Pentavalent vaccine

A major breakthrough in India's Universal Immunization Program

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Immunization is one of the most important public health interventions and a cost effective strategy to control the infectious diseases especially in children. Complete immunization coverage in India has increased from below 20% in the 1980s to nearly 61% at present, but still more than 1/3rd children remain un-immunized. Advent of combination vaccines has facilitated incorporation of additional vaccines into immunization schedule. Pentavalent vaccine, against five killer diseases—diphtheria, pertussis, tetanus, hepatitis B and *Hemophilus influenza* type B (Hib), has been introduced in almost all GAVI eligible countries by 2011. Government of India introduced the vaccine in two states in pilot phase and has given green signal to six more states. The use of pentavalent vaccine automatically raises the coverage level of hepatitis B and Hib vaccines. If the vaccines are provided individually, the coverage of hepatitis B and Hib vaccines usually lags behind DPT coverage. This gap can be filled by using pentavalent vaccine in routine immunization programmes.

Introduction

In 1974, WHO launched expanded program on immunization (EPI) with the aim of controlling these six childhood diseases: tuberculosis, diphtheria, pertussis, tetanus, polio and measles. Government of India (GoI) in 1978 adapted EPI with slight modification by replacing measles with typhoid. Later on typhoid was discontinued and measles included in the program and renamed as

universal immunization program (UIP) in 1985.¹

India is a developing country with a population of 1,210 million and high infant and under 5 mortality rate of 47 and 59 per 1,000 live births, respectively.^{2,3} Immunization is one of the most important public health interventions and a cost effective strategy to control the infectious diseases especially in children. Complete immunization coverage in India has increased from below 20% in the 1980s to nearly 61% at present, but still more than 1/3rd of the children remain un-immunized (Fig. 1).⁴⁻⁹ Immunization coverage for third dose of diphtheria, pertussis and tetanus (DPT3) and hepatitis B (Hep B) vaccine is 71.5 and 58.9% respectively.⁹ No data regarding *Hemophilus influenzae* type b (Hib) vaccine coverage is available in the country. US\$10–20 is the estimated cost to fully vaccinate a child and further by significantly reducing the total cost of treatment of diseases it offers opportunities for poverty reduction and social and economic development of the country.¹⁰

The advent of combination vaccines significantly reduced the volume of immunization activities by decreasing the number of injections, amount of pain and cumulative exposure to preservatives and stabilizers that may contribute to adverse events. In addition, it has facilitated incorporation of additional vaccines into immunization schedule, thereby higher immunization coverage.^{11,12} Pentavalent vaccines (a combination vaccine which protects against five killer diseases: diphtheria, pertussis, tetanus, hepatitis B and Hib) have been launched in 65 out of 67

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Figure 1. Trends in immunization coverage, India.

GAVI eligible countries by 2011.^{13,14} The pentavalent vaccines provide a golden opportunity to curb Hib disease and hepatitis B along with diphtheria, pertussis and tetanus in the developing countries.

Disease Burden

During 2010, there were 3,129 reported cases of diphtheria with 177 deaths in India. Pertussis also contributed with 38,493 reported cases and 6 deaths in the same year. There were 1,574 reported cases and 136 deaths due to tetanus other than neonatal tetanus in the country.⁹ The disease burden of diphtheria, pertussis and tetanus decreased by 85, 95 and 75% respectively in last three decades after introduction of DPT vaccine in India.^{4,9}

Hib disease is a common infectious disease which can lead to serious morbidity and also mortality in pediatric age group. Hepatitis B infection in children results in significant mortality and morbidity later in life.

Hib is a leading cause of bacterial meningitis among infants (357/100,000) and young children (0–4 y; 86/100,000) with case fatality ranging from 20 to 29%. Nearly 30% survivors of Hib meningitis suffer from major disabilities. A study estimated 72,000 deaths per year due to Hib disease among children under five with a case fatality rate of 16% among invasive cases in India.^{15–21}

It has been estimated that, of the 25 million infants born every year in India, over one million run the lifetime risk of developing chronic hepatitis B infection. Moreover, every year > 100,000 Indians die due to illnesses related to hepatitis B infection.²²

Immunogenicity, Safety and Efficacy of Pentavalent Vaccine

Numerous immunogenicity studies have been performed in India, and have shown that immunogenicity against each of the vaccine component and reactogenicity is same as that of simultaneous but separate site administration of DPT, Hep B and Hib vaccines.^{23–27} In a study from India, on post-primary immunization with Serum Institute of India's (SII) and GSK's pentavalent vaccine, 100% seroprotection was detected for diphtheria, tetanus, hepatitis B and Hib components in both SII and GSK groups and for pertussis, efficacy was 96.1% in SII group and 95.4% in GSK group.²³

The vaccines have excellent tolerability profile with only minor adverse events. All the infants who reported common systemic reactions i.e., fever, irritability and unusual crying, recovered with symptomatic treatment. No vaccine-related neurological, hypersensitivity reactions or other serious adverse events were reported in infants.^{23–27}

Cost Effectiveness

A preliminary cost-effectiveness analysis from India indicated that Hib vaccine introduction into the UIP is highly cost-effective. With conservative burden of disease assumptions and the UNICEF price (2008) of US\$3.60 per Hib vaccine dose, this analysis showed that costs per DALY averted is US\$254. Based on trends of other vaccines in national programs, prices would be expected to fall significantly from current levels. With a price of US\$2 per dose of pentavalent vaccine, the cost per DALY averted will be US\$26.²⁸ The SII has announced in June 2011 to sell the vaccine at US\$1.75 per dose, it is expected that the other manufacturers will follow suit.²⁹

A cost-effectiveness analysis study in Haryana State for Hib vaccine from 2010 to 2024 concluded that using UNICEF pricing, the incremental cost of Hib vaccine introduction from a government and a societal perspective was estimated to be US\$81.4 and US\$27.5 million, respectively. Vaccination of 73.3, 71.6 and 67.4 million children with first, second and third dose of pentavalent vaccine, respectively, would avert 7,067,817 cases, 31,331 deaths and 994,564 DALYs. Incremental cost per DALY averted from a government (US\$819) and a societal perspective (US\$277) was found to be less than the per capita gross national income of India in 2009.³⁰

Progress Toward Implementation

In 2008, National Technical Advisory Group on Immunization recommended the inclusion of pentavalent vaccine in UIP, depending on the availability of vaccines.³¹ Following the recommendation, the GoI decided to launch Hib containing pentavalent vaccines in ten states. The decision was hailed internationally by public health practitioners as India constitutes 34% of the birth cohort in GAVI-eligible countries and even in the absence of population-based data, the country is estimated to have the highest number of deaths due to Hib in children under 5 y of age.²⁹

After initial controversies, India has introduced pentavalent vaccine in 2 states

(Tamilnadu and Kerala) through routine immunization program in the year 2011. Acknowledging the significance of Hib vaccination, now the GoI has decided to introduce Hib vaccine in UIP as liquid pentavalent vaccine in six states, namely, Gujarat, Haryana, Karnataka, Goa, Jammu, Kashmir and Puducherry from October 2012 to December 2014.³²

Scope

The use of pentavalent vaccine automatically raises the coverage level of hepatitis B and Hib vaccines. If the vaccines are provided individually, the coverage of hepatitis B and Hib vaccines usually lags behind DPT coverage. This gap can be filled by using pentavalent vaccine in routine immunization programs. This will help India in combating a large but preventable burden of Hib disease as well as hepatitis B and achieving Millenium Development Goal 4 of reducing child mortality.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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