e-ISSN: 2319-9865
p-ISSN: 2322-0104
Research and Reviews: Journal of Medical and Health Sciences

Current status of vaccines against Diphtheria, Pertussis, Tetanus, Hepatitis B and Hib: A Review.

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Review Article

Received: 17/02/2014
Revised: 15/03/2014
Accepted: 18/03/2014

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Keywords: Immunization, pentavalent vaccine, hypotonic hyporesponsive episodes, immunogenicity, safety, India

ABSTRACT

A liquid pentavalent vaccine containing DTwP-HepB-Hib was incorporated in the Universal Immunization Program of India with the funding from Global Alliance for Vaccines and Immunization (GAVI). India introduced pentavalent vaccine in two states namely, Andhra Pradesh and Kerala in 2011. The combination vaccine offers simplification of immunization schedule, reduced cost, better acceptance and logistic benefits. However, some experts have been raising concerns regarding safety of pentavalent vaccine owing to incidents of deaths and adverse effects like hypotonic-hyporesponsive episodes following vaccine administration. Henceforth, there should be a vigilant approach towards prevention of potential adverse effects while spreading the coverage of pentavalent vaccine. The present article provides current status of potential benefits and risks associated with pentavalent vaccine against the diphtheria, pertussis, tetanus, hepatitis B and Haemophilus influenzae.

INTRODUCTION

The combination vaccine against diphtheria (D), pertussis (P) and tetanus (T) is the core part of the childhood vaccination in India. In 2010, more than 85% of infants have received DPT vaccine, representing 109 millions of immunized children. The spread of this vaccine has led to a marked reduction in these infections worldwide [1]. WHO recommended addition of HepB vaccination in the Expanded Program of Immunization (EPI) in 1992, to ensure reduction in overall incidence of hepatitis B infection and to reduce chronic carriage in endemic zones. In 1998, it was followed by addition of *Haemophilus influenzae type B* (Hib) vaccination considering the increasing burden of disease [2]. With advent of various new vaccines for combating infectious diseases, promotion of combination vaccines seems essential for simplifying the increasing complexity of immunization program of any country. To ensure continuous availability and uninterrupted supply of safe and effective DTP, HepB and Hib vaccines, which are essential for smooth functioning and success of any immunization program created a motive for the vaccine manufacturers to develop pentavalent combination vaccines.

Introduction of pentavalent vaccine in India

With the recommendation from National Technical Advisory Group on Immunization (NTAGI), the Ministry of Health and Family Welfare (MoHFW), Government of India (GoI), decided to incorporate pentavalent vaccine containing DTwP-HepB-Hib in Universal Immunization Program of India (UIP) in 2009. This incorporation of pentavalent vaccine is funded for the first two years of its introduction by a non-government organization; Global Alliance for Vaccines and Immunization (GAVI) [3]. These grants were meant for utilization of pentavalent vaccine in ten states namely; Andhra Pradesh, Himachal Pradesh, Jammu & Kashmir, Madhya Pradesh, Maharashtra, Kerala, Karnataka, Punjab, Tamil Nadu and West Bengal and were expected to benefit more than 18 million children. This move of introduction of pentavalent vaccine in UIP was praised vociferously internationally, as India constitutes 34% of birth cohort in GAVI-eligible countries [4].

Immunization schedule

Pentavalent vaccine has been recommended for all infants in a three dose schedule. The first dose is scheduled at 6 weeks and the next dose is administered after a gap of at least 4 weeks and the last dose is given 4

e-ISSN: 2319-9865
p-ISSN: 2322-0104

weeks later. (Table 1) The vaccine is offered to all children younger than 1 year of age and booster dose is not recommended in UIP. (Table 2) The administration is based upon progressive birth cohort whereby all children who present for the first dose of DPT (DPT1) will be provided first dose of pentavalent vaccine. The infants who are already been immunized with DPT + Hep B shall complete their respective schedule.

