MIXED IMMUNIZATION WITH TWO TBE VACCINE BRANDS INCREASES THE NEUTRALIZATION TITERS AGAINST A VARIETY OF TBE-EU STRAINS

Background

Two vaccines are available in Europe to protect against TBE. These vaccines are inactivated whole virus vaccines based either on the European subtype strain K23 (Encepur®, Bavarian Nordic) or on strain Neudörfl (FSME-IMMUN®, Pfizer). These TBE vaccines are highly effective with protection rates of more than 90% (see, e.g., Newsletter August 2022, Newsletter June 2022, Snapshot week 15/2023). The vaccine strains differ in 32 amino acids of the whole viral polyprotein and in four amino acids in the glycoprotein E (gE) which induces neutralizing (NT) antibodies against TBE virus and cross-reacting, but non-neutralizing antibodies against a variety of flaviviruses. A study has been carried out to assess the neutralizing activity of sera from individuals immunized with Encepur or FSME-IMMUN against virus strains from different genetic clades of the European subtype (TBE-EU).

Results

Sixteen TBE-EU virus strains (13 genotypic clades) were tested by a micro-neutralization test against a panel of 33 sera from healthy donors who had a complete basic TBE vaccination according to the recommended vaccination scheme of the manufacturers or who had in addition up to four booster injections. The vaccinees had received solely Encepur (N=12) or FSME-IMMUN (N=11) or a mixture of both vaccines (N=10). While the vaccine strain K23 was not available for the study, the related strain K2 was used for NT assays.

Except for one serum from an individual vaccinated with FSME-IMMUN, all serum-strain samples resulted in a NT titer of at least 10. The medium titer was 160. There was a weak positive correlation between the number of immunizations and the NT titer. No significant differences in NT titers could be seen between sexes of the donor samples. The variance of the NT titers for individual virus strains was broader than it was for individual serum samples. There was no significant phylogenetic signal of NT titers that were detectable along the tree topology, as well as no significant variation of NT titers in individual genotypic clades.

The highest NT titers were observed in sera from the mixed group (Encepur plus FSME-IMMUN) and the lowest NT titers for the Encepur group. The overall variances of NT titers differed significantly between the groups with lower intra-sample variances for sera from individuals immunized with both vaccines. No correlation among the amount of amino acid substitutions to Neudörfl and K23 and the NT titers was found. Furthermore, four virus strains with identical gE protein sequences but different NT titers were identified.

Discussion

The goal of vaccination is to protect the vaccinee from infection with a wild-type virus. Even small changes in the amino acid sequence or other virulence determining regions may cause alterations in the pathogen's epitope structure or replication capacity which may result in reduced vaccine efficacy or even vaccine failure.

The selected TBE-EU strains displayed an astonishing diversity and an unexpected level of

divergence in the performed in-depth phylogenetic analysis of the genomes despite geographical proximity. Nevertheless, sera from vaccinated individuals neutralized most of the TBE-EU strains used in this panel.

Both vaccines were able to induce antibodies that can neutralize a wide variety of TBE virus strains circulating in Central Europe. Notably, sera from a mixed vaccination (Encepur plus FSME-IMMUN) displayed the highest range of NT titers. Thus, the administration of vaccine injections from different brands might be an advisable way to address the immune system as broadly as possible and to reach higher NT titers and improved resilience against a broad spectrum of wild-type strains.

Literature

Bestehorn-Willmann et al.
Increased vaccination diversity leads to higher and less-variable neutralization of TBE viruses of the European subtype.
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