

CHEMOPROPHYLAXIS VERSUS IMMUNOPROPHYLAXIS IN TUBERCULOSIS AND LEPROSY INFECTION

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CHEMOPROPHYLAXIS VERSUS IMMUNOPROPHYLAXIS IN TUBERCULOSIS AND LEPROSY INFECTION

Bernadette Dian Novita ¹⁾

ABSTRACT

Tuberculosis (TB) and leprosy are mycobacterial diseases that still represent significant public health challenges. Bacille Calmette–Guérin (BCG), the only available TB and Leprosy vaccine use as Immunoprophylaxis and has already given in infants. However, the evidence of TB and Leprosy infection in Indonesia remain high. In the last 10 years, chemoprophylaxis for both TB and leprosy were extensively done. However the effectiveness between immunoprophylaxis and chemoprophylaxis remains unclear.

ABSTRAK

Tuberkulosis (TB) dan kusta merupakan penyakit *mycobacterium* yang masih menjadi tantangan kesehatan di masyarakat. Bacille Calmette–Guérin (BCG), satu-satunya vaksin yang tersedia untuk mencegah TB dan kusta yang tersedia, digunakan sebagai imunoprofilaksis dan telah diberikan pada bayi lebih dari 30 tahun. Namun, infeksi TB dan Kusta di Indonesia masih tetap tinggi. Dalam 10 tahun terakhir, kemoprofilaksis untuk TB dan kusta dilakukan secara luas. Efektivitas antara imunoprofilaksis dan kemoprofilaksis masih belum jelas.

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INTRODUCTION

Tuberculosis (TB) and leprosy are both airborne infections and Neglected Tropical Diseases (NTD) caused by *Mycobacteria* spp (1,2).

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis*, slow growing bacteria that has high affinity to human macrophage, especially lung's macrophage (3). Meanwhile, Leprosy and also known as Hansen's disease or Kusta is a NTD caused

by *Mycobacterium leprae*. It can affect the nerves, skin, eyes, and lining of the nose (nasal mucosa) (1).

By an early detection and proper treatment, both of TB and leprosy can be cured, continue to work and lead an active life during and after treatment (2,4,5). Tuberculosis (TB) and leprosy do not spread easily, however, once those neglect and untreated could cost more. When leprosy is left untreated, the nerve damage

can result in crippling of hands and feet, paralysis, and blindness. Leprosy is a disease that predominantly affects the skin and peripheral nerves, resulting in neuropathy and associated long-term consequences, including deformities and disabilities (6), also with TB, it can cause respiratory failure and end up with death (2). However, the transmission numbers of TB and leprosy remain high. In 2016, Indonesia was in the 3rd place for leprosy new cases, after India and Brazil, and 5th place for TB new cases(7).

Moreover, both of TB and leprosy still had big stigma issue in the community thus people whom affected with TB and leprosy, mostly were hide their symptoms and refused the treatment. Transmission of TB and leprosy could stop by treating the patients or index cases, and giving the contacts with immunoprophylaxis and chemoprophylaxis(3,8–10).

In order to support stop transmission of TB and leprosy, in 2016, the WHO launched the Global Leprosy Strategy 2016-2020 "accelerate world zero leprosy" (6).

Immunoprophylaxis versus Chemoprophylaxis as prevention in Tuberculosis and Leprosy

Basic interventions for TB and leprosy control strategy are the provision of multidrug therapy (MDT) (12–14).

Prevention in TB and Leprosy now are common to stop transmission of the infection. Both immunoprophylaxis and chemoprophylaxis or combines are the prevention strategies (3,9,15).

