

# What works for warts?



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Many doctors, including GPs, believe oral cimetidine is effective for common warts. But others are not so sure.

## CLINICAL SCENARIO

IN an online GP discussion board, cimetidine, a H<sub>2</sub>-receptor antagonist, is frequently suggested as a treatment for warts. Interestingly, this is met with both strong recommendations (anecdotes of personal experience and reports of approval from specialist colleagues), and scepticism (we know that most common warts will resolve in time and so there is a high 'placebo' response). So, what does the evidence say?

## CLINICAL QUESTION

What is the effectiveness of the oral cimetidine as treatment of common warts?

## What does the research evidence say?

### Step 1: The Cochrane Library

No Cochrane systematic review exists for the question. However, its search engine very helpfully listed 18 matches to the search term "cimetidine warts" from the Cochrane Central Register of Controlled Trials.

### Step 2: Trip database

I conducted a search using the TripDatabase PICO search tool: Participant: "wart"; Intervention: "cimetidine"; Comparator: "placebo"; Outcomes: blank.

The only useful response was a post published in April 2016 in the BMJ Evidence-based Medicine's Spotlight blog by Dr Geoffrey Modest, which looked at a study that was a retrospective analysis of the use of cimetidine for plantar warts.<sup>1</sup>

The blog author's conclusion "with some

trepidation" was that cimetidine "might be worth considering".

### Step 3: Selecting a paper review

However, I had some issues with the approach in Dr Modest's blog post. For instance, the study reviewed had no control group when there are several (admittedly problematic) randomised trials on

cimetidine for plantar warts that do exist.

After reviewing the list from the Cochrane Central Register of Controlled Trials, I decided to examine in detail Yilmaz et al's 1996 placebo-controlled double-blind study published in the *Journal of the American Academy of Dermatology*.<sup>2</sup>

My final analysis also considered data from Rogers et al's 1999 randomised trial

in adults, and Ardabili and Majid's 2014 paper, which was a randomised trial comparing cimetidine with placebo in addition to cryotherapy.<sup>3,4</sup>

## CRITICAL APPRAISAL

I used the randomised controlled trial appraisal sheet from the Centre for Evidence Based Medicine.<sup>5</sup>



## STAT FACTS: 95% CONFIDENCE INTERVALS

IN rough conceptual terms, the 95% confidence interval is the range of values that are still mathematically consistent with the estimate of effect found.

In other words, it tells us something about the degree of imprecision of the result. Confidence intervals are sometimes not reported for proportions, and this can be misleading, especially for small sample sizes where the imprecision can be large.

For instance, imagine if this study demonstrated that the cimetidine group had a 40% response rate.

Naively, this might seem a large proportionate difference, but is well within the uncertainty of the estimate.

Stat Facts

## PICO

### Participants: who was studied?

In total 70 people (children and adults) with at least five warts, who had received no topical or systemic treatment for at least four weeks. The setting of the study was not described, but the authors were academic dermatologists in Turkey. The mean age was about 15, with the mean duration of warts of roughly 2.5 years.

Important exclusions: pregnant and lactating women, renal and hepatic disease, and males aged over 16 (cimetidine was not specifically approved for use in men in Turkey).

### Intervention: what was the exposure?

The intervention group took cimetidine 25-40mg/kg daily, in three or four divided doses for up to three months. The treatment was discontinued if the lesions disappeared.

### Comparator: what was the control?

The placebo group were given an identical looking placebo, divided into three or four doses for up to three months.

### Outcomes: what was measured?

Primary outcome: this was not explicitly stated, but it appears that "complete cure", as defined by monthly clinical examinations, was the main outcome of interest.

## THE RESULTS

The primary outcomes showed the complete cure rate at three months was:

- Cimetidine group: 32% (9 of 28) (note: calculated 95% CI 16-52% - see StatFacts)
- Placebo group: 31% (8 of 26) (note: calculated 95% CI 14-52%)
- Interpretation: no meaningful difference between the groups were found

## DISCUSSION AND CONCLUSION

On its own, Yilmaz et al's small study cannot be considered as providing strong evidence (for or against) the efficacy of cimetidine on warts. That being noted, this study is consistent with the notion that cimetidine may be of placebo value in the treatment of warts as no meaningful difference was identified. In both groups, approximately one-third of participants had complete cure by the end of treatment.

## Internal validity: Are the results valid?

### Randomised patient assignment?

**Yes.** However, no description of how this was undertaken is given.

### Groups similar at the start?

**Yes.** There were no obvious differences between the intervention and placebo groups.

### Groups treated equally apart from assigned treatment?

**Yes.**

### All patients accounted for?

**No.** The investigators did not undertake an "intention-to-treat" analysis, with approximately 23% of participants not included in analyses.

### Measured objectives? Or were patients and clinicians kept blinded?

**Probably.** The presence or absence of warts is a reasonably objective outcome. The study is described as double-blinded, but little further detail is described.

There have been some suggestions that cimetidine is more effective in younger children.<sup>6</sup> However, this was not strongly supported by the limited randomised trial data and it should be recognised that younger children have higher/quicker wart resolution rates regardless of therapy.

A possible alternative hypothesis is that the impression of greater efficacy in children is simply due to association biases.

For adults, Rogers et al similarly didn't find a benefit from cimetidine compared with placebo.<sup>3</sup> As a treatment in addition to cryotherapy, cimetidine did not appear to provide benefit either.<sup>4</sup>

Cimetidine is typically considered to be a fairly benign treatment, although one-fifth of participants reported side effects in the Rogers et al study.

My interpretation of the research evidence is that it does not support the use of cimetidine as a treatment for warts. I recognise that there are anecdotes of seemingly miraculous responses for warts that have been present for a long period.

It is important to reflect that the placebo group in this study had a one-third completely cured rate, where the mean duration of warts was more than two years.

Cimetidine should not be used as routine treatment of common warts in primary care. ■

References on request