Table 1: Immunization schedule of pentavalent vaccine

Age	Current schedule	With Pentavalent vaccine
At birth	BCG, OPV-0, HepB-Birth dose	BCG, OPV-0, HepB-Birth dose
6 weeks	OPV-1, DPT-1, HepB1	OPV-1, Pentavalent-1
10 weeks	OPV-2, DPT-2, HepB2	OPV-2, Pentavalent-2
14 weeks	OPV-3, DPT-3, HepB3	OPV-3, Pentavalent-3
16-24 weeks	DPT-B1, MCV2, OPV-B1	DPT-B1, MCV2, OPV-B1
5-6 years	DPT-B2	DPT-B2

Table 2: Comparison between DTP vaccine and Pentavalent vaccine

DTP vaccine	Pentavalent Vaccine
Confers immunity against 3 diseases namely; • Diphtheria, • Pertussis and • Tetanus.	Confers immunity against 5 diseases namely; • Diphtheria, • Pertussis, • Tetanus, • Haemophilus influenzae type B and • Hepatitis B
Introduced in 1991	Introduced in 2009 in India.
0.5 ml as a single dose, Given deep intra-muscularly in antero-lateral aspect of the upper thigh	0.5 ml as a single dose, Given deep intra-muscularly in antero-lateral aspect of the upper thigh
Stored at 2-8^{0}C	Stored at 2-8^{0}C
Cheaper (Rs 17.13, Haffkine)	Expensive (INR 500, Serum Institute of India)
Dosing schedule • 6-10-14 weeks, followed by • Booster doses at 16-24 weeks and 5-6 years.	Dosing schedule • 6-10-14 weeks, followed by • Booster doses of DPT at 16-24 weeks and 5-6 years.
Contra-indications include, • Hypersensitivity. • History of encephalopathy within 7 days of vaccination with pertussis-containing vaccine. • Vaccine should not be used in patients with progressive neurologic disorder, progressive encephalopathy or uncontrolled epilepsy.	Contra-Indications include, • Hypersensitivity to any component of the vaccine. • It is a contraindication to use this or any other related vaccine after an immediate anaphylactic reaction associated with a previous dose. • Presence of any evolving neurological condition. Encephalopathy after a previous dose is a contraindication to further use. • Immunization should be deferred during the cause of an acute illness. • Vaccination of infants and children with severe, febrile illness should generally be deferred until recovery.
Adverse effects include, • Pain, swelling and redness at the injection site. • Persistent or unusual crying • Convulsions, signs of encephalopathy • Fever, headache, fatigue and • GI symptoms e.g. nausea, diarrhoea, abdominal pain.	Adverse effects include, • Local redness, warmth, oedema, and induration with or without tenderness, as well as urticaria and rash. • Systemic reactions such as fever, headache, drowsiness, weakness, nausea, vomiting, diarrhoea and anorexia, and rarely myocarditis.
Immune response to vaccines may be reduced in patients who are receiving immunosuppressive treatment e.g. cytotoxics, high dose corticosteroids, irradiation.	As with other intramuscular injections, use with caution in patients on anticoagulant therapy. Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses) may reduce the immune response to vaccines.

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p-ISSN: 2322-0104

Table 3: List of available vaccines

Name and manufacturer of vaccine	Diseases protected	Cost in Indian Rupees
DIPTHERIA, PERTUSSIS, TETANUS, (Haffkine)	Diphtheria, Pertussis, Tetanus	17.13
ADACEL, (Sanofi Pasteur)	Diphtheria, Pertussis, Tetanus	727
BOOSTERIX, (GSK)	Diphtheria, Pertussis, Tetanus	839
TRIPLE ANTIGEN (GSK)	Diptheria, Pertussis, Tetanus	16.65
TRIPVAC (Bio E)	Diptheria, Pertussis, Tetanus	11.65
INFANRIX (GSK)	Diptheria, Pertussis, Tetanus	699
EASY 4, (Chiron panacea)	Diphtheria, Pertussis, Tetanus, H. influenzae	575
TETRA HIBEST (Aventis Pasteur)	Diphtheria, Pertussis, Tetanus, H. influenzae	4505
Tetramune (Wyeth)	Diphtheria, Pertussis, Tetanus, H. influenzae	399
ECOVAC, (Panacea)	Diptheria, Pertussis, Tetanus, hepatitis B	1090
Q-VAC (Serum Institute)	Diptheria, Pertussis, Tetanus, hepatitis B	70.8
TRITANRIX-HB (GSK)	Diptheria, Pertussis, Tetanus, Hepatitis B	240
COMVAC, (Bharat Biotech)	Diphtheria, Pertussis, Tetanus, Hepatitis B, H. Influenzae type B	600
PENTAVAC, (Serum Institute)	Diphtheria, Pertussis, Tetanus, Hepatitis B, H. Influenzae type B	500
EASY 5, (Chiron panacea)	Diphtheria, Pertussis, Tetanus, Hepatitis B, H. Influenzae type B	635

