Adult Diphtheria Vaccination

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ABSTRAK

Cakupan imunisasi dewasa yang rendah mungin berperan pada kejadian luar biasa (KLB) difteria baru-baru ini di Indonesia. Meskipun dikenal sebagai vaksin anak, vaksinasi difteria harus diberikan sebagai ulangan pada remaja dan dewasa untuk pencegahan jangka panjang. Vaksin dewasa berbeda dari vaksin anak tetapi memiliki proteksi yang sama. Selain itu, dianjurkan pula vaksinasi untuk ibu hamil dan orang lanjut usia di atas 65 tahun.

Kata kunci: *difteria, vaksin, kehamilan, pediatrika, usia lanjut.*

ABSTRACT

Low adult vaccination coverage in Indonesia may contribute to a recent outbreak of diphtheria in Indonesia. Although well known as a pediatric vaccine, diphtheria vaccination should be administered as booster to adolescence and adults for longer prevention. Adult vaccine differs from pediatric vaccine but have similar protection. Additionally, there is special recommendation to vaccinate pregnant women and elderly people aged 65 years or more.

Keywords: *diphtheria, vaccine, pregnant, pediatric, elderly.*

INTRODUCTION

Diphtheria is regarded as a reemerging disease since an outbreak occurs in the Soviet Union in 1990s, more than 2 decades after universal childhood immunization was initiated and controlled the disease.[1] Recent outbreaks throughout the Indonesian archipelago last year reemphasizes the importance of childhood vaccination and adult boosters. During 2017, there were 954 cases of diphtheria with death toll reaching 44 (4.6%) cases.[2] Consequently, an outbreak response immunization (ORI) program has been launched in mid-December 2017 to control the spread of the disease further.[3]

Unpublished data from the Ministry of Health, Republic of Indonesia showed that diphtheria cases did occur sporadically from1988 to 2016 at the national level. Universal child immunization was launched in 1990 followed by vaccination for school-age children in 1999. Since 1990, diphtheria cases showed a fluctuation until an outbreak occurred in 2012. The outbreak was resolved in 2014, but it remained a potential problem due to a sociocultural resistance to vaccination among a small group of people.

DIPHTHERIA – THE DISEASE

Diphtheria is an acute bacterial disease caused by exotoxin-producing Corynebacterium diphtheria. Another toxin producing strain, i.e. *C. ulcerans* can cause a diphtheria-like illness.[4] It usually affects the tonsils, throat, nose and/or

skin. Respiratory diphtheria is the most common manifestation. It is characterized by a grayish-colored pseudomembrane on the pharynx, palate, or nasal mucosa that can fatally obstruct the upper airway. The overall case-fatality for diphtheria is 5–10%.[5] Cutaneous manifestation of diphtheria can occur, resulting in indolent skin infection. Transmission is by person-to-person contact through inhaling air droplets of infected person.

Symptoms of diphtheria may appear 2-4 days after infection with an incubation period of 1-10 days. Most adult cases occur among unvaccinated or inadequately vaccinated people. Immunity after contracting diphtheria may not lifelong, so patients recovered from diphtheria are still need to be immunized. Diphtheria remains a public health problem in developing countries and potentially causes an outbreak.

Diphtheria antitoxin is predominated by immunoglobulin (IgG) induced after vaccination with diphtheria toxoid. Antitoxin concentrations of >0.1 IU/mL are generally considered protective, while concentration <0.01 IU/L are not protective.[6] Periodic vaccination is required to maintain immunity. Immunity acquired from childhood vaccination wanes during adulthood if there are no decennial boosters. An American study showed that people with protective levels of diphtheria antibody decreased from 91% at 6-11 years of age to only 29.5% at 70 years.[7]

VACCINE RECOMMENDATION

A tetanus-diphtheria-acellular pertussis (Tdap) vaccination gives protection against tetanus, diphtheria and pertussis. A tetanus-diphtheria (Td) vaccination gives protection against both tetanus and diphtheria. The current recommendations are:[8]

- Tdap vaccine for adult >19 years: 1 dose if not vaccinated previously with Tdap;
- Td vaccine (booster) 1 dose every 10 years.

