Imiquimod versus podophyllotoxin, with and without human papillomavirus vaccine, for anogenital warts: the HIPvac factorial RCT

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Plain English summary

The HIPvac [Human papillomavirus infection: a randomised controlled trial of Imiquimod cream (5%) versus Podophyllotoxin cream (0.15%), in combination with quadrivalent human papillomavirus or control vaccination in the treatment and prevention of recurrence of anogenital warts] trial compared two commonly used creams to treat genital warts: 0.15% podophyllotoxin cream (Warticon®; GlaxoSmithKlein plc, Brentford, UK) and 5% imiquimod cream (Aldara®; Meda Pharmaceuticals, Takeley, UK). It also investigated whether or not a vaccine used to prevent human papillomavirus infection, quadrivalent human papillomavirus vaccine (Gardasil®, Merck Sharp & Dohme Corp., Merck & Co., Inc., Whitehouse Station, NJ, USA), could help treat warts or prevent them from coming back in patients whose warts had been cleared.

The HIPvac trial was a randomised controlled trial involving 503 patients with warts attending sexual health clinics in England and Wales. The creams and the vaccine were well tolerated; there was some soreness where the cream was applied, but no unexpected side effects.

When deciding which treatment was better, we looked at whether or not the warts had cleared by 16 weeks after starting treatment and, if cleared, whether or not they returned by 48 weeks. We compared the creams against each other, and the addition of vaccine against no vaccine (a placebo injection). Patients were allowed to have cryotherapy (freezing treatment) as well, if the investigator advised this. We also calculated the value for money of each type of treatment.

The two creams were very similar in how well they worked to clear the warts. One difference was that podophyllotoxin cream worked slightly quicker. The number of patients given cryotherapy was about the same for both types of cream. We had expected that recurrence of warts after treatment with imiquimod cream might be less than after treatment with podophyllotoxin cream, but, in fact, the two creams were similar.

Quadrivalent human papillomavirus vaccine did not improve clearance of warts or reduce the chance of recurrence, but the result remains inconclusive. If we had been able to recruit 1000 participants as originally planned, we might have been able to be more certain about whether there was any benefit of vaccination. Further research would be needed to investigate any possible effect.

The two creams offered similar value for money in treating warts. Giving patients the vaccine in addition to the cream is not good value for money at its current list price, given the uncertainty about the benefit it offers.
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