Immunoprophylaxis is a protection against infectious disease by immunizations acquired by individuals either passively or actively. Immunoprophylaxis effectively to prevention of infectious diseases. Both poverty-related mycobacterial diseases require better tools to improve disease control. For leprosy, there has been an increased emphasis on developing tools for improved detection of infection and early diagnosis of disease (16). For TB, there has been a similar emphasis on such diagnostic tests, while increased research efforts have also focused on the development of new vaccines (15). *Bacille Calmette–Guérin* (BCG), the only available TB vaccine, provides insufficient and inconsistent protection to pulmonary TB in adults. The impact of BCG on leprosy, however, is significant, and the introduction of new TB vaccines that might replace BCG could, therefore, have serious impact also on leprosy. Given the similarities in antigenic makeup between the pathogens *Mycobacterium tuberculosis* (*Mtb*) and *M. leprae*, it is well possible, however, that new TB vaccines could cross-protect against leprosy(15). Immunoprophylaxis

on tuberculosis and *Mycobacterium leprae* to date the BCG vaccine. The protective effect of BCG varied 2-83% to prevent pulmonary tuberculosis and 58-74% in preventing extra pulmonary TB. While the efficacy of leprosy is only around 26-41% in experimental studies about 61% in the observational studies, with a mild difference between the types of paucibacillary leprosy (62%) and multibacillary (76%) (17).

Immunotherapy has a dual role in the treatment of tuberculosis is increasing the success rate for the treatment of TB-MDR; shorten treatment for tuberculosis; and increasing immunity of individuals who have been treated with drug therapy, thereby preventing recurrent disease (either through relapse or reinfection). In patients with tuberculosis, immunotherapy aims to "reactivate" or enhance the immune response either by promoting protective (Th1) immunity or immune system by blocking the harmful response (Th2). Improving the Th1 response can lead to the release of Th1 cytokines related systemic necrosis lesions of tuberculosis (Koch phenomenon) (11).

New TB subunit vaccines currently evaluated in human phase I and II studies indeed often contain antigens with homologs in *M. leprae*. In this review, we discuss pre-clinical studies and clinical trials of subunit or whole mycobacterial

vaccines for TB and leprosy and reflect on the development of vaccines that could provide protection against both diseases. Furthermore, we provide the first preclinical evidence of such cross-protection by *Mtb* antigen 85B (Ag85B)-early secretory antigenic target (ESAT6) fusion recombinant proteins in *in vivo* mouse models of *Mtb* and *M. leprae* infection. We propose that preclinical integration and harmonization of TB and leprosy research should be considered and included in global strategies with respect to cross-protective vaccine research and development.

Chemoprophylaxis is the administration of the drug to prevent the development of a disease. The use of chemo-prophylactic agents is based on knowledge of the epidemiology and clinical implications of the infectious diseases from which protection is sought. Generally, chemoprophylaxis is taken for diseases that are common, or where the clinical impact of infection is high like tuberculosis and leprosy. Tuberculosis and leprosy are a diseases with high transmission rates, those increasing the risk of transmission to people in close contact with patients. Therefore it takes prevention by given chemoprophylaxis for prevention (6). In granting chemoprophylaxis as prevention of leprosy, in 1960-1970, giving dapsone as chemoprophylaxis leprosy. In 1988 began

at the tested use of rifampicin as chemoprophylaxis, due to noticeable decrease in cases of leprosy, then in 1990 combination of rifampicin ofloxacin-minocycline (ROM) given as prevention on adults and in children aged <15 years and in 2000 single doses of rifampicin (SDR) tested in 5 islands in Indonesia as chemoprophylaxis leprosy (18). In 1991 the multi-drug therapy (MDT), that three anti-bacterial drugs (rifampicin, dapsone, and clofazimine) provide a more effective, where MDT is reducing the number of leprosy patients ¹⁰ treated from 5.3 million in 1985 to 3.1 million in 1991. This decline of the prevalence gives hope to the world to achieve the target elimination of leprosy in 2000 (19).