Efficacy and safety data

Table 4: Incidence of adverse events after liquid pentavalent vaccine administration.[5] (n=245)

Adverse event	After 1st dose	After 2nd dose	After 3rd dose
Pain			
Any	141(57.6%)	127(51.8%)	102(41.6%)
Grade 3[a]	54 (22.4%)	53(21.6%)	38(15.5%)
Redness			
Any	52(21.2%)	42(17.1%)	36(14.7%)
>5.0 cm	48(19.6%)	38(15.5%)	32(13.0%)
Swelling			
Any	101(41.2%)	89(36.3%)	73(29.8%)
>5.0 cm	96(39.1%)	86(35.1%)	71(28.9%)
Nodule			
Any	4(1.6%)	1(0.1%)	0(0%)
Hindrance of limb movements			
Any	46(18.8%)	43(17.6%)	27(11.0%)
Fever			
Any	101(41.2%)	101(41.2%)	70(28.6%)
37.5-<38.0°C	58(23.6%)	58(23.6%)	38(15.5%)
>38.0°C	43(17.5%)	43(17.5%)	32(13.0%)
Persistent crying			
Any	29(11.8%)	18(7.3%)	12(4.9%)
Irritability			
Any	70(28.6%)	53(21.6%)	46(18.8%)
Loss of appetite			
Any	5(2.0%)	7(2.9%)	5(2.0%)
Refusal of feeds			
Any	1(0.4%)	0(0%)	2(0.8%)
Vomiting			
Any	9(3.7%)	6(2.4%)	4(1.6%)
Diarrhoea			
Any	6(2.4%)	5(2.0%)	4(1.6%)

[a] The highest grading

e-ISSN: 2319-9865
p-ISSN: 2322-0104

150 countries across the globe that have already introduced HiB vaccine have reported a dramatic decline in the incidence of invasive HiB disease and death.

A pre-licensure, open label, phase III, randomized controlled study in three tertiary care hospitals of India in 2008-2009 with regard to immunogenicity and tolerability of LPV in Indian infants showed that the vaccine meets all criteria for childhood vaccination. A 100% seroprotection rate was obtained with LPV in 484 infants aged 6-8 weeks, except pertussis for which the response was 95%. The incidence of adverse reactions like pain at injection site and restricted limb movements were less frequent ($p<0.001$) among the recipients.[5] (Table 4) The study documented neither immunological interference nor increased reactogenecity due the vaccine administration.

A review on the first five years of introduction of pentavalent vaccine by Schmid et al (*Penta 004 study*) [6,7] has documented that the vaccine was highly immunogenic. One month after primary immunisation course, over 97% of vaccinated children were protected against diphtheria, tetanus, pertussis and Hib (anti-PRP≥0.15µg/ml) and 91.4-98.0% of the children were protected against HBV. (Table 5) At the higher anti-PRP cut off level of ≥1 µg/ml (an indicator of long term protection), more than 88% of children were seroprotected.

