Prevalence and Prevention of Contact Dermatitis Caused by FreeStyle Libre: A Monocentric Experience

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OBJECTIVE

Cutaneous adverse events (CAE) from FreeStyle Libre include allergic contact dermatitis (ACD) caused by the allergen isobornyl acrylate (IBOA). We aim to report CAE from this glucose sensor, ACD to IBOA in particular, and the outcome of using barrier films as a prevention.

RESEARCH DESIGN AND METHODS

A monocentric, retrospective review of medical files from adult and pediatric patients with diabetes using Freestyle Libre, in the period between December 2016 and April 2019, was performed with a focus on CAE.

RESULTS

Fifty-seven of 1,036 patients with diabetes (5.5%) were referred to our dermatology department because of CAE from FreeStyle Libre. Thirty-nine of 1,036 (3.8%) had ACD due to IBOA. Only two patients, of whom one sensitized to IBOA, had a benefit from using barrier films.

CONCLUSIONS

CAE occurred in 5.5% of FreeStyle Libre users, and 3.8% suffered from ACD due to IBOA. Barrier films had limited value in the prevention.

FreeStyle Libre (Abbott Diabetes Care, Witney, U.K.) is a sensor-based, flash-continuous glucose monitoring system applied on the skin for up to 14 days (1). However, it contains isobornyl acrylate (IBOA), a newly discovered allergen, which may cause allergic contact dermatitis (ACD) (2–5). We report a single-center experience of cutaneous adverse events (CAE) from this glucose sensor, including ACD due to IBOA, and the outcome of using barrier films as a prevention in these patients.

RESEARCH DESIGN AND METHODS

The medical files of 614 adult and 422 pediatric patients with diabetes, using FreeStyle Libre in the period between December 2016 and April 2019, were retrospectively reviewed with a focus on CAE. In our center, patients are usually referred to the dermatology department for an allergy workup, including patch tests with IBOA 0.1% dispersed in petrolatum according to published guidelines (6). Whenever a barrier film (Cavilon No Sting Barrier Film) had been used to prevent the CAE (7), applied according to the manufacturers' recommendations, its impact on the CAE was verified.

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RESULTS

Fifty-seven of 1,036 patients with diabetes (5.5%), i.e., 34 of 614 adult patients (5.5%) and 23 of 422 children (5.5%), had been referred to our dermatology department because of CAE. Patch tests showed ACD to IBOA in 39 patients, indicating that the prevalence of ACD in Freestyle Libre users is at least 3.8% (39 of 1,036). The remaining 18 patients with no sensitization to IBOA were considered to have irritant contact dermatitis (ICD) or ACD to an unidentified or untested allergen. Sixteen patients, 13 females and 3 males with a median age of 24.5 years (range 9–53), of whom 14 (88%) showed ACD to IBOA, had tried Cavilon to prevent their CAE (Table 1). Five of these 16 patients (31%), all children, reported some improvement with Cavilon, but only 2 continued its use. The first child, sensitized to IBOA, reported residual but acceptable itch and erythema, whereas the other child, not sensitized to IBOA, became completely free of symptoms. One of the three remaining children was successfully switched to Dexcom (San Diego, CA), whereas the other two, despite stopping the use of Cavilon, had continued the use of the Freestyle Libre sensor and had noticed spontaneous improvement of their CAE. The 11 of 16 remaining patients (71%), all adults, experienced no benefit from Cavilon. They tried corticosteroid nebulizers or hydrocolloid dressings underneath the sensor (8) or were switched to other devices, such as Dexcom or Eversense (Roche, Basel, Switzerland) (9,10).