² This time by providing the use of single doses of rifampicin (SDR) as a preventive treatment for adults and children (2 years and above) in contact with the patients, by ensuring there is no TBC as contraindications and make sure no other contraindications. This intervention is carried out ² with the following requirements: (i) adequate management of contacts, and (ii) there is informed consent given chemoprophylaxis for the prevention of leprosy (19). The results showed that if the third intervention (detection and treatment of subclinical infection, chemoprophylaxis, and BCG), ¹⁵ when applied consistently to individual contacts

of leprosy patients, will reduce the incidence of disease in populations (18).

Based on the research results of the main benefits of prophylaxis SDR gave to leprosy patient's contact or as post-exposure prophylaxis (PEP), which can reduce the risk of leprosy by 60%. Given of the ² SDR in leprosy contacts associated with a 57% reduction in the risk of leprosy after 2 years and 30% after 5-6 years, with that none of TBC infection in individuals because SDR in individuals who showed symptoms of active tuberculosis, can caused the risk of resistance in tuberculosis to be MDR-TB (20). The risk of leprosy infected for individuals who live together and close contact with patients *multibacillary* (MB) is 5-10 times higher, and 2-3 times higher in patients with *paucibacillary* (PB), compared to people who are not close contacts (5). The result in combining BCG and rifampicin for leprosy was also shown no different compare to SDR.

⁷ A study testing the effectiveness of the SDR as chemoprophylaxis leprosy (COLEP) in Bangladesh. The result is the effectiveness of chemoprophylaxis SDR as leprosy (COLEP) is SDR ¹² does not have significant protection against the development of leprosy on contact. Furthermore, SDR does not protect against the development of multibacillary leprosy (MB), but protects against the development

of paucibacillary leprosy (PB) and single-lesion leprosy (SLL) where protection only lasted 2 years. These findings indicate that the SDR treatment is only effective when the patient has a low load mycobacterial(10).

While on TB chemoprophylaxis is a therapy for the prevention of infection with *Mycobacterium tuberculosis* or to avoid the development of disease in individuals already infected with *Mycobacterium tuberculosis*. Isoniazid therapy is most commonly used, however, the use of rifampicin and pyrazinamide also been carried out. Investigation of contacts in giving chemoprophylaxis is also very important (21). In a research found that

there are effects of isoniazid therapy on cytokine responses reflecting mycobacterial burden reduction in close contact, and therefore should be taken as a positive response to the prevention and treatment(19). In giving chemoprophylaxis isoniazid (INH) is effective given to groups ILTB (infection latent tuberculosis), children's age <5 years close contact with TB patients (infected individual secondary), and in HIV/AIDS prevention, for people living with HIV/AIDS-susceptible tuberculosis (8). As conclusion, herewith in table 1 the comparison for using immunoprophylaxis and chemoprophylaxis in order to prevent tuberculosis and leprosy infection.

Tabel 1 : Comparison The Use of Immunoprophylaxis versus Chemoprophylaxis in Tuberculosis and Leprosy Prevention

Type of Preventive	Diseases	% of protection
Immunophrophylaxis (BCG)	Pulmonary tuberculosis	2-83%
	Extra pulmonary tuberculosis	54-78%
	Leprosy	26-41%
Chemophrophylaxis (Single Dose Rifampicin)	Tuberculosis	unknown
	Leprosy	60% (within 5 years, and need to be repeated if still be exposed

Future work

Preventing in TB and Leprosy is an important strategy to stop the diseases transmission. Immunoprophylaxis is one of strategy, however, the prevention rate remains less than 80%. Also with chemoprophylaxis, Isoniazid and rifampicin in TB gave low efficacy, also

with SDR in Leprosy, around 60%. As shown by the combination treatment strategies, provision and administration of chemoprophylaxis and immunoprophylaxis suggested as an active control strategy in reducing the incidence of leprosy. Some studies suggest that BCG produces relatively common protection to be used as

a preventive vaccination leprosy disease, especially in the contact. Because there is no great benefit as leprosy disease prevention WHO does not recommend revaccination BCG as prevention of disease leprosy (9). Giving a single dose of rifampicin and BCG to contact without symptoms, can prevent many potential cases and reduce ongoing transmission (5).

