Immunization Dialogue

Measles Vaccination: Is the EZ Strain Safe?

For the past several years the measles vaccine has been administered as early as 6-9 months of age, the aim being to minimize the risk of measles which commonly occurs at a young age in the developing world. It is a well accepted fact that transplacental antibodies against the measles virus reach rather low levels by 6-9 months and there is a distinct "window period" of lack of protection before the measles vaccine is given. The older strains of measles vaccines *(e.g.,* Schwarz) were ineffective when given before 9 months. Hence the quest for a new more potent vaccine lead to the discovery of the Edmonston Zagreb strain (EZ) which is effective between 6 and 9 months and probably even earlier. EZ vaccine administered at a concentration of at least $10^{4.7}$ pfu per dose was more effective than other vaccine strains in overcoming the interferring effects of passively acquired maternal antibodies in young children^). Hence the introduction of this strain into routine immunization occurred several years ago and is being used extensively throughout the country for some time now. However, are we handling a safe virus and should we be using the EZ strain at all? Recent reports state otherwise.

In 1990, the Global Advisory Group of the Expanded Programme on Immunization (EPI) recommended vaccination at 6 months of age with high dose EZ measles vaccine(2), because studies of medium and high titer EZ vaccine had shown good antibody response and clinical protection(3,4). In the developing world, where measles in the first year is such an important health problem, the EZ vaccine was grabbed with tremendous enthusiasm(5) and reports regarding its safety and efficacy continue to appear(6). Soon reports of increased morbidity and mortality from unrelated diseases began appearing in the medical literature in patients who had received the high titer EZ vaccine. Such reports appeared from Senegal(7), Guinea Bissau(8) and Mexico(9). However, there was no excess measles related mortality or atypical measles like disease(9). Also morbidity and mortality was distinctly more in females(l,7,8). The reason for such an event in still not clear. It has been seen that measles in Bengali children has a significant negative effect on growth that persists for years(10). Infact, high titer vaccine receipients had a lower percentage of circulating CD4+ lymphocytes and a consistently lower mitogen induced lymphoproliferation and DTH response(l). Many of the short term immunogenic abnormalities that accompany natural infection are also seen to a lesser degree after immunization and re-immunization with standard dose measles vaccine(l). Thus high titer measles vaccine may induce long term disruption of the hosts ability to respond to infections. The patient becomes more vulnerable or susceptible to common infectious diseases^). Eventually, the EPI Global Advisory Board recommended that high titer measles vaccine usage be stopped(ll,12). Yet the EZ strain continues to be widely used in India and even trials still continue(6).

Have we, then, lost our way in the EPI measles programme. Certainly, because

most clinicians are still immunizing for measles at 9 months and not between 6 and 9 months. At this age, other strains are equally effective yet we are exposing infants to an extremely dangerous attenuated measles strain, the EZ strain. So, let us continue vaccinating at 9 months with other strains, and drop the EZ strain immediately!

Mukesh U. Sanklecha,
Consultant Pediatrician,
51, Poornima, Colaba,
Mnmbai 400 005.

REFERENCES

1. Leon ME, Ward B, Kanashiro R, Hernandez H, Vaisberg B. Immunogenic parameters two years after high titer measles immunization in Peruvian children. J Infect Dis 1993; 168:1097-1104.
2. Expanded Programme on Immunization. Global Advisory Group. Wkly Epid Rec 1990; 65: 5-11.
3. Markowitz LE, Sepulveda J, Diaz Orterge JL. Imunization of 6 months old infants with different dose of EZ and Schwarz measles vaccine. N Engl J Med 1990; 322: 580-587.
4. Whittle HC, Campbell H, Reghman SM, Armstrong JRM. Antibody persistence in Gambian children after high dose EZ, measles-vaccine. Lancet 1990; 336: 1046-1048.
5. Bhargava I, Chhaparwal BC, Phadke MA, Irani SF, Chakladhar BK, Maheshwari CP. Reactogenicity of indigineously produced measles vaccine. Indian Pediatr 1996; 33: 827-831.
6. Parmar VR, Sood AK, Goyal A, Sharma V, Singh T. Immunogenicity of Edmonston Zagreb measles vaccine. Indian Pediatr 1996; 33: 845-850.
7. Gorenne M, Leroy O, Beau JP, Sene I. Child mortality after high titer measles vaccine: Prospective study in Senegal. Lancet 1991; 338: 903-907.
8. Aaby P, Knudsen K, Whittle H, Lisse I, Tharrup J, Poulsen A, *et al.* Long term survival after EZ measles vaccination in Guinea Bissau: Increased female mortality rates. J Pediatr 1993; 122: 904-908.
9. Diaz-Ortega JL, Luna AM, Valdespino J. Mortality and morbidity after high titer measles vaccine in Mexico. Lancet 1992; 340: 924-925.
10. Koster FJ, Curlin GC, Aziz KM A, Hague A. Synergistic impact of measles and diarrhea on nutrition and mortality in Bangladesh. Bull WHO 1981; 51: 901-908.
11. Expanded Programme on Immunization. Safety of hight titer measles vaccines. Wkly Epid Rec 1992; 67: 357-361.
12. Expanded Programme on Immunization Recommendations: High titer measles vaccine dropped. Lancet 1992; 340: 232.

Comments

Dr. Sanklecha has raised some important issues regarding measles immunization policies and practices in India. They are regarding the choice of the strain of vaccine virus, the virus titre per dose and the age at immunization.

There are several strains of measles vaccine viruses. The parent of many strains in current use was called Edmonston, after the child from whom it was isolated by the Nobel laureate Dr. Enders and his