Table 5: Seroprotection/Seroconversion rates 1 month after 3rd vaccination (6-10-14 weeks.[6,7]

Antibody	Penta 004 study [14,15] (n=320)	SIIL group [17] (n=152)	GSK group [17] (n=152)
Hepatitis B (≥10 IU/L)			
% SP	91.4	100	100
95% CI	87.7,94.3	(97.60–100)	(97.60–100)
Diphtheria (≥0.1 IU/L)			
% SP	99.0	100	97.37
95% CI	97.2,99.8	(97.60–100)	(93.40–99.28)
Tetanus (≥0.1 IU/L)			
% SP	100	99.34	98.68
95% CI	98.8,100	(96.39–100)	(95.33–99.84)
Pertussis (≥20 EIU/mL)			
% SC@	97.4	96.06	95.40
95% CI	95.0,98.9	(91.61–98.54)	(90.74–98.13)
Hib *(Anti-PRP≥0.15 µg/ml)*			
% SP	99.0	100	100
95% CI	97.2,99.8	(97.60–100)	(97.60–100)
(Anti-PRP≥1 µg/ml)			
% SP	88.2	100	96.06
95% CI	84.1,91.5	(97.60–100)	(91.61–98.54)

%SP: seroprotection rate, @%SC=seroconversion rate (pertussis only)

An open labelled, multicentre, randomized, comparator controlled study was conducted during 2006–08 at Maulana Azad Medical College & Hospital, New Delhi and Bharati Vidyapeeth University Medical College & Hospital, Pune; on post-primary immunization with Serum Institute of India ltd. (SIIL) and Glaxo Smith Kline's (GSK) pentavalent vaccine. Post vaccination, seroprotection rate for diphtheria, tetanus, Hib and hepatitis B components was 100% in both SIIL and GSK groups. For pertussis, the vaccine response was 96.1% in SIIL and 95.4% in GSK. In terms of long-term sufficient acquired protection, 100% infants in SIIL & 96% in GSK group exceeded the level of ≥1.0 µg/ml for anti-PRP antibodies and this difference was statistically significant ($p = 0.04$) [8]. (Table 5)

A phase III, single arm, open label study by Eregowda et al in 2013 at a tertiary care hospital in India have demonstrated that the pentavalent vaccine was highly immunogenic and has a acceptable safety profile for use in Indian infants [9]. The study showed that at one month after third vaccination, percentage of infants achieving predefined protective antibody levels were 99% diphtheria; 100% tetanus; 98% Hepatitis B; 100 % Hib short term (≥0.15µg/mL); 95% Hib long-term (≥1.0µg/mL) protection; and relevant immune response was 99 % for pertussis. The investigators documented no vaccine related serious adverse events and the vaccine was well tolerated. The most frequently reported reactions were mild to moderate tenderness and erythema. The frequencies of all adverse events declined with subsequent vaccinations.

An open-label, randomized, phase II study was conducted in 2006 at the Gülveren Health Centre in Ankara, Turkey by Kanra et al with the objective to assess the safety and immunogenicity of the new DTPw-HepB-Hib combination vaccine in comparison with the separate administration of licensed DTPw-Hib and hepatitis B vaccines

in order to exclude the possibility of antigenic interference and to ensure that the safety profile was comparable to that achieved with separate administration. The author demonstrated non-inferiority of the DTPw-HepB-Hib vaccine to separately administered DTPw-Hib + HepB was confirmed for each antigen at one month after the third vaccination. The investigators found no evidence of interference in the immunoresponse to diphtheria or tetanus with the DTPw-HepB-Hib vaccine in their study [10].

A post-licensure, open-label study was carried out in 2011-12 at two tertiary care hospitals of India to assess the long-term persistence of the diphtheria, tetanus, pertussis, HBV, and Hib antibodies in children at 15–18 months of age who had completed their three-dose primary immunization schedule at 6–10–14 weeks of age.

The antibody persistence was compared between the pentavalent vaccine produced by two different manufacturer viz. Serum Institute of India Ltd. (SIIL; Pentavac®) and Panacea Biotech (Easyfive®). Also the response to the booster dose of DTwP–Hib (Quadrovax®) vaccine was analysed. The study showed that the primary immunisation with pentavalent vaccine induced an excellent immunity lasting till second year of life. The study documented that regarding Hib, suggested short term (≥0.15 µg/ml) protection was shown by 99–100% of vaccines in both groups. The higher antibody level (≥1.0 µg/ml), which suggests long-term protection, was slightly better (83%) in the SIIL Pentavac® than Easyfive® (76%) group. For diphtheria, 90%vaccinees in both groups showed seroprotection; for tetanus the proportion of vaccinees with likely clinical protection was 89% and 87% in the SIIL Pentavac® and Easyfive® groups, respectively; for pertussis, these percentages were 49% vs. 54%, and hepatitis B 94% vs. 88%. Following the booster dose, a strong immune response was induced, as 100% of vaccinees achieved seroprotection for diphtheria, tetanus, and Hib; for pertussis, the vaccine response was 79% in the SIIL Pentavac® and 78% in the Easyfive® group.

