A varicella-zoster virus vaccine reduced the burden of illness of herpes zoster in older adults

Oxman MN, Levin MJ, Johnson GR, et al. **A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults.** N Engl J Med. 2005;352:2271-84.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Infectious Disease ★★★★★★★

QUESTION

In persons ≥ 60 years of age, does a live attenuated varicella-zoster virus (VZV) vaccine decrease the burden of illness caused by herpes zoster and the incidence of postherpetic neuralgia?

METHODS

Design: Randomized placebo-controlled trial (Shingles Prevention Study).
Allocation: {Concealed}†.*
Blinding: Blinded (clinicians and participants, {data collectors, outcome assessors, data analysts, and monitoring committee}†).*
Follow-up period: Mean 3.13 years.
Setting: 22 sites in the United States.
Participants: 38 546 persons ≥ 60 years of age (median age 69 y, 59% men) who had a history of varicella or had resided in the United States ≥ 30 years. Immunocompromised persons were excluded.
Intervention: 1 subcutaneous injection of 0.5 mL of Oka/Merck VZV vaccine (n = 19 270) or placebo (n = 19 276). The vaccine had median estimated potency of 24 600 plaque-forming units.
Outcomes: Vaccine efficacy with respect to the severity of illness caused by herpes zoster, defined as the relative reduction in burden-of-illness score (VE_{BOI}) based on the severity and duration of herpes zoster pain, comparing the vaccine and placebo groups. For the vaccine to be considered a success, the VE_{BOI} point estimate had to be ≥ 47% with the lower limit of the 95% CI > 25%. The secondary outcome was vaccine efficacy with respect to the incidence of post-herpetic neuralgia (VE_{PHN}) defined as pain rated as ≥ 3 on a scale ranging from 0 (no pain) to 10 (pain as bad as you can imagine). The vaccine was considered a success if the VE_{PHN} point estimate was ≥ 62% with a 95% CI lower limit > 25%.
Patient follow-up: 95% (modified intention-to-treat analysis).

MAIN RESULTS

Herpes zoster developed in 315 participants in the vaccine group and 642 in the placebo group. The incidence of herpes zoster was lower in the vaccine group (Table). The herpes zoster burden-of-illness score was lower in participants who received the vaccine than in those who received placebo (score 2.21 vs 5.68, 61% reduction, $P < 0.001$). The results were not affected when stratified by sex or age. Postherpetic neuralgia developed in 27 participants in the vaccine group and 80 in the placebo group (Table), and the results were not affected by sex or age.

CONCLUSIONS

In persons ≥ 60 years of age, a live attenuated varicella-zoster virus vaccine decreased the burden of illness caused by herpes zoster and the incidence of postherpetic neuralgia. The incidence of herpes zoster was also reduced to a greater extent in vaccine recipients than in the placebo recipients.

Sources of funding: Cooperative Studies Program, Department of Veterans Affairs; Merck; James R. and Jesse V. Scott Fund for Shingles Research.

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*See Glossary.

†Information provided by author.

Varicella-zoster vaccine (VZV) vs placebo to prevent herpes zoster at mean 3.13 years‡

Outcomes	Incidence per 1000 person-y		NNT (95% CI)	Vaccine efficacy (CI)
	VZV vaccine	Placebo		
Incidence of herpes zoster	5.42	11.12	59 (50 to 72)	51% (44 to 58)
Incidence of postherpetic neuralgia	0.46	1.38	364 (259 to 577)	67% (48 to 79)

‡Abbreviations defined in Glossary; NNT and CI calculated from number of confirmed cases of herpes zoster and postherpetic neuralgia in article.

COMMENTARY

The study by Oxman and colleagues may be the first to look at a vaccination strategy to prevent expression of a disease caused by reactivation of a latent infection acquired decades earlier. While zoster is seldom fatal, morbidity from postherpetic neuralgia can be high, and the disease requires physician visits and prescriptions for antiviral drugs and analgesics. In persons with previous varicella, zoster can occur at any time, although risk increases with age (especially after 60 y). The participants in this study (immunocompetent adults > 60 y) seem representative, with a rate of zoster (among placebo recipients) similar to that previously described in a population-based study (1). A single dose of vaccine substantially reduced the risk for herpes zoster (by 51%) and postherpetic neuralgia (by 67%) over the 5.5 years of the double-blinded study. Given that vaccination caused very few adverse events, the vaccine seems to be both safe and effective. Cost-effectiveness will depend on the price of the vaccine and the costs of various outcomes (which have not yet been analyzed). However, if the vaccine is available to the target population at a price similar to that of the pediatric vaccine, a strong case could be made for administering it universally without regard to patient-specific risk factors because the cost of treating zoster and its sequelae can be substantial. The biggest caveat would be for immunocompromised adults because neither safety nor efficacy has been measured yet in such persons. Encouragingly, the pediatric vaccine has been fairly safe in children with moderate immune-deficiency (2).

For this new vaccine, the optimal age at first administration still needs to be determined. The duration of protection is unknown. While the relatively high NNT of 59 may seem unappealing, a vaccine with 100% protection against zoster would still have an NNT of 30.

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References

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