In addition, there is an off-label use of Tdap, i.e. for pregnant women, 1 dose each pregnancy preferably given at 27 – 36 weeks of gestation.

The Advisory Committee on Immunization Practices (ACIP) provides these recommendations in accordance to recommendations of the American Academy of Family Physicians (AAFP), the American College of Obstetricians and Gynecologists (ACOG), and the American College of Physicians (ACP).

AVAILABLE VACCINES

In general, there are 4 vaccines that include protection against diphtheria, i.e. DTaP, DT, Tdap and Td. The DTaP and DT are pediatric vaccines for infants and young children. Tdap is an inactive vaccine for adult primary vaccine, while Td is a booster vaccine. Compared with infant formulations DTaP and DT, Tdap and Td contains reduced quantities (10–50%) of all toxoids and antigens. The reduced antigen content is designed to avoid the increasing reactogenicity historically seen with the fourth and fifth doses of infant vaccine.

In the global market, there are 2 Tdap vaccines available, i.e. Adacel® (Sanofi Pasteur) for persons aged 11 – 64 years (16) and Boostrix® (GlaxoSmithKline) for persons aged 10 – 18 years (17). Both vaccines are licensed for single-dose administration. They do not contain thimerosal or other preservative.

Each 0.5-mL dose of Adacel® contains 5 limit of flocculation (Lf) tetanus toxoid, 2 Lf diphtheria toxoid, and acellular pertussis antigens (2.5 µg detoxified PT, 5 µg FHA, 3 µg pertactin, 5 µg FIM). Each 0.5-mL dose of Boostrix® contains 5 Lf of tetanus toxoid, 2.5 Lf of diphtheria toxoid, 8 µg of inactivated PT, 8 µg of FHA, and 2.5 µg of pertactin (69 kiloDalton outer membrane protein).

Tetanus and diphtheria toxoids (Td) are also available for adults and adolescents in Indonesia, which is produced by Bio Farma Company as single dose (Bio Td) and multiple dose vials (Adsorbed Td Vaccine 10 doses). Each dose of 0.5 mL vaccine contains 7.5 Lf of tetanus toxoid and 2 Lf of diphtheria toxoid. Bio Farma is the only vaccine manufacturer in Indonesia recognized by World Health Organization and member of the Developing Countries Vaccine Manufacturers Network (DCVMN).[9]

Dose of Tdap or Td is 0.5 mL administered intramuscularly, preferably into the deltoid muscle.[10] Simultaneous injections with other vaccine can be safely done at a different anatomical site.

VACCINE IMMUNOGENICITY AND EFFECTIVENESS

No controlled clinical trial of the efficacy of the toxoid in preventing diphtheria has ever been conducted. There is, however, strong evidence from observational studies to support the effectiveness of vaccination, although effectiveness of diphtheria toxoid does not reach 100%:

Immunogenicity of the first dose Tdap vaccine given to adults is very good. The postvaccination antibody levels >0.1 IU/mL were achieved by 96.1% of participants. For those who have received Tdap vaccine 10 years before, 98.5% participants achieved the protective antibody.[11]

Seroprotective diphtheria antibody levels were similar between TdaP and Td. The seroprotective concentration (> 0.1 IU/mL) can be achieved by 98% of adults receiving TdaP and Td vaccines.[12]

CONTRAINDICATIONS AND PRECAUTIONS

Tdap vaccine is contraindicated in:[8]

- Severe allergic reaction (e.g. anaphylaxis) after a previous dose or to a vaccine component.
- Encephalopathy (e.g. coma, decreased level of consciousness, or prolonged seizures) not attributable to another identifiable cause within 7 days of administration of previous dose of DTP, DTaP, Tdap. This is specifically a contraindication for the pertussis component of Tdap. If present, the person should receive Td instead of Tdap.

Td (and DT) is contraindicated in severe allergic reaction (e.g. anaphylaxis) after a previous dose or to a vaccine components.