CONCLUSIONS

The FreeStyle Libre sensor may provoke CAE, including ACD due to the allergen IBOA (2). However, the number of patients suffering from CAE from Freestyle Libre, and the proportion of these with ACD to IBOA, is largely unknown. The French governmental agency ANSM (Agence Nationale de Sécurité du Médicament et des Produits de Santé) stated that only 0.2% of such patients require a medical follow-up (11), and a Finnish study reported that 1–5% of Freestyle Libre users may develop CAE, including ACD in ~0.7% (12). We here confirm that, notwithstanding a potential referral bias, 57 of 1,036 (5.5%) Freestyle Libre users develop CAE (12). Contrary to the 0.7% of ACD in the Finnish study, we show that at least 3.8% of Freestyle Libre users is affected by ACD from IBOA in our center. This figure may even be higher, as ACD can take months to even years to develop, and some FreeStyle Libre users from our cohort may not yet have developed allergic symptoms at the time of this review. In many patients reported, here and in the literature, Freestyle Libre was often the first diabetes device that caused CAE, including ACD (2).

The percentage of patients with CAE who were found to be sensitized to IBOA (39 of 57 [68%]) is lower than previously reported (2,12). In the Finnish study, 51 of 63 Freestyle Libre users (81%) with severe CAE were sensitized to IBOA. The 18 patients in our study who were not shown to be sensitized to IBOA may have been affected by ICD, or by ACD from currently unidentified or untested allergens present in the device (13,14). Alternatively, the manufacturer may meanwhile have changed the composition of the device (11,15), although it remains to be seen whether a recently updated version of the FreeStyle Libre sensor will effectively result in fewer cases of CAE, including ACD. Nevertheless, this might explain why two of our patients (patients 4 and 5) (Table 1) noticed a spontaneous improvement of their skin symptoms, despite the continued use of the glucose sensor.

In case of CAE, many patients try plastic or hydrocolloid barrier dressings, acrylate-based film-forming sprays, corticosteroid nebulizers, and combinations thereof. One case of ACD from FreeStyle Libre due to IBOA was claimed to be successfully managed by the use of Cavilon (7). In our cohort of 57 patients with CAE, only 16 patients, of whom 14 with ACD to IBOA, had tried the use of this barrier film. Eleven patients had no benefit at all, possibly related to the fact that the barrier effect is incomplete and transient (72 h), whereas FreeStyle Libre is worn on the skin for up to 14 days. Premature replacement of the glucose sensor was often necessary, and most patients eventually stopped the use of the device. They returned to finger pricks or were switched to IBOA-free sensors (9). Only two patients (patients 1 and 3) (Table 1) reported that the barrier film alleviated or even completely prevented their cutaneous symptoms, the latter patient not being sensitized to IBOA and potentially suffering from ICD instead of ACD. Our experience with barrier films only concerns a small sample of 16 patients who suffered from potentially more severe CAE, the majority being affected by ACD to IBOA. We feel that in patients with only minor CAE, barrier films may still be tried, although some manufacturers state that these might affect the performance of the sensors (15).

Table 1—Overview of 16 patients with CAE from FreeStyle Libre, the result of a patch test with IBOA, and the outcome of using barrier films in prevention*

Patient	Age (years)	Sex	IBOA 0.1% pet on day 4	Improvement with barrier films*
1	9	M	+ +	Yes
2	24	F	+ +	No
3	17	F	Neg	Yes
4	13	M	+	Yes**
5	16	F	Neg	Yes**
6	24	M	+ +	No
7	16	F	+ +	Yes**
8	27	F	+	No
9	18	F	+ + +	No
10	40	F	+	No
11	25	F	+ +	No
12	28	F	+	No
13	46	F	+	No
14	53	F	? +	No
15	29	F	+ +	No
16	26	F	+	No

F, female; M, male; Neg, negative; pet, petrolatum; ? + to + + +, a positive patch test. *Barrier films or film-forming agents: Cavilon No Sting Barrier Film. **Only temporary improvement.

In conclusion, this monocentric and retrospective study shows that 57 of 1,036 (5.5%) of FreeStyle Libre users may suffer from CAE and that 39 of 1,036 (3.8%) are affected by ACD due to IBOA. Barrier films only seem to have a limited value in preventing CAE, especially in cases of severe (vesicular, oozing) ACD. Our approach does show the potential benefit of multidisciplinary cooperation between endocrinologists and dermatologists and highlights that clinicians should examine patients' sensor sites routinely so that CAE, including ACD, would be noticed earlier.