The safety analysis of the pentavalent vaccine showed that the Pain at injection site (50.6%), redness (15.2%), swelling (32.7%), and fever (29.6%) were the most common reported adverse events (Table 6). Other noted adverse events were nodule (0.8%), irritability (23.5%), loss of appetite (6.1%), vomiting (2.1%), diarrhoea (1.3%) and drowsiness (0.8%). The authors mention that there were no any serious adverse events or any case of anaphylaxis. All the reactions were mild in intensity and resolved with or without medications (analgesics) or by application of cold compress [11].

Table 6: Adverse events profile of pentavalent vaccine [11].

Adverse event	Total (n=229)	% of AE	95% CI
Pain [a]	**116**	**50.6**	**42.0, 60.5**
Grade 1	22	9.6	6.44, 14.12
Grade 2	84	36.6	30.70, 43.10
Grade 3	10	4.3	2.41, 7.85
Redness (cm)	**35**	**15.2**	**10.8, 21.0**
Up to 2.5	25	10.9	7.51, 15.62
2.5-5.0	10	4.3	2.41, 7.85
Swelling (cm)	**75**	**32.7**	**26.0, 40.8**
Up to 2.5	51	22.2	17.37, 28.10
2.5-5.0	21	9.1	6.09, 13.61
>5.0	03	1.3	0.47, 3.76
Nodule (cm)	**2**	**0.8**	**0.15, 2.89**
<0.5	1	0.4	0.10, 2.39
0.5-<1.0	1	0.4	0.10, 2.39
Fever (°C)	**68**	**29.6**	**23.2, 37.4**
<38.0	19	8.3	5.39, 12.59
38.0-38.4	28	12.2	8.60, 17.11
38.5-38.9	12	5.2	3.04, 8.93
39.0-39.4	9	3.9	2.10, 7.29
Irritability	54	23.5	17.9, 30.5
Drowsiness	2	0.8	0.15, 2.89
Loss of appetite	14	6.1	3.5, 10.0
Vomiting	5	2.1	0.80, 4.84
Diarrhea	3	1.3	0.33, 3.57

AE –Adverse events; **CI**- Confidence interval

[a] **Grade 1:** present, but leg movement not affected; **grade 2**: discomfort, interferes with or limits leg movement; and **grade 3:** disabling, unable to move leg.

An open label, phase IV single group study carried out at *K. E. M. Hospital, Mumbai*, *M.S. Ramaiah Medical College, Bangalore,* and *St. John's Medical College Hospital, Bangalore, India* carried out by Bavdekar et al [12]

demonstrated that the pentavalent vaccine offers 99% seroprotection against hepatitis B infection and 100% seroprotection against *H. influenzae* type b with a robust increase in Geometric Mean Concentrations (GMCs) for both anti-HBs and anti-PRP (polyribosol ribitol phosphate; the Hib capsular polysaccharide) antibodies, after the three-dose primary vaccination course. The study also demonstrated that the vaccine has excellent tolerability profile with only minor adverse events such as local swelling (33.5% of doses) and irritability (29.0% of doses) being commonly reported. Severe adverse events were highly uncommon. The incidence of symptoms (solicited/unsolicited; local/general) observed in this study was similar to those reported in other studies [13,14]. The investigators concluded that the combined DTPw-Hep B/Hib vaccine is immunogenic for the antigens tested, safe and well-tolerated in Indian infants when immunized according to the recommended 6-10-14 week's schedule.

