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Review Article

Why treat? Better prevent: Adult immunization

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Abstract
Immunization is a safe, effective and simple way to prevent life threatening illnesses not only in children but also in adults. Vaccines are some of the safest medicines available which can relieve suffering costs related to these preventable diseases. The reason for underutilization of vaccines in adults are 1) Low prioritization of the importance of vaccines preventable diseases among adults 2) Uncertainty or lack of knowledge about the safety and efficacy 3) Lack of universal recommendations for all adults and 4) Financial constraints, especially in developing countries.
Adult immunizations are administered in primary series like previously immunized, booster doses and periodic doses. Agents include Toxoids (Diphtheria and Tetanus), Live Virus Vaccines (Measles, Mumps and Rubella), and inactivated virus vaccines (Influenza), Inactive viral particles (Hepatitis B), inactivated bacterial polysaccharide vaccine (Pneumococcal) and Conjugate / Polysaccharide vaccine (Meningococcal). And also vaccines like Hepatitis A, Polio and Varicella may be recommended in some.
Since the economy and literacy rate has shown a steady rise in the South Asia and people are being aware of different health problems through the recently advanced global communication, the education and awareness for immunization not only in children but also in adults need a special consideration.
Keeping in view the statistical data of suffering costs related to the non-utilization of immunization in adults, the need of hour has come for utilization of immunization to emphasize its importance.

Key words: Adult immunization, Vaccines**.**

Vaccines are preparations of antigenic materials which are administered with the objective of inducing the recipient active immunity to specific infecting agents or toxins or antigen produced by them. They may contain living or killed microorganisms, bacterial toxoid or antigenic material from particular parts of the infecting organism which may be derived from the organism or produced by the recombinant DNA technology. Vaccine may be single component vaccines or mixed combined vaccines[1,2]. Vaccination and immunization are often used as interchangeable terms. However, the former one denotes only the administration of a vaccine or toxoid, whereas the latter describes a state of inducing or providing immunity by any means, whether active or passive[3].

Why an adult also be immunized? – global burden: Adults are more likely to die from vaccine preventable diseases than children. The statistical data of the diseases that could be prevented among adults in U.S.A, a developed country both in economy and literacy, is itself alarming for the developing countries to realize the need to initiate the preventive strategies in dealing with the preventable disease among adults. The data is as follows: Influenza itself is responsible for 20,000 to 40,000 deaths annually and an estimated 200,000 excess hospitalization at a cost of around $1Billion during epidemic years[4,5].

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In America, among adults with community-acquired pneumonia (CAP) requiring hospital admission, *S pneumoniae* ranks first as a cause and accounts for most of such cases. Pneumococcal disease is estimated to account for 3,000 cases of meningitis, 50,000 cases of bacteremia, 500,000 cases of pneumonia, and 7 million cases of otitis media each year[6]. The pharyngeal colonization rate is 5-10% of healthy adults. In Canada, an overall incidence 11.8-16.1 cases per 100,000 persons was reported between 1995-1997[6].

Hepatitis B Virus (HBV) infection is a worldwide health problem. The prevalence of HBV infection varies in different geographic areas of the world, with carrier rates ranging from 0.1 to15%[7]. Tetanus is found to affect 95% of the adults older than 20years, with 100% deaths during 1991-94[8]. A massive diphtheria epidemic (more than 157,000 cases and 5000 deaths) occurred recently in the states of the former Soviet Union and accounted for more than 80% diphtheria cases reported worldwide during that interval. A majority of cases throughout this epidemic occurred in persons ≥ 15 yrs old, and adults from 40 to 49 yrs old had very high incidence and death rates[9]. An estimated 6%-11% of younger adults are unprotected against rubella with 85% of cases during 1994-'96 in only 15years of age or older[10].

In Malaysia, the overall incidence of hepatitis A was 4.72 in 1997 per 100,000 populations. Similarly about 1.1 million Malaysians are thought to be chronically infected with HBV[11].

In Nepal, diseases that are preventable by adult vaccination have been reported by researchers recently. A study from Patan hospital, Kathmandu reported Enteric fever as the leading cause for patients with febrile illnesses visiting the hospital. Enteric fever was followed by pneumonia. The most common putative pathogens were *Salmonella enterica* serotype Typhi and *S. enterica* serotype Paratyphi A[12]. Similarly, another study from Kathmandu have noticed Multi Drug Resistant (MDR) Salmonella isolated from the cases of enteric fever in Kathmandu showing resistance to all three first line antibiotics, Ampicillin, Chloramphenicol and Cotrimoxazole[13].

The present article provides an overview of some of the adult vaccine schedule, their dosage form, availability and efficacy based on the data available with the ultimate objective of emphasizing the need for adult immunization in a developing country like Nepal. The details of the indications, dosage, cost and availability of the vaccines are tabulated in the Table 1. The cost of the vaccines is obtained from the selling price of the products as per the label or from the drug index books available in Nepal.

