor use was also associated with a worsening of DM control. Patient characteristics and patch tests results are depicted in Table 1.

DISCUSSION

Contact dermatitis in response to medical devices for patients with diabetes may be irritant or allergic.⁷ Irritant reactions are more common and are influenced by individual (age or predisposition to dry skin) and physical factors (skin occlusion, sweating, or damaged epidermis by rapidly tearing off the adhesive).^{8,9} ACD is less common but has a greater clinical significance. These reactions may be due to one or more allergens present in the medical device itself and/or in the adhesive that fixes it to the skin.⁹⁻¹¹

FreeStyle Libre consists of a sensor applied on the upper arm with an adhesive film, which analyzes interstitial glucose levels through a central catheter inserted in the subcutaneous tissue.¹² The first skin reactions to FreeStyle Libre were described some months after its appearance, but the major allergen responsible for ACD to this device, IBOA, was identified in only 2017.^{10,11} IBOA is widely used in coatings, inks, and paints.^{10,13,14} It can easily be released into materials¹¹ and is not present in the adhesive part of FreeStyle Libre, but originates from the plastic part of the sensor and subsequently diffuses through the plaster to the skin, aided by occlusion and sweating.^{4,10,11} This explains why patients may not react to the adhesive part of the sensor itself, but do react to the whole device.⁴ In 2018, *N,N*-dimethylacrylamide was identified as another potential allergen in FreeStyle Libre.¹⁵

In our study, 8 out of 10 patients presented a positive reaction to IBOA, similar to previously reported results.^{13,16} Furthermore, the

mean time between first use of the sensor and development of dermatitis was 7 months, and most of our patients were female with DM type 1, similar to other studies.^{13,14,17} Five patients were patch tested with a piece of the adhesive part of the sensor, all of them exhibiting negative reactions.

Two of our patients did not react to IBOA. On the one hand, these patients may have developed irritant and not allergic contact dermatitis. In favor of this notion, patient 4 developed the reaction immediately after starting to use the sensor, and therefore without time for sensitization to occur. On the other hand, these patients may have developed ACD to an allergen other than IBOA.⁴

None of our patients reacted to other acrylates, which is consistent with previous observations on the lack of cross-reactivity between IBOA and other acrylates.^{2,14,18} One of our patients showed a positive reaction to sesquiterpene lactone (SL) mix. Cross-reactions between IBOA and SL mix have been reported previously.¹⁷

In our series, five patients with confirmed ACD to IBOA decided to continue using the sensor, all of them with the aid of some protective material such as adhesives or barrier products. Obvious limitations of these alternatives include the costs, potential for reduced comfort, and the short duration of action.^{19,20}

Contact dermatitis to FreeStyle Libre is probably underestimated, given that only patients with severe cutaneous adverse reactions are brought to dermatologists' attention. When these patients consult, patch tests with at least IBOA and other acrylates should be conducted, and contact allergies reported to the manufacturers and local health authorities, in order to obtain alternatives in the future.¹³

AUTHOR CONTRIBUTIONS

Catarina Queirós: Conceptualization; formal analysis; methodology; writing-original draft. **Maria Alexandre:** Data curation; methodology; writing-original draft. **Pedro Garrido:** Data curation; writing-original draft. **Teresa Correia:** Project administration; validation; writing-original draft. **Paulo Filipe:** Resources; supervision.

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