

Still no place for depot triamcinolone in hay fever?

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Key learning points

- ▶ In 1999, *DTB* noted that despite the likelihood that a single injection of triamcinolone acetonide will relieve hay fever symptoms, there was uncertainty about the efficacy and safety of repeated administration.
- ▶ A systematic review from 2005 that reviewed data on corticosteroid injections suggested that a single dose of an intramuscular injection has a statistically significant effect on symptom relief, generally lasting for up to 5 weeks, without any safety concerns, though all the data were from old studies.
- ▶ A retrospective study from 2013 that used Danish National Registry data warned that regular use of depot corticosteroid injections to treat allergic rhinitis was associated with an increased risk of being diagnosed with diabetes and osteoporosis.
- ▶ UK guidance recommends a short course of oral corticosteroids rather than depot injectable preparations that cannot be removed if adverse effects occur.
- ▶ Allergen immunotherapy is recommended as a treatment option for patients requiring frequent oral corticosteroid rescue.

Introduction

Triamcinolone acetonide (Kenalog) intramuscular injection used to be commonly prescribed for the treatment of hay fever in UK general practice, particularly in patients who had insufficient relief from other treatments. A *Drug and Therapeutics Bulletin* (*DTB*) article published in 1999 concluded that a single dose is likely to relieve hay fever symptoms, but it is unclear for how long any benefit is likely to last, what unwanted effects might develop and how it compares with standard therapy.¹ The article recommended that until there is clear evidence of its advantages over other hay fever treatments, use of depot injections of triamcinolone is no longer acceptable. Due to continued interest by patients in using this treatment, a search for new evidence was conducted to determine if the conclusions of the *DTB* article remain valid.

Triamcinolone acetonide injection

Triamcinolone acetonide injection is licensed for intramuscular use for the treatment of allergic states.² The suggested initial dose is 40 mg and subsequent dosage depends on the patient's response and period of relief. The product information suggests that patients who do not respond to conventional therapy may obtain remission of symptoms lasting throughout the pollen season after a single dose of 40–100 mg given when allergic symptoms appear.² A 4 mg dose of triamcinolone has anti-inflammatory activity equivalent to about 5 mg of prednisolone.¹

It is reported that 20%–25% of people in UK suffer from hay fever, of whom 10% do not obtain symptom relief from use of over-the-counter medicines.^{3,4} In 2018, 220 000 prescriptions for triamcinolone acetonide injection were dispensed in primary care in England.⁵ However, triamcinolone is licensed for intramuscular and intra-articular use for a range of indications and it is not known how many prescriptions were issued for treatment of hay fever. In addition, some patients may seek treatment privately if they are unable to obtain it on the National Health Service.

What did *DTB* say in 1999 and why?

The *DTB* article identified one randomised double-blind placebo-controlled trial, which included 38 patients with severe symptoms of hay fever and reported an improvement or resolution of symptoms in 16 of 17 (94%) patients given triamcinolone compared with 2 of 21 (10%) given placebo after 10 days.¹ It was noted that triamcinolone given intramuscularly might cause any of the unwanted effects of systemic corticosteroids, but there was a marked lack of controlled trial data on the likelihood of such effects when used to treat hay fever. *DTB* recommended a brief course of oral prednisolone in patients with severe hay fever, as this allows flexibility in dosing and the option to stop treatment if unwanted effects occur.¹

What evidence is available and what has been published since that review?

A systematic review from 2005 examined the efficacy and safety of a single dose of an intramuscular injection of a corticosteroid (dexamethasone, betamethasone, methylprednisolone or triamcinolone).⁶ Of the 18 studies included in the review, nine were double-blind randomised controlled trials (RCTs), two were single-blind RCTs and seven were open label studies. With one exception, the clinical results of the studies were based on the patients' subjective validation of the relief of hay fever symptoms (eg, 'excellent, good, poor or none effect'). In all the double-blind placebo-controlled trials, a statistically significant effect on symptom relief was shown. Generally, the effect lasted from the first or second day until 3–5 weeks.

