

Two flushing-like reaction cases from calcium pidolate who tolerated calcium carbonate

To the Editor,

The calcium salts associated to vitamin D are widely employed for osteoporosis prevention and treatment.

We present two cases of a flushing-like reaction related to the intake of Osvical D effervescent granulate® (calcium pidolate 4500 mg equal to calcium 600 mg, cholecalciferol 4 mg, aspartame, sodium bicarbonate, sodium carbonate, citric acid, sodium citrate, orange flavour, lemon flavour, S yellow orange colorant, povidone 30). To our knowledge there is no calcium pidolate skin reaction reported, although there has been a case of urticaria.¹

Case 1: A 60-year-old woman, diagnosed of hypothyroidism under treatment with levothyroxine, suffered, immediately after the first Osvical D® ingestion, facial erythema and burning sensation, headache and non-pruritic rash on extremities. It resolved spontaneously in 12 h without scaling. She had not previously been treated with calcium salts. She no longer took calcium or vitamin D.

After previous signed informed consent was obtained, we performed a full-dose open oral challenge with Osvical D®. After 20 min facial and neck erythema appeared, together with a burning sensation. It swiftly spread to extremities and bra pressure area. She did not complain of itching. The reaction was treated with dexchlorpheniramine 5 mg and methylprednisolone 40 mg i.m. resolving in about 2 h.

In order to identify the component which elicited the reaction (calcium pidolate or cholecalciferol) we conducted an open oral challenge with one tablet of Ibercal effervescent® (calcium pidolate 1852 mg equal to calcium 250 mg, sodium bicarbonate, citric acid, lactose, macrogol 6.000, sodium benzoate, lemon flavour, saccharine) causing a similar reaction. To discard the possible implication of other components, apart from calcium pidolate, which Osvical D® and Ibercal® share, i.e. sodium bicarbonate and citric acid, we performed an open oral challenge, with both of them and the tolerance was good. We looked for an alternative to pidolate salt, since the patient needed calcium for her osteoporosis. Therefore an open oral challenge with Mastical tablet® (calcium carbonate 1250 mg equal to calcium 500 mg) was carried out without adverse reactions.

Case 2: A 49-year-old woman, suffering from spondylitis and hypothyroidism upon treatment with celecoxib, infliximab and levothyroxine began osteoporosis preventive treatment with Osvical D®. Three days after the start of therapy and 1 h after the Osvical D® intake, she developed a non-itching facial erythema which quickly spread towards extremities. The reaction resolved spontaneously in about 8 h. She did not take calcium nor vitamin D again.

We performed the same study described earlier with the same result.

In addition, 90 min after the open oral challenge reaction with Osvical D®, a normal serum tryptase value was obtained.

Both patients were diagnosed with flushing-like reaction to calcium pidolate, and calcium carbonate was further recommended.

Regarding adverse reactions with calcium pidolate, there is a previous report of a skin reaction which is described as an itchy maculopapular rash with hives and mild angio-oedema finally diagnosed as urticaria. The authors determined good tolerance to calcium carbonate as well.¹

In our patients, the features of the reaction, meaning the absence of pruritus and hives, the presence of burning sensation and the normal levels of serum tryptase observed in the second case, almost rule out an IgE-mediated or a mast cell degranulation mechanism and it suggests a vascular picture more than an immunological one.

It has been reported, although not confirmed by further study, that calcium pidolate achieves higher concentrations of serum calcium than other available calcium salts such as calcium carbonate.^{2,3} Calcium itself might have been the direct mediator of the reaction.

Although both cases happened to be hypothyroid, a firm relationship has not been stated between this condition and the flushing. Anyway we highlight this association to be kept in mind when evaluating future cases.

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Conflict of interest

The authors declare no conflict of interest.

References

- Domínguez-Ortega J, Abad-Schilling C, Kindelan C. Urticaria due to calcium pidolate. *Allergol Immunopathol.* 2007;35: 38–9.
- Farrerons J, Olazabal A, Díaz López C, López Ciudad A, Rams A. An analysis of calcium pidolate absorption and a comparison with that of a salt in common use, gluconate–lactate–carbonate, in postmenopausal osteoporosis. *Ann Med Interne.* 1989;6:361–5.
- Deroisy R, Zartarian M, Meurmans L, Nelissen N, Micheletti MC, Albert A, et al. Acute changes in serum calcium and parathyroid hormone circulating levels induced by the oral intake of five currently available calcium salts in healthy male volunteers. *Clin Rheumatol.* 1997;16: 249–53.

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