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Could mometasone furoate be a viable glucocorticoid with fewer metabolic adverse effects?

Glucocorticoids are medications widely used to treat inflammation and allergies, and in contexts of immunosuppression such as after transplants. They are well-established and safe. The problem is that, when used for a long time, or in high doses, they cause several side effects, which can even lead to diabetes and dyslipidemia. In some cases, the problems are irreversible.

Mometasone furoate (MF) is an anti-inflammatory of the glucocorticoid class, widely used to treat respiratory diseases, such as rhinitis and asthma, and skin problems, such as dermatitis – always with local application, in the form of nasal sprays, creams, or ointments. These routes are because MF was elaborated to be less bioavailable, avoiding systemic side effects.

However, in a previous in vitro study (not from our group) authors suggested MF might be a good candidate to act as a systemic anti-inflammatory with possibly fewer metabolic adverse effects in vivo. Thus, we investigated the possibility of using it orally or by intraperitoneal injection, so that it is systemically absorbed and spreads throughout the body.

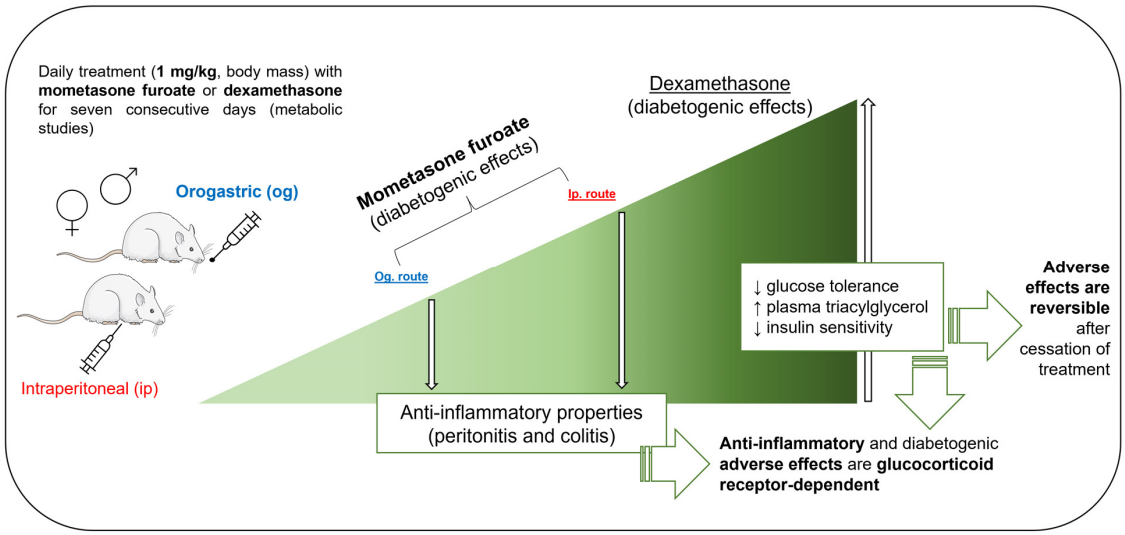

Fig. 1. Treatment and outcomes caused by mometasone furoate in rats. Both male and female adult rats were treated daily (1 mg/kg, body mass) with mometasone furoate (MF) or dexamethasone (DEX) for six consecutive days through oral (intragastric) or intraperitoneal routes to evaluate the metabolic outcomes. A separate group of rats was submitted to protocols of peritonitis or colitis to verify the anti-inflammatory action of MF and DEX and to define the better dose and systemic route of drug application. MF was as effective as DEX in preventing or mitigating the inflammatory processes associated with peritonitis and colitis, respectively. DEX treatment, as expected, caused several metabolic side effects such as reduced glucose tolerance, insulin sensitivity, and dyslipidemia. MF reproduced most of these alterations only when administered intraperitoneally, although with outcomes of lower severity. These MF side effects on metabolism were reversible after 10 days of MF administration or were absent in the presence of an antagonist of the glucocorticoid receptor. When treated by the oral route (males) or both routes (females), MF caused minor side effects.

For that, we induced two types of inflammation in rats – a short-lasting one, called peritonitis, and a longer-lasting one, called colitis. In some groups, MF was applied in different doses (diluted in corn oil); others received dexamethasone (DEX), another medication from the glucocorticoid class, but DEX is already widely known and used for systemic applications for the most varied types of inflammation. Control groups were also established, which received only a placebo: corn oil.

We observed that, both orally and intraperitoneally, MF was as efficient as DEX in preventing short-term inflammation (peritonitis) and even better than DEX in alleviating longer-lasting intestinal colitis. After demonstrating that MF can work when applied systemically, we began studying possible side effects.

For that, rats received specific doses of DEX or MF orally and intraperitoneally for six consecutive days, which, in humans, would be equivalent to a prolonged treatment. This period was enough for DEX treatment, regardless of the route of administration, to cause an increase in triglycerides and insulin, and glucose intolerance (features that resemble prediabetes). The same side effects from DEX treatment were observed in male rats that received MF intraperitoneally, although in lower magnitude. However, none of the females treated with MF developed a situation equivalent to prediabetes, nor did the males that received the MF orally.

Nevertheless, it is worth mentioning that, even among males using the intraperitoneal route, all undesirable effects were prevented under blockage of the glucocorticoid receptor or reversed after ten days without MF (Fig. 1). We warn, however, that the results should be interpreted with caution, as longer treatments, higher doses, or previous illnesses can cause side effects to persist for longer.

We also carried out in vitro studies with nanoparticles charged with MF – tiny capsules, made from corn protein, and capable of resisting stomach acids and intestinal enzymes, which could be a manner to deliver the MF to the patient's intestine. Our results with cells indicated that the nanoparticle was compatible with fat-soluble MF and exhibited good adherence to intestine cells, with a gradual release of MF into the medium.

Therefore, carried out in cells and animal experiments, we indicate that MF can be a good option for treating intestinal inflammation, presenting the same benefits and fewer side effects as other corticosteroids.

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Publications

Oral mometasone furoate administration preserves anti-inflammatory action with fewer metabolic adverse effects in rats
Zimath PL, Almeida MS, Bruxel MA, Rafacho A
Biochem Pharmacol. 2023

Zein nanoparticles as oral carrier for mometasone furoate delivery
Zimath P, Pinto S, Dias S, Rafacho A, Sarmento B
Drug Deliv Transl Res. 2023