
Interferon for the treatment of genital warts: a systematic review

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CRD summary

The authors concluded that interferon was fairly well tolerated for treating genital warts. Local administration was more effective than systemic administration or placebo in improving the complete response and reducing recurrence. The review was well conducted, but the relative efficacy of local and systemic administration was not based on direct comparisons and so this conclusion may not be reliable.

Authors' objectives

To evaluate the efficacy and safety of interferon for treating genital warts.

Searching

The Cochrane Sexually Transmitted Diseases Group's Trials Register, Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, EMBASE, CBM, CNKI and VIP database were searched for articles from inception to 2009. Search terms were reported and reference lists of relevant trials were screened. Organisations and researchers were contacted for details of additional published, unpublished, or ongoing trials and confidential reports. Only citations in Chinese or English were screened.

Study selection

Randomised controlled trials (RCTs) were eligible for inclusion if they compared locally or systemically administered interferon with placebo in human papillomavirus (HPV)-infected patients with clinically or experimentally diagnosed genital warts. The primary review outcomes were complete response rates and recurrence rates. Secondary review outcomes included adverse effects. All of the included trials were of parallel design and most of them compared locally-applied interferon with placebo; the remaining trials compared systemically-applied interferon with placebo.

Two reviewers independently selected trials and disagreements were resolved by discussion.

Assessment of study quality

Two reviewers independently assessed validity by considering the potential for selection, performance, attrition, and detection biases. Based on these criteria, trials were classified as at low, moderate, or high risk of bias. Disagreements were resolved with the help of a third reviewer or by consensus among the review group.

Data extraction

The numbers of events were extracted, for dichotomous data, and the means and standard deviations were extracted, for continuous data. Two reviewers independently extracted the data using a standardised form. Differences were resolved by consensus and trial authors were contacted if further information was required.

Methods of synthesis

Pooled relative risks and 95% confidence intervals were calculated, for dichotomous data, and pooled weighted mean differences and 95% confidence intervals were calculated, for continuous data. Heterogeneity was assessed using the χ^2 and I^2 statistics. Fixed-effect models were used in the absence of significant statistical heterogeneity and random-effects models were used in its presence ($p < 0.10$, $I^2 > 50\%$). Locally and systemically administered interferon trials were analysed separately as well as together. The authors stated that there were too few trials to assess publication bias.

Results of the review

Twelve parallel-group RCTs were included ($n=1,445$) and the sample size ranged from 42 to 257. All trials were classified as at moderate risk of bias. Three used computer-generated allocation sequencing and one described allocation concealment. All were described as double-blind, but none reported blinded assessment of the outcome. Two RCTs described losses to follow-up and used intention-to-treat analysis and seven described withdrawals, drop-outs, and losses to follow-up, but did not use intention-to-treat analysis.

Complete response rate: Locally applied interferon was associated with a statistically significant increase in complete response rate (44.4%) compared with placebo (16.1%; RR 2.68, 95% CI 1.79 to 4.02; seven trials). There was no significant difference in complete response rate between systemically administered interferon (27.4%) and placebo (26.4%; five trials).

Recurrence rate: There was no significant difference in recurrence rate between interferon (21.1%) and placebo (34.2%; seven trials). Locally applied interferon was associated with a significant reduction in recurrence rate compared with placebo (RR 0.57, 95% CI 0.38 to 0.88; four trials), but there was no significant difference between systematically administered interferon and placebo (three trials).

Significant heterogeneity ($p < 0.10$) was found for most outcomes, except systemically administered interferon.

Adverse events: The most commonly reported adverse event was flu-like symptoms. Intralesional interferon was associated with application-site reactions. In some trials, systemically administered interferon was associated with leucopenia and thrombocytopenia. There were no significant differences between treatment and placebo groups in liver-function tests, blood urea nitrogen, and creatinine levels.

Authors' conclusions

Interferon was fairly well tolerated and locally applied interferon appeared to improve the complete response rates and reduce the recurrence rates, compared with either systemically administered interferon or placebo, in patients with genital warts.

CRD commentary

The review question was clearly stated and the inclusion criteria were appropriately defined. Several relevant sources were searched and attempts were made to minimise publication bias. It appeared that some language restrictions were applied and language bias may have resulted. Methods were used to minimise reviewer errors and bias in the selection of studies, extraction of data, and assessment of validity. Only RCTs were included and their validity was assessed, using appropriate criteria, and the results were reported. Little information was provided about the included trials; the duration of follow-up for the assessment of recurrence rates, the participant characteristics, and dose and duration of treatment would have aided the interpretation of the review results. Appropriate methods were used for the meta-analyses, heterogeneity was assessed, and forest plots were presented.

The review was generally well conducted, but was limited by a lack of information on the primary trials and their methodological flaws. The authors' conclusions about the relative efficacy of locally and systemically administered interferon were not based on direct comparisons and so may not be reliable.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that more high-quality RCTs were required to evaluate the different routes of administration of interferon and combined treatment with interferon plus other therapeutic agents for genital warts. These trials should clearly describe their methods of randomisation and allocation concealment.

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