Ali et al demonstrated that pentavalent vaccine has a good immunogenic potential with high levels of antibodies to the specific antigens and a very good seroprotection rate for all the vaccine components, i.e., diphtheria, pertussis, tetanus, hepatitis B and Hib [15]. (Figure 1, 2)

Figure 1: Pre and post immunization antibody titres.[15]

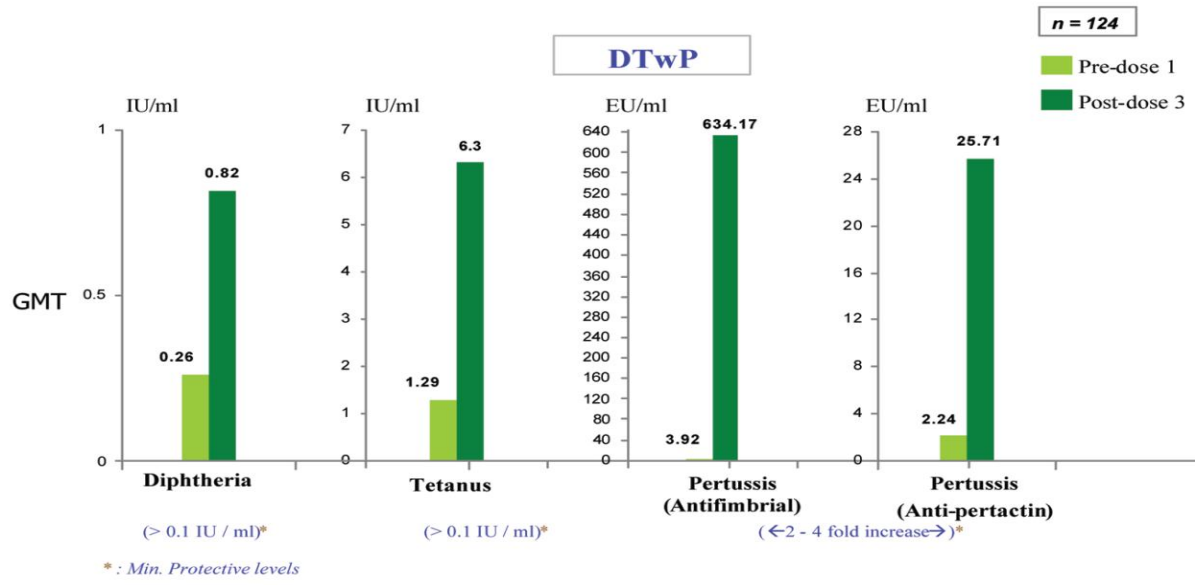
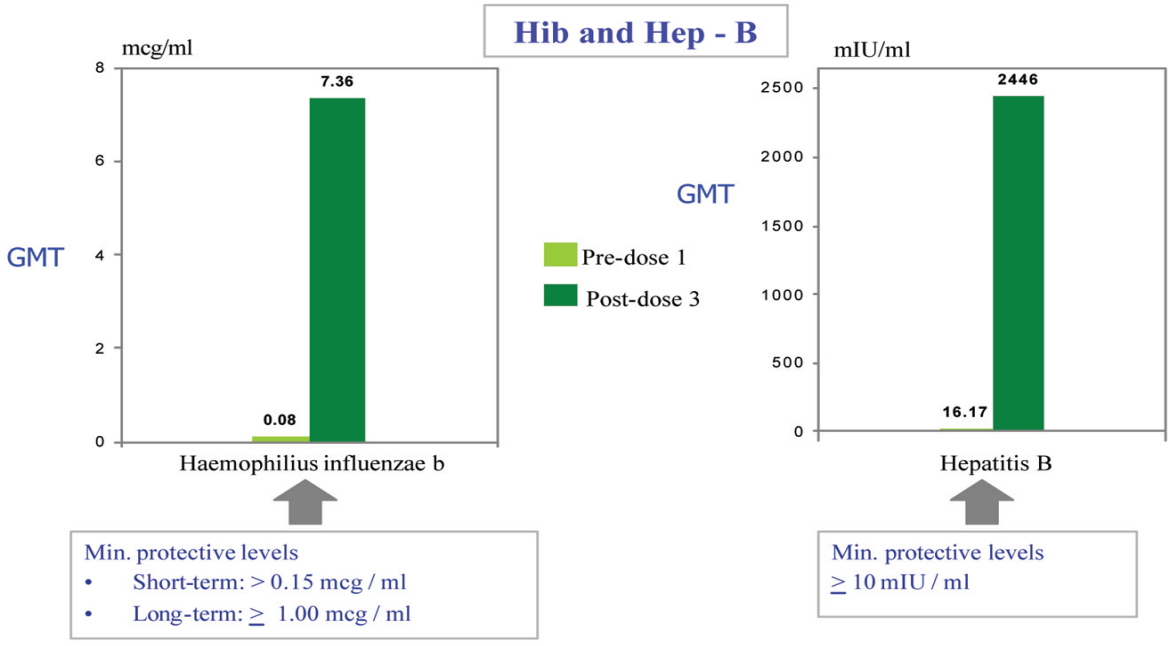


