

EFFECTIVENESS OF TBE VACCINES

Background

On More than twenty-five countries in Europe have one or more TBE endemic areas. Using the EU TBE case definition (laboratory confirmed infection with symptoms of CNS inflammation), there were a total of 3,734 TBE cases reported to the European Centre for Disease Prevention and Control in 2020. In 2020, the highest incidence rates were in Lithuania (23.6/ 100,000, Slovenia (8.7/100,000) and the Czech Republic (7.9/100,000).

Two TBE vaccines with pediatric and adult formulations are available in Europe with various schedules for primary and booster immunization. Randomized controlled clinical trials for demonstration of efficacy were not conducted as part of the clinical development program for licensure, but approval was granted following demonstration of safety and immunogenicity data (antibody formation).

Various observational studies have been conducted to assess vaccine effectiveness (VE) in different age groups and across different countries. A review has recently been published about the reported estimates of TBE VE generated in Europe.

Results

Information extracted from each VE study included country, study design, study period, study population, study participant age, number of TBE virus infected cases, and the number in the comparator group. Estimates also included VE against TBE virus infection outcomes (e.g., With/without CNS involvement, moderate/severe illness, hospitalization, prolonged hospitalization).

On initial screening of the literature, thirteen publications met the inclusion criteria (one study was a cohort milk-borne outbreak) and were

analyzed. The studies were conducted in Austria, the Czech Republic, Latvia, Germany, and Switzerland. Eleven of the twelve studies (the outbreak not included) used the screening method, and two used a case-control study design to estimate the VE, and one study used both analytical approaches.

In six studies which estimated the VE against TBE virus infection, estimates ranged from 91.5% (three doses) to 98.8% (four or more doses). There was only a little difference in VE between studies using the screening methods compared to studies with the case-control design. TBE vaccines were highly effective against serious infections including protection against prolonged hospitalization. The lowest estimate of VE was a study in Latvian children (94.9% against hospitalization).

TBE vaccines were highly protective in all age groups, e.g., in the oldest age group (≥ 60 years of age) from 91.7% in Austria to 99.5% in Latvia. In the youngest age strata, VE estimates range from 88.6% in Austria to 100% in Germany.

Four studies described little differences in VE at ≤ 10 or ≥ 10 years after the last vaccine dose. VE at ≥ 10 years after last dose ranged from 86.8% in Germany to 99.6% in Latvia. There was little difference in VE between the two TBE vaccine brands (FSME-Immun, Encepur). In an alimentary-transmitted outbreak in Germany, the VE was estimated 81% protection against virus infection and if one individual whose last vaccine shot was more than 10 years overdue was excluded from the analysis, VE would be 100% against TBE virus infection by consumption of non-pasteurized milk.

Four studies have estimated the number of TBE cases converted by vaccination, e.g., in Austria: approximately 333 cases per year from 2000 to 2011 among a population of 8.2 million.

Discussion

This review clearly demonstrates that TBE vaccines are highly effective across Europe in preventing infection, disease and serious outcomes. The studies also indicated that the booster interval may be prolonged to 10 years to those who have received three or more vaccine doses. The public health aspect of TBE vaccination is notable in terms of cases and hospitalizations averted.

It is likely that thousands of TBE cases are averted each year in TBE endemic regions of Europe. Studies in Latvia suggest that TBE vaccines are protective against the three TBE virus subtypes (European, Siberian, Far Eastern). VE estimates against specific subtypes are yet not available and with increasing emerging of *Ixodes persulcatus* in the Baltic countries and Scandinavia, and the increased risk of infections by Siberian and Far Eastern subtypes, estimations of VE against the latter virus subtypes are warranted.

Measures to increase TBE vaccine uptake and enhancement of compliance with TBE vaccination schedules should be implemented in all endemic regions in Europe and in travelers to these regions.

Literature

Angulo FJ, Zhang P, Halsby K, et al. A systematic literature review of the effectiveness of tick-borne encephalitis vaccines in Europe. *Vaccine*. 2023;41(47):6914-6921. doi:10.1016/j.vaccine.2023.10.014

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