



Herpes zoster

News for daily clinical practice

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Herpes zoster is a common painful disorder characterised by a unilateral dermatomal rash resulting from reactivation of latent varicella zoster virus. [1] Reactivation is thought to occur because of immunosenescence, with ageing and immunosuppression being well established risk factors for zoster. [2] Herpes zoster is an important diagnosis as it is very common, affecting 30% of people during their lifetime and 50% of individuals aged 85 years or greater. [3] With an ageing population in the UK and the Netherlands, the burden related to zoster and its complications is likely to increase over time. The main complication of zoster is persisting pain lasting for months to years after zoster, termed post-herpetic neuralgia (PHN); the likelihood of developing PHN increases with ageing. [4] PHN has a major effect on quality of life and treatments are relatively ineffective. [5] Zoster is also less frequently associated with other serious complications, including ophthalmological and neurological complications, with recent studies showing a transient increase in stroke following zoster. [6-8]

HERPES ZOSTER VACCINE

The development of a live attenuated herpes zoster vaccine was a major breakthrough for prevention of the morbidity associated with herpes zoster. Oxman *et al.* demonstrated in the phase 3 Shingles Prevention Study (n=38,546) that the live attenuated vaccine was efficacious and well tolerated, reducing the incidence of zoster by 51% (95% confidence interval, 44-58) and PHN by 67% (48-79). [9] Vaccine efficacy depends on the age at vaccination, reducing zoster by almost 70% (54-81) in those aged 50-59 years, 64% (56-71) in individuals aged 60-69 years and by 38% (28-52) in those aged 70 years or greater. The zoster vaccine was introduced into routine clinical practice in the USA in 2006 and in other countries including the UK in 2013, Australia, Greece and France.

Effectiveness of the zoster vaccine in routine clinical practice was similar to the phase 3 clinical trials. [10] Vaccine uptake has been a major issue in the USA, with initial uptake of only 4% rising to almost 20% in 2013. [10, 11] Contributing factors to the low uptake include patient and provider issues with reimbursement complexities and storage issues being frequently cited provider issues, while perception of risk are issues from a patient and provider perspective. [12,13] Loss of zoster vaccine efficacy over time has been an important finding from the Long Term Persistence Study. [14] This study reported that the vaccine efficacy against incident zoster was only 21% (11-30) and PHN 35% (95% CI 9-56) respectively 5-11 years after vaccination. [14,15] Loss of vaccine effectiveness over time has implications for cost-effectiveness analyses, as they may lead to the possible need for a booster dose, although this strategy would require further formal assessment.

UK EXPERIENCE

The live zoster vaccine was introduced into UK routine clinical practice in September 2013 for immunocompetent individuals aged 70 years with those aged 79 years being targeted as a catch up regime. [16] Vaccine uptake has been relatively high; when the vaccine was first introduced, uptake was 62%, with more recent research showing a slight decline in uptake to 52%. [17] The majority of UK vaccinations took place during seasonal influenza vaccination season, consistent with guidance provided to general practitioners to concomitantly administer these vaccines. [17] The latter strategy was based on studies of the immune response when these vaccines were administered together rather than separately, which showed no major alteration in the vaccine immune response. [17] Concomitant administration is also a pragmatic approach to maximise vaccine uptake. Vaccine effectiveness in routine UK clinical practice has been similar to that observed in the clinical trials and observational studies undertaken in other settings. [9,10,17,18]

NEW HERPES ZOSTER SUBUNIT VACCINE

The live attenuated zoster vaccine is contraindicated in those who are severely immunosuppressed, who are at the highest risk of both developing zoster and major complications including PHN following zoster. [2,19] A new adjuvanted subunit vaccine (HZ/su) has recently been approved by the US Food and Drug Administration and the European Medicines Agency. In late 2017, the US Advisory Committee on Immunization Practices recommended that the subunit vaccine be used in preference to the live attenuated vaccine on the basis of superior efficacy (>90%) in clinical trials in a range of age

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groups, with efficacy maintained during a mean 3.7 year follow up. [20,21] The subunit vaccine is administered in two doses, and current cost estimates are \$140 USD per dose plus administration costs. Cost-effectiveness analyses from the USA have supported the use of this vaccine as a cost-effective intervention. [22] The subunit vaccine is associated with more side effects than the live attenuated vaccine, however, side effects are short-lived. [21] Further research is needed focused on the long-term efficacy and effectiveness of the new subunit vaccine, adherence to the new vaccine given the requirement for two doses and side effects in the context of the use of a novel vaccine adjuvant.

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SUMMARY

Herpes zoster is an important disease resulting from reactivation of latent varicella zoster virus decades after childhood varicella. Zoster is associated with substantial morbidity, in particular prolonged pain, known as post-herpetic neuralgia. A live attenuated zoster vaccine has been introduced into clinical practice in the US, the UK and other countries. In phase 3 trials, this vaccine reduced incident zoster by 51% and post herpetic neuralgia by 67% with similar effectiveness in real world settings. However, this vaccine is limited by waning efficacy over time and by its use being contraindicated in severely immunosuppressed individuals who are at greatest risk of both zoster and complications following zoster. The development of a new highly efficacious recombinant subunit zoster vaccine which may be useful for immunosuppressed individuals is an important development with public health consequences for countries with ageing populations.

KEYWORDS

herpes zoster – post-herpetic neuralgia – vaccine effectiveness

DISCLOSURE

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