Antibiotics 2019: Antigenic diversity of type 1 polioviruses and its implications for efficacy of inactivated polio vaccines - Konstantin Chumakov - Food and Drug Administration

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Statement of the Problem:

Two vaccines against poliomyelitis??? Inactivated Polio Vaccines (IPV) and live Oral Polio Vaccine (OPV) are among the most successful vaccines ever. They define paradigms for vaccine protection against viral diseases, and brought about virtual elimination of the disease in most of the world. Nevertheless, some questions about the correlates of their efficacy remain. Polio eradication will lead to discontinuation of OPV use and its replacement with IPV. To ensure IPV supply for resource-limited countries a new generation of IPV based on attenuated Sabin strains (sIPV) was developed. This raised important questions about determining its efficacy and potency. How can these new vaccines be compared to the conventional IPV (cIPV) made from immunochemically different strains? Can we use the same benchmarks for potency and protectiveness for both types of IPV? These questions prompted us to undertake the study.

Following the assertion of wild-type 2 poliovirus destruction in 2015, the sort 2 part was expelled from the live-constricted oral polio antibody (OPV). This change suggests a need to improve worldwide inclusion through routine vaccination with inactivated polio antibody (IPV), to guarantee type 2 insusceptibility. A few makers use Sabin OPV strains for IPV creation (sIPV), as opposed to the standard wild-type strains utilized for regular IPV (cIPV). Be that as it may, as opposed to cIPV, strength tests for sIPV have not been normalized, no worldwide references exist, and no antigen units have been characterized for a sIPV human portion. Therefore, sIPV items from various makers can't be looked at, and the connection among antigenicity and immunogenicity of sIPV isn't surely known.

Methodology & Theoretical Orientation:

We assembled a panel of wild and vaccine-derived polioviruses and used it to determine titers neutralizing antibodies in sera from healthy previously immunized subjects, as well as in immunized animals. In addition, we have used a transgenic mouse model to determine the minimal level of antibodies needed for protection. Findings: antibodies against poliovirus present in sera of experimental animals as well as healthy vaccinated subjects exhibited a significant strain bias when tested in neutralization reaction. Maximum neutralization titers were observed when neutralization tests were performed against the strain used for vaccine manufacture, while titers against heterologous strains tended to be lower. In some extreme cases the difference in titers was more than 10-fold. As a result, while the level of seroprotection in a group of vaccine recipients was sufficiently high when measured against the homologous strain, it was significantly lower when heterologous strains were used. A booster dose of IPV increased all titers, and the seroprotection level was acceptable even when measured against heterologous strains. We will also present experiments to identify the minimal protective level of neutralizing antibodies by passively immunizing transgenic mice expressing the human poliovirus receptor.

Conclusion & Significance:

The results demonstrate that strains of type 1 poliovirus have different ability to be neutralized by vaccine-induced antibodies. This suggests that while people with minimal levels of neutralizing antibodies can be protected against viruses that are immunologically similar to the strains used in vaccine manufacture, they may have undetectable levels of neutralizing antibodies against other strains and thus not be fully protected. Therefore to ensure protection against a wide range of viruses, clinical trials must include measuring seroconversion using both homologous and heterologous strains. The antigen intensity of a lot of 7 sIPV tests was resolved utilizing various strategies accessible in the same number of research facilities. The essential point of this examination was to think about the result of various power appraisals, utilizing distinctive immunizer reagents and reference principles, and to describe the D-Ag substance of 2 potential applicant sIPVs, to choose a proposal for the foundation of the first IS for sIPV. The same applies to performing pre-clinical evaluation and measuring potency of IPV, as well as to performing seproprevalence studies. The results also suggest that to ensure robust protection against all strains the level of neutralizing anti-poliovirus antibodies must be maintained at a level higher than the commonly accepted minimum of 1:8.