Table1: Indications, dosage, availability and cost of vaccines[14-17]

Vaccine	Indication	Adult dosage and Route	Cost (NRs) for single dose
Pneumococcal Vaccine* (PPV23 - A polyvalent 23-Valent conjugate vaccine)	**Prophylaxis**: • Persons aged > 65 years • Any chronic illness involving any system • Both anatomical and functional asplenia • Immunocompromised states • Conditions with Immunosuppressive therapy • Organ Transplantations	0.5 mL as single dose Route – Intra Muscular or Sub Cutaneous *One time revaccination for at highest risk patients	1679.68
Influenza vaccine*	**Prophylaxis**: • Persons aged > 50 years • Any adult wishing for immunity • Any chronic illness • Any condition with compromised respiratory status (Eg. COPD) • Health care workers providing direct care • Travelers from and to the current influenza active countries	0.5 mL by IM route every year	635.00

Vaccine	Indication	Adult dosage and Route	Cost (NRs) for single dose
Hepatitis B vaccine* (Hep B) (Recombinant)	**Prophylaxis** • Any adult wishing for immunity • Persons at risk for sexual transmission • Persons at risk for transmission by percutaneous/ Mucosal exposure to blood • Persons with chronic liver disease, including persons with hepatitis C	20 mcg 3 doses at 0, 1, and 6 months by IM route In dialysis patients, 40 mcg 3 doses at 0,1,2 and 6 months by IM route	
Tetanus, diphtheria, pertusis vaccine *	**Prophylaxis** • Those adults who were not given at least 3 doses of tetanus and diphtheria • In wound management as early as 5 years after receiving the previous dose as a booster	3 doses in those who are not vaccinated with primary series at 0, 1-2m, 6-12m intervals; *Booster with Td every 10yrs after the primary series Route – Intra muscular	289.18 (for 1 adult dose)
Measles, Mumps and Rubella *	**Prophylaxis** • Those who have not received on or after the first birthday • Health care workers • Women of child bearing age	Measles-mumps-rubella vaccination: 0.5 mL SC	13.75
Rabies vaccine*	**Prophylaxis - Post-exposure** • If the domestic animal develops rabies in 10 days • If the animal is rabid or suspected to be rabid • If the rabies is endemic in the species involved • Rabies immunoglobulin (RIG) is administered along with the vaccine **Prophylaxis - Pre-exposure** • Veterinarians, animal handlers, persons staying >1 month in endemic rabies areas	**Post-exposure** HDCV 1mL per day on day 0, 3, 7, 14, 28 Booster doses on days 0 and 3 if already immunized. Route: IM RIG- 20 IU/kg (Half dose I.M other half infiltrated at wound site) **Pre-exposure** HDCV, 0.1 mL Intra Dermal or 1 mL Intra Muscular on days 0, 7, 28 Booster dose every 2 years	153.49
Typhoid vaccine	**Prophylaxis** • Patients traveling to endemic areas • Patients with expected exposure to household contacts (eg, family members) • Workers in microbiology laboratories with expected frequent contact with Salmonella typhi	1 capsule orally x 4 doses on days 1,3,5, and 7; booster dose (4-capsule course) every 5 years (same schedule)	482.61
Meningococcal vaccine* (Conjugate-MCV4; Polysaccharide-MPSV4)	**Prophylaxis** • Both anatomical and functional asplenia • Persons traveling to or residing in hyper endemic or epidemic areas • Health workers routinely getting exposed e.g., Microbiologist • Military recruits	0.5 mL as 1 dose; Revaccinate after 5yrs if risk continues Route – MCV4 - Intra Muscular; MPSV4 – Sub Cutaneous	
Hepatitis A vaccine (Hep A)	**Prophylaxis – Pre Exposure** • Any adult wishing for immunity • Injecting and Non-Injecting drug users • Homosexual men • Persons with clotting factor disorders • Persons with chronic liver disease, including persons with hepatitis B and C • Food handlers **Prophylaxis – Post Exposure** • Within 14 days of known exposure of high-risk persons	Vaqta(R), 1 mL (50 Units); Havrix(R), 1 mL (1440 ELISA Units) Route: Intra Muscular single dose; Booster dose 6 to 18 or 24 months later	538.24

*= Available in Nepal

Effectiveness of immunization: The effectiveness of some of the commonly used vaccines are discussed below:

1. Influenza vaccine: Some uncontrolled studies of influenza vaccination are very much in favor, the incidence of clinical illness in vaccinated persons has been 70% to 90% less than expected in healthy individuals <65 years of age, elderly in nursing homes experienced 30% to 40% reduction in the incidence of illness, a 50% to 60% reduction in hospitalization and pneumonia and a 70% to 100% reduction in mortality[6,17]. Immunization with influenza vaccine was associated with a reduction in the rates of asthma exacerbation in children (1 to 6 years of age) during 3 influenza seasons[18].

2. Pneumococcus vaccine (Polyvalent): The Pneumococcal vaccine was found to be effective for preventing Pneumococcal bacteremic disease. However, the vaccination was not associated with a reduced risk of community-acquired pneumonia due to any cause in older adults[19].

