IN SILICO PREDICTIVE STUDY OF ROTAVIRUS EPITOPES OF CIRCULATING *VS* VACCINE STRAINS.

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Introduction. Rotavirus is the leading cause of acute gastroenteritis in children under the age of five (1). Since 2004 frequency rotavirus strains have been detected, being in the city of Chihuahua strains G3P[8] and G2P[4] the main cause of gastroenteritis. The antigenic proteins, VP8* and VP7 are the main target to elicit antibodies that prevent infection. Two live attenuated rotavirus vaccines have been applied since 2006 in Mexico; Rotarix® (monovalent includes the strain G1P1A[8]) and RotaTeq® (pentavalent includes strains G1-G4 along with genotype P7[5], and G6P1A[8]. Four antigenic epitopes has been reported in VP8* and three in VP7 (2), which are recognized by antibodies elicited with vaccination. The aim of this work was to study the antigenic variability of VP8* and VP7 of rotavirus through *in silico* prediction analyses.

Methods. Rotavirus VP8* and VP7 aminoacid sequences obtained from hospitalized infants with severe acute gastroenteritis, were aligned against the aminoacid sequences of both rotavirus vaccines monovalent and pentavalent, analyzed in Clustal X and Bioedit to find aminoacid changes in the antigenic regions of both proteins. Tridimensional structures were modeled on Esypred3D basing on crystallographic models, using model 2DWR to model VP8* sequences and 3FMG for VP7 models and compared the physical protein structures calculating the RMSD value (3) and then measuring the distances between alpha carbons of each antigenic aminoacid, both between the detected proteins and the vaccine proteins.

Results. The aminoacid alignments against the VP8* component of Rotarix and RotaTeq showed that there are 7, 14 and 7 aminoacid changes between the VP8* of the circulating genotypes P[8]-3, P[4]-3 and P[8]-1, respectively. Sequence comparison between G1 genotype of Rotarix and RotaTeq showed 3 aminoacid changes against circulating G1 genotype, 4 changes between Rotarix G2 and circulating G2 and 3 changes between circulating G3 and RotaTeq G3.
RMSD valued calculated for VP8* ranked between 0.11-0.19 and 0.38-1.13 Å for VP7. Alpha carbon distances for antigenic aminoacids of VP8* ranked from 0.08-0.53 Å and 0.65-3.14 Å for VP7.

Conclusions. Aminoacid differences in VP8* and VP7 demonstrate variability in the sequence of the epitopes of VP8* and VP7, through *in silico* prediction analyses specific aminoacid changes in the antigenic epitopes, that leads to escape antigen recognition by antibodies elicited with vaccination, that weakens avidity of antigen-antibody interaction, though there is no significant structural differences between circulating and vaccine proteins of rotavirus.

References.

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