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DENGUE FEVER VACCINES: AN UPDATE AND MINI REVIEW

General Medicine

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KEYWORDS

INTRODUCTION

Dengue one of the commonest mosquito-borne diseases affects millions every year.[1]It is caused by Flavivirus and is transmitted by Aedes aegypti and Aedes albopictus mosquitoes and has 4 genetically distinct serotypes .Dengue is a major problem also due to mosquitoes which are resistant to commonly used insectisides.[2,3,4]Last 2 decades have seen several problems of vaccine development due to difficulty of performing long term studies to find out the risk of dengue shock syndrome and dengue haemorrhagic fever mostly in children .Moreover, to avoid antibody dependant enhancement(ADE) in repeat infections and protection against all 4 serotypes is a real challenge.

Dengue has various clinical manifestations ranging from fever with headache and a wide spectrum of clinical features. Secondary infection by a different serotype may lead to serious disease due to ADE[5]due to antibodies which cross react forming immune complexes and thus causing severe disease.

Development of Vaccines

Several vaccines are developed among which 3 are the most studied.[6]The 3 vaccines are

1. Dengvaxia[R]
2. TV003/TV005
3. TAK-003

1. Dengvaxia-It is created on the backbone of yellow fever in which pre- membrane and envelope genes of Yellow Fever Virus have been altered by similar genes from every DEN V serotypes.
2. TV003/TV005 was made by deleting 30 nucleotides of DENV -4 and DENV-1.DENV-2 and DENV-3 parts were made from the Rden4 delta30 backbone[7,8].
3. TAK-003/DENvax is modulated on a live attenuated DEN V-2 strain in which the genes of the pre membrane and the envelope region of the Yellow Fever Virus have been substituted by similar genes from every DEN V serotypes[9].

Clinical Evaluation

Till recently, 2 vaccines for dengue have received license for use, Dengvaxia R(CYD-TDV)(Sanofi Pasteur) and Qdenga R.(TAK-003)[10]

CYD-TDV was first vaccine to get license which is given in a 3 -dose pattern in a 0/6/12 month schedule .Screening before vaccination for dengue seropositivity is a must and only positive tested persons are eligible for vaccination restricting it's widespread use.

TAK-003,a live attenuated vaccine contains weakened dengue virus serotypes1-4, produced by Takeda using DENV2 as the backbone of the genome.It is a 2 dose series,3 months apart.

DSV-4(dengue subunit vaccine) is a tetravalent vaccine which is a single component nonreplicating 4 in 1 based on virus like particle made using the methylotrophic yeast Pichia pastoris.It is serotype specific with absence of undesirable epitopes with low or absent ADE phenomenon.[11]It is being developed .

Recommendations

TAK-003 is recommended in children,6-16 years of age in zones of high dengue transmission .As it has lower efficacy below 6 years of age, it is not recommended in that age group and also because seropositivity is low in children below 6 years of age. The interval should not be reduced between the 2 doses, but if 2nd dose is missed, it should be administered at the earliest.

WHO recommends vaccination from 6-60 years of age also in persons in dengue endemic regions , having comorbid conditions.

Contraindications

1. Pregnancy or females planning pregnancy at least 1 month post vaccination
2. Breastfeeding females
3. Persons with congenital or acquired immunodeficiency including patients on immunosuppressives or on systemic corticosteroids.
4. Persons with symptomatic HIV infection or asymptomatic HIV with impairment of immunity

TAK-003 can be given with hepatitis and yellow fever vaccines. It will not prevent all cases and so vaccination is used for disease control. Vector control is very important.

Travel Vaccination

Frequent travellers of non endemic countries, infected earlier by one of the serotypes ,travelling to endemic countries may benefit from TAK 003 vaccine which may prevent 2nd infection which may be fatal.

CONCLUSION

Dengue fever is a viral disease with widespread clinical manifestations with morbidity and mortality among different age groups .Though vector control is very important the development of safe and effective vaccines are very important to avoid complications as there is no definite treatment apart from supportive therapy Progress has been made in the field of dengue vaccination, but much more research is needed for safe and effective vaccines, which is the importance of this mini review.

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