Duality of Interest. C.D.B. is a consultant for Abbott, A. Menarini Diagnostics, Lilly, Medtronic, Novo Nordisk, and Roche Diagnostics. No other potential conflicts of interest relevant to this article were reported.

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References

1. Bolinder J, Antuna R, Geelhoed-Duijvestijn P, Kröger J, Weitgasser R. Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial. Lancet 2016;388:2254–2263
2. Herman A, Aerts O, Baeck M, et al. Allergic contact dermatitis caused by isobornyl acrylate in Freestyle® Libre, a newly introduced glucose sensor. Contact Dermatitis 2017;77:367–373
3. Kamann S, Aerts O, Heinemann L. Further evidence of severe allergic contact dermatitis from isobornyl acrylate while using a continuous glucose monitoring system. J Diabetes Sci Technol 2018;12:630–633
4. Raison-Peyron N, Mowitz M, Bonardel N, Aerts O, Bruze M. Allergic contact dermatitis caused by isobornyl acrylate in OmniPod, an innovative tubeless insulin pump. Contact Dermatitis 2018;79:76–80
5. Aerts O, Herman A, Bruze M, Goossens A, Mowitz M. FreeStyle Libre: contact irritation versus contact allergy. Lancet 2017;390:1644
6. Johansen JD, Aalto-Korte K, Agner T, et al. European Society of Contact Dermatitis guideline for diagnostic patch testing - recommendations on best practice. Contact Dermatitis 2015;73:195–221
7. Shinkawa E, Washio K, Tatsuoka S, Fukunaga A, Sakaguchi K, Nishigori C. A case of contact dermatitis caused by isobornyl acrylate in FreeStyle Libre: the usefulness of film-forming agents. Contact Dermatitis 2019;81:56–57
8. Kamann S, Oppel E. Hydrocolloid blister plaster decreases allergic contact dermatitis caused by Freestyle Libre and isobornyl acrylate. Contact Dermatitis 2019;81:380–381
9. Oppel E, Kamann S, Reichl FX, Högg C. The Dexcom glucose monitoring system-an isobornyl acrylate-free alternative for diabetic patients. Contact Dermatitis 2019;81:32–36
10. Deiss D, Szadkowska A, Gordon D, et al. Clinical practice recommendations on the routine use of Eversense, the first long-term implantable continuous glucose monitoring system. Diabetes Technol Ther 2019;21:254–264
11. Mise à disposition de dispositifs FreeStyle Libre avec des capteurs modifiés – Point d'Information [Internet], 2019. Available from https://ansm.sante.fr/S-informer/Points-d-information-Points-d-information/Mise-a-disposition-de-dispositifs-FreeStyle-Libre-avec-des-capteurs-modifies-Point-d-Information. Accessed 25 June 2019
12. Hyry HSI, Liippo JP, Virtanen HM. Allergic contact dermatitis caused by glucose sensors in type 1 diabetes patients. Contact Dermatitis 2019;81:161–166
13. Passanisi S, Lombardo F, Barbalace A, et al. Allergic contact dermatitis and diabetes medical devices: 2 clinical cases. Contact Dermatitis 2018;79:115–117
14. Mowitz M, Herman A, Baeck M, et al. N,N-dimethylacrylamide-a new sensitizer in the FreeStyle Libre glucose sensor. Contact Dermatitis 2019;81:27–31
15. Medicines & Healthcare products Regulatory Agency. Medical Device Alert: MDA/2019/003: FreeStyle Libre Flash Glucose Sensor – Use of Barrier Methods to Reduce Skin Reactions to the Sensor Adhesive [Internet], 2019. Available from https://assets.publishing.service.gov.uk/media/5c4f35e1ed915d7d51fd5a35/MDA-2019-003_Final13.pdf. Accessed 25 June 2019