In the future, doing research in preventing TB and Leprosy remains high priority, whether, find more effective vaccines for both TB and Leprosy nor provide better combination of chemoprophylaxis.

REFERENCES

1. Chaptini C, Marshman G. Leprosy : a review on elimination , reducing the disease burden , and future research . Lepr Rev. 2015;86(4):307–15.
2. World Health Organization. Guidelines for surveillance of drug resistance in tuberculosis. 5th ed. 2015.
3. Pineda NIS, Pereira SM, Matos ED, Barreto ML. Chemoprophylaxis in the prevention of tuberculosis. J Bras Pneumol. 2004;30(4):485–94.
4. CDC. CDC core Curriculum complete. In: What The Clinician Should Know. sixth edit. CDC Publisher; 2016. p. 21–47.
5. Chaptini C, Marshman G. Leprosy: a review on elimination, reducing the disease burden, and future research. Lepr Rev. 2015;86(4):307–15.
6. WHO. WHO Guidelines for the Diagnosis, Treatment and Prevention of Leprosy. In: 2nd ed. New Delhi; 2018. p. 87.
7. Kementerian Kesehatan Republik Indonesia. Data dan Informasi Profil Kesehatan Indonesia Tahun 2016. 2017. p. 100.
8. Smith WCS. Chemoprophylaxis in the prevention of leprosy. Bmj. 2008;336(7647):730–1.
9. Duthie M, Balagon MF. Combination chemoprophylaxis and immunoprophylaxis in reducing the incidence of leprosy. Risk Manag Healthc Policy. 2016;9:43–53.
10. Lockwood DNJ, Krishnamurthy P, Kumar B, Penna G. Single-dose rifampicin chemoprophylaxis protects those who need it least and is not a cost-effective intervention. 2018;10–3.
11. WHO. Report of the expert consultation on immunotherapeutic interventions for tuberculosis. In: 1. Geneva: WHO Publications; 2007.
12. Laurence B, Chapner B, Knollmann B. The Pharmacological Basis of Therapeutics-Goodman & Gillman-Ed. 12th ed. California: McGraw-

- Hill Companies; 2011.
13. Golan D, Tahjian A, Armstrong E, Armstrong A. Principles of Pharmacology : The Pathophysiologic Basis of Drug Therapy. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2012.
 14. Katzung BG. Basic & Clinical Pharmacology. 14th ed. San Fransisco: McGraw-Hill Education; 2018.
 15. Coppola M, van den Eeden S, Robbins N, Wilson L, Franken K, Adams L. Vaccines for Leprosy and Tuberculosis : Opportunities for Shared Research , Development , and Application. *Front Immunol.* 2018;9(February):1–12.
 16. Smith C, Aerts A, Kita E, Virmond M. Time to define leprosy elimination as zero leprosy transmission? •. *Lancet Infect Dis.* 2019;3099(16):1–6.
 17. Coppola M. Vaccines for Leprosy and Tuberculosis : Opportunities for Shared Research , Development , and Application. 2018;9(February):1–12.
 18. Richardus JH, Oskam L. Protecting people against leprosy : Chemoprophylaxis and immunoprophylaxis. *Clin Dermatol.* 2015;33(1):19–25.
 19. Metrics P. Time to define leprosy elimination as zero leprosy transmission? •. 2019;3099(16):1–6.
 20. Mieras L, Anthony R, van Brakel W, Bratschi MW, van den Broek J, Cambau E, et al. Negligible risk of inducing resistance in Mycobacterium tuberculosis with single-dose rifampicin as post-exposure prophylaxis for leprosy. *Infect Dis Poverty.* 2016;5(1):1–5.
 21. Biraro IA, Egesa M, Kimuda S, Smith SG, Toulza F, Levin J, et al. Effect of isoniazid preventive therapy on immune responses to mycobacterium tuberculosis : an open label randomised , controlled , exploratory study. *BMC Infect Dis.* 2015;1–12.

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