Figure 2: Pre and post immunization antibody titres.[15]



e-ISSN: 2319-9865
p-ISSN: 2322-0104

Benefits as a combination vaccine

Combination vaccines offer an effective solution to the increasing complexity of childhood immunization, which is increasing as newer vaccines are being developed and added to the universal immunization schedules. The benefits of these combination vaccines includes i) simplification of immunization programmes, ii) improved compliance for the vaccines from the infants and parents, iii) decrease in fear and pain among the infants and toddlers, iv) logistic benefits; v) reduced cost, vi) reduced clinical visits and vii) chance to include more vaccines in the tight immunization schedules.

Experience and safety issues over pentavalent vaccines in Asian Countries [16]

Sri Lanka, Bhutan, Vietnam and India were the first Asian countries who introduced pentavalent vaccine in their immunization schedules. Sri Lanka introduced the pentavalent vaccine from Crucell in January 2008. Within 3 months, 4 reports of deaths and 24 reports of suspected hypotonic-hyporesponsive episodes (HHE) prompted regulatory attention and precautionary suspension of the initial vaccine lot. HHE is a recognised side effect to whole cell and acellular pertussis-containing vaccines, and to Hib and hepatitis B vaccine. A subsequent death that occurred with the next lot in April 2009 led the authorities to suspend pentavalent vaccine use and resume DTwP and HepB vaccination.

Bhutan introduced pentavalent vaccine from Panacea in September 2009. The identification of 5 cases with encephalopathy and/or meningo-encephalitis shortly after pentavalent vaccination prompted the authorities to suspend vaccination on 23 October 2009. Subsequently 4 additional serious cases related to vaccine administration were identified and investigated.

Vietnam introduced pentavalent vaccine from Crucell in June 2010. Through May 2013, a total of 43 serious AEFI (serious adverse events following immunization) cases were investigated, including 27 fatalities. Following receipt of reports of 9 deaths following vaccination between December 2012 and March 2013, health authorities suspended use of the vaccine.

India introduced pentavalent vaccine from Serum Institute of India in the two states of Tamil Nadu and Kerala in December 2011. This was followed up with expansion of vaccine usage in the states of Goa, Pondicherry, Karnataka, Haryana, Jammu and Kashmir, Gujarat and Delhi during the second half of 2012 to the 1st quarter of 2013. To date, 83 AEFI cases, some of which were associated with fatality, have been reported after vaccine introduction from some states.

In each country the serious AEFIs were reviewed with independent national and international experts. Based on those reviews, none of the fatal cases could be classified as having a consistent causal association with immunization. The WHO panel also concluded that “the reporting rate of HHE following the pentavalent vaccine (14.9 cases per 100 000 doses) was found to be well within the reported estimates of HHE following whole-cell pertussis-containing vaccines (21–250 cases per 100 000 doses)”[17]. In Sri Lanka, after a comprehensive investigation and review, the same pentavalent vaccine product was re-introduced in 2010. However some experts have objected the methodology of assessment and classification of adverse drug reactions used by WHO experts for establishment of causality [18]. Since then and up to 2012, another 14 deaths were reported among infants who had received the Crucell pentavalent vaccine. In addition, 6 of 19 infant deaths were found at autopsy to have severe congenital heart disease. Following this finding, in Sri Lanka children with known severe congenital heart disease are now vaccinated under close medical supervision, and no additional deaths among these children have since been reported in temporal association with pentavalent vaccine administration. In Bhutan, following a similar investigative process, the vaccine was reintroduced in 2011. Vietnam is currently reviewing clinical, epidemiological and vaccine quality issues.