When there is a history of anaphylactic reactions to the vaccine, the patient should be referred to an allergist to confirm the presence of specific allergy to tetanus toxoid and whether or not a desensitization therapy can be done.

In addition, there are several precautions of giving Tdap and Td vaccines, i.e.:[8]

- Progressive or unstable neurological disorder, uncontrolled seizures, or progressive encephalopathy until a treatment regimen has been established and the condition has stabilized; these precautions are for pertussis components (only for Tdap);
- Guillain-Barré syndrome <6 weeks after a previous dose of tetanus toxoid–containing vaccine;
- History of Arthus-type hypersensitivity reactions after a previous dose of tetanus or diphtheria toxoid–containing vaccines; defer vaccination until at least 10 years have elapsed since the last tetanus toxoid–containing vaccine;
- Moderate or severe acute illness with or without fever.

ADVERSE REACTIONS OF VACCINATION

Several adverse reactions have been reported after TdaP or Td vaccination. A study comparing TdaP and Td vaccines showed comparable post-vaccination symptoms. Among persons receiving TdaP and Td vaccines respectively, the reported local reactions are pain (30.7% and 35.7%), swelling (4.2% and 2.5%), and erythema at the injection site (2.0% and 3.2%). The most frequent general symptoms were headache (20.4% and 15.7%), fatigue (17.0% and 14.5%), and myalgia (10.0% and 12.5%).[12]

Other studies have compared post-vaccination adverse events between the naïve and repeat-dose groups. The reported adverse reactions were injection-site pain (84.4% and 87.8%), erythema (29.7% and 23.1%), swelling (23.3% and 20.5%), and myalgia (53.5% and 60.1%), headache (37.6% and 40.6%), malaise (29.0% and 29.4%), and fever (4.9% and 4.2%).[11]

VACCINATION DURING PREGNANCY

The ACIP recommends pregnant women to receive Tdap vaccine between 27 and 36 weeks of gestation.[8,13] This time period was consistently protective against acute respiratory infection (ARI) in the first 2 months of the infant's life. A retrospective cohort study has included 99,434 infants and compared the infants born from mothers vaccinated with Tdap during pregnancy and mothers who did not receive vaccination. The risk of ARI at <2 months of age was 9% less likely (relative risk [RR] = 0.91; 95% confidence interval [CI] = 0.84-0.99) in infants from mothers

who received Tdap vaccination. Furthermore, the risk was 17% lower if the mother was vaccinated between 27 and 36 weeks of pregnancy (RR = 0.83; 95% CI = 0.74-0.93).[14]

VACCINATION FOR ELDERLY PEOPLE

Initially, Tdap vaccination or booster was recommended until the age of 64 years. Elderly people > 65 years of age was not recommended due to a lack of safety and immunogenicity data. However, lack of standalone pertussis vaccine has force the use of Tdap for people > 65 years due to prevent pertussis epidemic in this group of age.[15] Immunizing older adults with Tdap not only reduce the risk of pertussis in the elderly but also prevent transmission to infants having close contact with them.

Study showed that in elderly people aged >65 years, Tdap and Td vaccine showed comparable safety. The most frequent adverse events were local injection-site reaction.[16] There is no increased risk of reactogenicity after Tdap vaccination to people with a history of receiving Td vaccine within 5 years.[17] Tdap vaccine can also be co-administered with influenza vaccine to subjects >65 years of age without compromising of either the reactogenicity or immunogenicity profiles of both vaccines.[18]

CONCLUSION

Diphtheria vaccination should be given to adults aged ≥ 19 years with a decennial Td booster dose. A single dose of Tdap should be given to persons without a history of diphtheria vaccination. Continued protection against diphtheria (and tetanus) is provided by booster doses of Td every 10 years throughout life. Pregnant women should have Tdap vaccine in each pregnancy. Tdap vaccination is also recommended for elderly people >65 years of age. Tdap or Td vaccine is administered as a single dose of 0.5 mL, intramuscularly into the deltoid muscle.

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