3. Hepatitis B vaccine: It is suggested that, although antibody titers are achieved with the intradermal administration schedule (at 1/10th the recommended intramuscular dose), revaccination may be indicated at more frequent intervals due to the lower levels achieved[20].

4. Tetanus toxoid: Tetanus antibody titer can be raised to protective levels in the elderly by a single immunization. Fifty percent of 129 individuals over the age of 65 had non-protective levels of tetanus antibody. Of the 35 of those who agreed to immunization with follow-up antibody testing, 86% developed protective tetanus antibody titers[21].

5. Measles, Mumps and Rubella vaccine **(combined vaccination/MMR vaccination):** The vaccine combination provides long lasting immunity to measles in at least 95% of recipients. In case of mumps, the incidence of clinical illness reduces by 75% to 95%. It has also demonstrated a similar effectiveness to that of measles (in at least 95% of recipients) in assuring immunity[22].

6. Rabies vaccine: Rabies vaccine is an inactivated virus vaccine which promotes immunity by inducing an active immune response. The production of specific antibodies requires about 7 -10 days to develop[23].

7. Typhoid vaccine: Typhoid vaccine estimated to have a protective efficacy of 95% against Salmonella typhi and 70% to 75% against Salmonella paratyphi A in a study done on the visitors to Nepal for the prevalence of Salmonella typhi and Salmonella paratyphi A infections over a 16-month period. While a direct comparison was not performed, the parenteral vaccine was judged to be more effective than the oral vaccine[24].

8. Meningococcal vaccine: In a study 40 volunteers of age 19 to 27 (25 males; 15 females), tetravalent meningococcal vaccine with polysaccharides A, C, W-135, and Y induced the elevation of antibodies following a single 0.5-milliliter dose administered subcutaneously. The seroconversion rates for the polysaccharides were 92%, 92%, 97% and 95%, respectively[25].

9. Hepatitis A vaccine: In a study involving 42 males, intramuscular administration of 3 doses (0, 1, and 6 months) or 4 doses (0, 1, 2, and 6 months) of inactivated hepatitis A vaccine (HM-175 strain) produced detectable neutralizing antibodies to hepatitis A virus in 36 subjects (86%) by month 8. Antibody titers of at least 1:40 were observed in 34 of these subjects (95%). There was no difference in immunogenic efficacy between the 2 regimens[26].

Precautions and use in special population:

Vaccines should always be given exactly as recommended on the package insert; however, the interval between a series of doses may be lengthened without losing efficacy. The vaccines in general should be avoided in moderate or severe acute illnesses and also in those who are hypersensitive to the previous dose or to any components of that particular vaccine. Live-microbial vaccines should not be given simultaneously with immunoglobulin ideally; such vaccines should be given 2 week before or 6-12 week after the immunoglobulins. Live vaccines usually should not be given to immunocompromised persons or pregnant women**.** The commonly used vaccines are classified under the US FDA class C pregnancy category. In all the vaccine mentioned in the table 1, it was found to have minimal risk on the infant if used during pregnancy[27].

Problems in getting immunized

Even in case of pediatric vaccination programs, **t**he developed countries themselves are facing the difficulties in implementing the vaccination programs. They also impose legislation to improve the vaccination rates[28]. Thus, it is evident that implementing adult immunization is more difficult in

the developing countries where significant population is uneducated and illiterates with financial constraints. The family physicians and the treating doctors who are well informed about the benefits and cost effectiveness in the adult immunization may in turn be able to convince the patients, in the form of counseling, for the same.

Underutilization of adult vaccines

Though adult immunization is a potential need for the growing community, many times it is ignored. Hardly people appreciate the importance of adult immunization. Many times the healthcare professionals also do not have sufficient information regarding the safety and efficacy of these vaccines. There is also a lack of universal recommendations for all adults and in many developing countries there is lack of financial support which is a potential cause for underutilization of adult vaccines. One American study randomly selected 54 nursing homes from Washington and surveyed about pneumococcal vaccine utilization and policies. The survey concluded that Pneumococcal vaccine appears to be underutilized in Washington state nursing homes[29]. Another study from Jerusalem, Israel reported that Influenza vaccine uptake in vaccine eligible in Jerusalem is low, about 30% in the sick and elderly and considerably lower in medical personnel[30]. However, we did not get any data from South Asia or Nepal.

Newer vaccines

Besides these vaccines there are several other newer vaccines which are under development and may be available in the market in couple of years. Some of them include vaccine for malaria, HIV, bird flu etc. The success of these vaccines depends on their efficacy, safety and affordability.

Conclusion

Adult immunization, if properly utilized will be cost effective by reducing or preventing morbidity and mortality related to the preventable diseases in the society. Adult immunization is a potent area which is neglected in developing countries like Nepal. Keeping in view the statistical data of suffering costs related to the non-utilization of immunization in adults, the need of hour has come for utilization of immunization with a literary review to emphasize its importance. It is the time for us to understand that the cost involved in adult immunization is relatively high and is usually difficult for the patient to afford and the physician to convince individuals in countries like Nepal. But it has potential advantage in terms of disease prevention and disease free condition which is ultimately the objective of every healthcare professional.

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