A public Interest Litigation was filed in Supreme Court of India over the 15 infant deaths after immunisation with the pentavalent vaccine in Kerala and Tamil Nadu.[19] Following which a national-level Adverse Events Following Immunisation (AEFI) Committee of the Ministry of Health and Family Welfare is in the process of holding a study on safety of the vaccine, which was introduced in India in 2011, as well as to ascertain the background under which the deaths were reported within 72 hours of vaccination [20].

The other issue regarding incorporation of pentavalent vaccine into UIP is uncertainty regarding long term sustainability of this program. There is no clear information regarding funds to introduce the vaccine in whole country, guarantee of uninterrupted vaccine supply in adequate amounts. In India, there are certain states where the full immunization coverage is atrociously low at 30-40% like Uttar Pradesh, Madhya Pradesh, and Bihar. Henceforth, there is a need for assessment of beneficial impact of pentavalent vaccine in these poorly immunised sates.

e-ISSN: 2319-9865
p-ISSN: 2322-0104

Cost effectiveness of pentavalent vaccine

It has been argued by many, that the introduction of pentavalent vaccine is influenced by financial terms rather than medical needs. India being one of the biggest developing markets, this move can be viewed suspiciously. It has been noted that manufacturers who produce pentavalent vaccine, are the key constituents of GAVI alliance [21]. Potential links between manufacturers and the agencies which might play a pivotal role in decision making should not be ignored prior to taking strategic decisions.

While the doubts regarding the costs are legitimate, recent data suggest that the cost of the vaccine has reduced substantially. At present there are at least five Indian companies manufacturing the vaccine. With one of the Indian manufacturers, the Serum Institute of India, announcing in June 2011 that they plan to sell the vaccine at US$ 1.75 (€1.2; approximately Rs 79 as on June 2011) per dose, it is expected that the other manufacturers will follow suit.[22] By virtue of a welcome move by an Indian manufacturer Biological E to supply the pentavalent vaccine at a cost of $1.19 (Approximately Rs 73 as on April 2013) per dose, the scenario is more promising [23]. In the future the price will reduce even further – as a result of bulk procurement by the Government and competition between the manufacturers. It has already been demonstrated that any price lower than US$ 2 (€ 1.4, Rs 122 approximately) per dose is highly cost effective [24].

In India, incremental costs of pentavalent vaccine were estimated at US$ 81.4 million for the year 2010 [25]. Incorporating Hib vaccination as a pentavalent vaccine, would avert up to 994,564 DALYs if all three doses were given, amounting to an incremental cost per DALY averted of US$ 819 and US$ 277 from a governmental and societal perspective, respectively. These figures are less than the per capita gross national income of India, which makes this strategy particularly cost-effective.

In a study performed at the Institute of Child Health in Calcutta, India [26] using a fully-liquid pentavalent vaccine resulted in savings of an estimated 107,000 working days/year, due to faster vaccine delivery, and cost savings over the entire supply chain of an estimated US$ 55.5 million/year.

CONCLUSION

Even today, especially in developing world, not all children get the vaccines they need, which is a harsh reality. A partial solution to this problem would be to expand the use of multivalent vaccines based upon the cost-benefit analysis. Combination vaccines no doubt simplify the national immunisation schedules. With heavy load of disease in the resource-poor countries, urgent efforts are needed to provide these so easy-to-use vaccines to children residing in those areas and thus saving millions of lives.

The pentavalent vaccine provides a golden opportunity to curb Hib disease and hepatitis B along with diphtheria, pertussis and tetanus in the developing countries. However there should be a vigilant approach towards prevention of potential adverse effects while spreading the coverage of pentavalent vaccine. Acknowledging the significance, now the GoI has decided to introduce liquid pentavalent vaccine as a part of UIP in six states, namely, Gujarat, Haryana, Karnataka, Goa, Jammu, Kashmir and Puducherry from October 2012 to December 2014 [27].

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