Triamcinolone studies

The authors of the systematic review noted that the data did not highlight any concerns regarding long-lasting suppression of plasma cortisol, the possibility of a longstanding influence on stress reaction, or the risk of serious tissue atrophy following a single intramuscular injection of corticosteroid for hay fever, but acknowledged the lack of current evidence on this intervention and the need for studies

comparing it with current first-line therapies.⁶ The systematic review included five studies involving triamcinolone (see table 1). The conclusions of this review have been challenged on the basis that the trials had methodological limitations. These limitations included only a minority of patients in the trials had severe disease and use of an inappropriate main outcome measure of a global satisfaction scale, which has been superseded by well validated rhinitis specific symptom scores.⁷

Any safety concerns?

The systematic review reported no statistically significant differences in adverse effects between the groups.⁶ In the comparative studies, the clinical adverse effects were generally regarded as minor and similar with different systemic corticosteroid injections. In several studies, miscellaneous adverse effects of minor importance were reported in a few participants, consisting of pain at the site of injections, menstrual irregularities, flushing, tiredness, nervousness and blue skin marks. The physiological effect on plasma cortisol indicated significant but minor and short-lasting depression and no longstanding influence on stress reaction. There was no clinically significant effect on blood glucose, body weight or blood pressure noted. An editorial commented that some papers reporting adverse events were not included in the systematic review.⁸ It highlighted postinjection flare, facial flushing, and skin and fat atrophy as the most common adverse effects of injectable corticosteroids, and though systemic complications are rare, they do exist, and a more persistent and possibly greater effect on bones or eyes, lasting for weeks, cannot be excluded. Furthermore, if the season is exceptionally severe, or if the patient experiences prolonged symptoms as a result of multiple allergies, several injections may be necessary, which increases the risk of severe adverse events.

A retrospective study based on Danish registry databases (1995–2011) investigated whether depot corticosteroid treatment of allergic rhinitis was associated with an increased risk of steroid-related diseases compared with the use of immunotherapy.⁹ It included 47 382 individuals with rhinitis: 55.8% treated with corticosteroids (agent not defined), 37.6% with immunotherapy and 6.7% with both, and covered corticosteroid use defined as a minimum of one injection during April to July for at least three consecutive years. Treatment with specific immunotherapy against grass, birch or both was used as a non-corticosteroid control group. Regular use of depot corticosteroid injections was associated with increased risk of being diagnosed with diabetes (rate ratio [RR] 1.5, 95% CI 1.3 to 1.8; $p<0.001$), incidence 3.9 per 1000 patient years (95% CI 3.5 to 4.3), and osteoporosis (RR 1.2, 95% CI 1.0 to 1.5; $p=0.023$), incidence 2.8 per 1000 patient years

(95% CI 2.5 to 3.1) compared with immunotherapy. Risk of diabetes culminated within the first 2 years of start of treatment. No significant differences in infections or tendon rupture were observed. The authors concluded that there was evidence of an association between depot corticosteroid injections and increased risk of osteoporosis and diabetes.⁹

A case of avascular necrosis of the hips has been reported in a patient on long-term depot corticosteroids for severe and disabling hay fever.¹⁰ He had received 16 injections between 1987 and 1997, nine of which were of triamcinolone 40 mg and seven of methylprednisolone 80 mg. After each injection, symptoms were relieved for up to 6 weeks. Avascular necrosis of both hips developed in 1997, with a possibility of the need for hip replacements in the future. The authors of the report suggested that it was a failure in management that the patient was not referred to an allergy specialist sooner and pollen immunotherapy considered.

What do guidelines recommend?

The British Society for Allergy and Clinical Immunology guideline recommends intranasal corticosteroids for the first-line therapy of moderate-to-severe persistent symptoms.¹¹ The original guideline published in 2008 did not recommend the use of injectable corticosteroids except under exceptional circumstances because the risk–benefit profile was considered poor compared with other treatments.¹² The updated guideline published in 2017 recommended a short course of oral corticosteroids over depot injectable preparations, that cannot be removed if adverse effects occur.¹¹ It was noted that use of oral corticosteroids is rarely indicated in the management of allergic rhinitis except for severe nasal obstruction where in order to obtain control, short-term rescue medication is used during severe exacerbations despite compliance with conventional pharmacotherapy. Intranasal corticosteroid therapy should be co-administered with oral corticosteroids with or without a short-term decongestant spray to allow intranasal drug penetration. There is no consensus on the dose and duration of oral corticosteroid therapy but a suggested regime for adults is 0.5 mg/kg prednisolone for 5–10 days. Allergen immunotherapy is recommended as a treatment option for patients requiring frequent oral corticosteroid rescue. The guideline suggests that it can improve symptoms, reduce medication requirements and improve quality of life, and is the only treatment that can modify the course of allergic rhinitis, with long-term remission following discontinuation.¹¹

