Imiquimod for anogenital warts in non-immunocompromised adults

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Key findings

- Findings should be treated with caution due to the low quality and high risk of bias of the included trials.
- Imiquimod and patient-applied treatments conferred similar benefits.
- Imiquimod resulted in fewer systemic adverse reactions.
- However, effects of imiquimod when compared to placebo were imprecise, and local adverse reactions and frequency of pain were increased with imiquimod.

Evidence included in this review

10 trials with a total of 1734 participants were included in the review. Studies were included from Austria (1), Germany (1), Greece (1), India (1), Turkey (1) and the USA (5). Six trials were at risk of bias due to being funded by pharmaceutical companies.

Imiquimod was compared to placebo (6 studies, 1294 patients), other patient-applied treatment (2 studies, 105 patients), or other provider-applied treatments (2 studies, 335 patients).

Quality assessment

The quality of included trials was very low, and all trials were at a high risk of bias.

Clinical implications

Review findings should be treated with caution due to the low quality of the included trials, the high risk of bias, and the limited confidence in the effect estimates of the review.

Further research

High quality RCTs will be required in order to guide treatment for patients with anogenital warts comparing imiquimod to other patient- or provider-administered treatments. Future research should minimize sources of bias and ensure that important clinical outcomes are reported in order to ensure that results can provide clear guidance on optimal treatment for these patients.

Cochrane review
30% of people with anogenital warts (AGW) have spontaneous regression of lesions but there is no way to determine whether a specific lesion will remain. There are a wide range of options available for treating people with AGW and selection is based on clinician's experience, patient preferences and adverse effects. The imiquimod could offer the advantages of patient-applied therapies without incurring the limitations of provider-administered treatments.

To assess the effectiveness and safety of imiquimod for the treatment of AGW in non-immunocompromised adults.

We searched the Cochrane Sexually Transmitted Infections Group Specialized Register (15 April 2014), CENTRAL (1991 to 15 April 2014), MEDLINE (1946 to 15 April 2014), EMBASE (1947 to 15 April 2014), LILACS (1982 to 15 April 2014), World Health Organization International Clinical Trials Registry (ICTRP) (15 April 2014), ClinicalTrials.gov (15 April 2014), Web of Science (2001 to 15 April 2014) and OpenGrey (15 April 2014). We also handsearched conference proceedings, contacted trial authors and reviewed the reference lists of retrieved studies.

Randomized controlled trials (RCTs) comparing the use of imiquimod with placebo, any other patient-applied or any other provider-administered treatment (excluding interferon and 5-fluorouracil which are assessed in other Cochrane Reviews) for the treatment of AGW in non-immunocompromised adults.

Three review authors independently assessed trials for inclusion, extracted data and assessed risk of bias. We resolved any disagreements through consensus. The quality of the evidence was assessed using the GRADE approach.

Ten RCTs (1734 participants) met our inclusion criteria of which six were funded by industry. We judged the risk of bias of the included trials as high. Six trials (1294 participants) compared the use of imiquimod versus placebo. There was very low quality evidence that imiquimod was superior to placebo in achieving complete and partial regression (RR 4.03, 95% CI 2.03 to 7.99; RR 2.56, 95% CI 2.05 to 3.20, respectively). When compared with placebo, the effects of imiquimod on recurrence (RR 2.76, 95% CI 0.70 to 10.91), appearance of new warts (RR 0.76, 95% CI 0.58 to 1.00) and frequency of systemic adverse reactions (RR 0.91, 95% CI 0.63 to 1.32) were imprecise. We downgraded the quality of evidence to low or very low. There was low quality evidence that imiquimod led to more local adverse reactions (RR 1.73, 95% CI 1.18 to 2.53) and pain (RR 11.84, 95% CI 3.36 to 41.63).

Two trials (105 participants) compared the use of imiquimod versus any other patient-applied treatment (podophyllotoxin and podophyllin). The estimated effects of imiquimod on complete regression (RR 1.09, 95% CI 0.80 to 1.48), partial regression (RR 0.77, 95% CI 0.40 to 1.47), recurrence (RR 0.49, 95% CI 0.21 to 1.11) or the presence of local adverse reactions (RR 1.24, 95% CI 1.00 to 1.54) were imprecise (very low quality evidence). There was low quality evidence that systemic adverse reactions were less frequent with imiquimod (RR 0.30, 95% CI 0.09 to 0.98).

Finally, two trials (335 participants) compared imiquimod with any other provider-administered treatment (ablative methods and cryotherapy). There was very low quality of evidence that imiquimod did not have a lower frequency of complete regression (RR 0.84, 95% CI 0.56 to 1.28). There was very low quality evidence that imiquimod led to a lower rate of recurrence during six-month follow-up (RR 0.24, 95% CI 0.10 to 0.56) but this did not translate in to a lower recurrence from six to 12 months (RR 0.71, 95% CI 0.40
to 1.25; very low quality evidence). There was very low quality evidence that imiquimod was associated with less pain (RR 0.30, 95% CI 0.17 to 0.54) and fewer local reactions (RR 0.55, 95% CI 0.40 to 0.74).

The benefits and harms of imiquimod compared with placebo should be regarded with caution due to the risk of bias, imprecision and inconsistency for many of the outcomes we assessed in this Cochrane Review. The evidence for many of the outcomes that show imiquimod and patient-applied treatment (podophyllotoxin or podophyllin) confer similar benefits but fewer systematic reactions with the Imiquimod is of low or very low quality. The quality of evidence for the outcomes assessing imiquimod and other provider-administered treatment were of very low quality.

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Home > Imiquimod for anogenital warts in non-immunocompromised adults