In 2018, an international consensus statement considered the evidence for corticosteroid injections in the management of allergic rhinitis.¹³ The authors included a review of five randomised

Table 1 Trials of a single intramuscular dose of triamcinolone to treat hay fever

Year	Number of patients	Design	Interventions	Response	Effect duration	Clinical adverse effects	Physiological adverse effects
1964	418	Open label	Triamcinolone 80 mg	75% good to excellent	>5 weeks	6%	Urine cortisol depressed
1971	18	Open label	Triamcinolone 80 mg	90% good to excellent	12–48 hours to 3 weeks	Minor	Plasma cortisol depressed<3 weeks
1971	220	Double blind	Triamcinolone 40 mg vs. dexamethasone 8 mg	Equally good; 70% good or excellent	8 hours to 4 days	Minor	Not measured
1972	38	Double blind	Triamcinolone 40 mg vs. placebo	Good; $p<0.001$ (16/17 vs 2/21)	>20 days	Minor	Not measured
1973	92	Open label comparative	Triamcinolone 80 mg vs. methylprednisolone 80 mg	90% complete or substantial relief	90%>4 weeks	Minor	Not measured

Adapted from Østergaard *et al.*⁶

Information for patients

- Kenalog injection, which contains the corticosteroid triamcinolone, has been used to treat hay fever that has not responded to usual treatments. It is no longer offered due to a lack of information comparing it with modern, safe and effective treatments, and also concerns about safety. Once the injection has been given, the drug cannot be removed from the body if adverse effects are experienced.
- For severe symptoms that do not respond to usual treatments, steroid tablets, taken for a few days can help to relieve symptoms, in conjunction with a nasal spray containing a steroid or an antihistamine.
- If steroids do not work some people may require specific allergen immunotherapy (or desensitisation), which must be prescribed and supervised by a hospital allergy specialist, as there are some risks involved.
- Factsheets and information about hay fever are available from: Allergy UK: https://www.allergyuk.org/information-and-advice/conditions-and-symptoms/11-hay-fever-allergic-rhinitis#download_access NHS website: <https://www.nhs.uk/conditions/hay-fever/>

studies published between 1979 and 1988 (none of which included triamcinolone) and the Danish national registry data. Injectable corticosteroids were considered to be effective at improving symptoms of allergic rhinitis, but have known adverse effects on the hypothalamic-pituitary axis, cause growth suppression, osteoporosis, hyperglycaemia and other systemic adverse effects.¹³ Therefore, the authors concluded that adverse effects outweigh the demonstrated clinical benefit, and given the availability of effective alternatives, injectable corticosteroids were not recommended for routine treatment of allergic rhinitis.

Conclusion

Despite the likelihood that a single injection of triamcinolone acetate will relieve hay fever symptoms, there remains uncertainty about the efficacy and safety of repeated administration. No new studies have been conducted and the excess risk compared with treatments such as short courses of oral corticosteroids remains to be established. The conclusion of the *DTB* article from 1999 remains unchanged in that this product should not be used, until clear evidence of its advantages over other hay fever treatments, including oral prednisolone, become available. This view is supported by British guidelines and an international consensus statement. Topical corticosteroids are the mainstay of anti-inflammatory treatment of allergic rhinitis. For people with severe nasal obstruction, a short course of oral corticosteroids is recommended over a depot injectable

preparation for severe exacerbations. Allergen immunotherapy may be an option for patients requiring frequent oral corticosteroid rescue.

Correction notice This article has been corrected since it was published online. The previous version was an uncorrected paper and it has now been updated.

Editor's note This article is based on a UKMi Medicines Q&A document 'Is there a place in therapy for Kenalog (triamcinolone acetate) intramuscular injection for seasonal allergic rhinitis (hay fever)?'

Competing interests None declared. Refer to the online supplementary files to view the ICMJE form(s).

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