ORIGINAL RESEARCH

Analysis of Effects of Preventive Therapy for Latent Tuberculosis Infection and Factors Associated with Treatment Abandonment at a Tertiary Care Centre

[1]Dr. Ashok Sudam Bansode, [2]Dr. Animesh Dubey

[1,2]Associate Professor, Department of Pulmonary Medicine, L N Medical College & J K Hospital, Kolar Road, Bhopal, Madhya Pradesh, India

Corresponding Author
Dr. Animesh Dubey
Associate Professor, Department of Pulmonary Medicine, L N Medical College & J K Hospital, Kolar Road, Bhopal, Madhya Pradesh, India

ABSTRACT
Background: The present study was conducted for assessing the effects of preventive therapy for latent tuberculosis infection and factors associated with treatment abandonment.
Materials &Methods: A total of 400 subjects, 200 staff and 200 school going children (within the age group of 14 to 16 years) were enrolled in the present study. Screening of all the subjects was done for clinical symptoms andwere subjected to purified protein derivative (PPD) skin testing and chest X-ray examination for evaluating LTBI.The individuals were split into two groups: a PT group and a control group, in accordance with the principle of voluntariness and whether the subject agreed to receive preventative therapy (PT). The 210 cases in the PT group all underwent PT. A total of 190 cases who did not receive PT made up the control group. For three continuous months, participants in the PT group took INH tablets along with RFP capsules. This was followed by a questionnaire survey. All the results were analysed.
Results: A total of 400 subjects, 200 staff and 200 school going children(within the age group of 14 to 16 years) were enrolled. The 210 cases in the PT group all underwent PT. A total of 190 cases who did not receive PT made up the control group. Active pulmonary tuberculosis was seen in one student and two staff members. However; PT suggested absence of LTBI.While evaluating the risk factors with PT abandonment, it was seen that occurrence of PT adverse effects, illiterate parental education and rural residence were significant risk factors associated with PT abandonment.
Conclusion: The authors inferred that PT adoption for LTBI populations at high risk is advantageous based on the aforementioned findings. But PT must begin concurrently with "source of infection" control efforts.
Key words: Tuberculosis, Latent, Preventive Therapy.

INTRODUCTION

Tuberculosis (TB) is a leading cause of death worldwide, with 10.4 million cases and 1.8 million deaths in 2015. Infected individuals are classified as either having latent tuberculosis infection (LTBI), an asymptomatic clinical state that is not transmissible, or active TB disease, characterized by the presence of clinical symptoms arising from infection that can occur in multiple organs. While Mycobacterium tuberculosis, the bacterium that causes TB, can infect many parts of the body, pulmonary TB is primarily the transmissible form. Our understanding of M. tuberculosis infection as a clear binary condition that is either active or latent has recently shifted, and the more modern view treats infection as spectrum of disease states.[1-3] Latent tuberculosis infection refers to a state of persistent immune response to stimulation by Mycobacterium tuberculosis antigens with no evidence of clinically manifest active TB. There is no gold standard test for direct identification of Mycobacterium tuberculosis infection in humans. The vast majority of infected people have no signs or symptoms of TB but are at risk for active TB disease.[4]Hence; the present study was conducted for assessing the effects of preventive therapy for latent tuberculosis infection and factors associated with treatment abandonment.

MATERIALS & METHODS

The present study was conducted in Department of Pulmonary Medicine, L N Medical College & J K Hospital, Kolar Road, Bhopal, Madhya Pradesh

1259

(India) for assessing the effects of preventive therapy for latent tuberculosis infection and factors associated with treatment abandonment. A total of 400 subjects, 200 staff and 200 school going children (within the age group of 14 to 16 years) were enrolled in the present study. Screening of all the subjects was done for clinical symptoms andwere subjected to purified protein derivative (PPD) skin testing and chest X-ray examination for evaluating LTBI.Three sputum samples from patients with reactive PPD induration diameters 15 mm, papules, blisters, and a normal chest X-ray image were required in order to microscopically test for acid-fast bacilli. To rule out pulmonary TB, a consultation and a chest CT scan were performed if necessary. The individuals were split into two groups: a PT group and a control group, in accordance with the principle of voluntariness and whether the subject agreed to receive preventative therapy (PT). The 210 cases in the PT group all underwent PT. A total of 190 cases who did not receive PT made up the control group. For three continuous months, participants in the PT group took INH tablets along with RFP capsules. Prior to starting PT, all enrolled patients in the PT group had normal liver function, and monthly liver function tests and full blood counts were conducted. For two years, the two subject groups were routinely observed, and at the conclusion of the second year, a chest X-ray was performed on each patient. Suspected subjects were required to submit three sputum samples for smear testing. We looked into the risk variables for treatment relapse using an updated epidemiology questionnaire.All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPS software.

RESULTS

A total of 400 subjects, 200 staff and 200 school going children (within the age group of 14 to 16 years) were enrolled. The 210 cases in the PT group all underwent PT. A total of 190 cases who did not receive PT made up the control group. Active pulmonary tuberculosis was seen in one student and two staff members. However, PT suggested absence of LTBI.While evaluating the risk factors with PT abandonment, it was seen that occurrence of PT adverse effects, illiterate parental education and rural residence were significant risk factors associated with PT abandonment.

Table: 1 PPD results

Groups	PPD			Active pulmonary tuberculosis	PT suggested for LTBI
	Screening numbers	Numbers of <15 mm	Numbers of ≥15 mm		
Students (n=200)	195	180	15	1	0
Staff (n=200)	190	179	11	2	0

Table: 2 LTBI and PT results

Variable	PT abandonment (n=210)	PT completed (n=190)	p-value
Males (n)	138	62	0.12
Females (n)	148	52	0.25
Positive History of BCG vaccination	173	168	0.84
Occurrence of PT adverse effects	9	3	0.00*
Parental education- Illiterate	83	52	0.04*
Rural residence	53	27	0.03*

*: Significant

DISCUSSION

Tuberculosis is one of the most prevalent infections of human beings and a formidable public health challenge that shows little sign of abating. Primary infection with M. tuberculosis leads to clinical disease in only ~ 10% of individuals. In the remaining cases, the ensuing immune response arrests the further growth of M. tuberculosis. However, the pathogen is completely eradicated in only ~ 10% people, while the immune response in the remaining ~ 90% individuals only succeeds in the containment of infection as some bacilli escape killing by blunting the microbicide mechanisms of immune cells and remain in no replicating (dormant or latent) state in old lesions. The process is termed as latent tuberculosis infection (LTBI) and is defined as a state of persistent immune response to stimulation by Mycobacterium tuberculosis antigens without evidence of clinically manifested active TB.[5, 6]Latent tuberculosis infection (LTBI) is defined by the detection of a specific immune response to Mycobacterium tuberculosis complex (MTC) antigens in a healthy subject (i.e., with no symptoms or signs of active tuberculosis [TB]). As M. tuberculosis can only be isolated from humans when it is in an active phase, causing illness, the detection of the presence of LTBI is wholly reliant

on indirect measurements of immune reactivity to antigenic challenge. By evading both innate and adaptive immunity, bacteria of the MTC are able to persist in a dormant phase for several decades, or even for the lifetime of the host. In ∼10% of all infected individuals, a LTBI will progress to active replication and cause TB disease. This can be prevented with antibiotic treatment; globally standard regimens are of 6−9-mo duration with a single drug, or at least 3 mo of two antibiotics. Increasing the number of drugs within the regimen increases the potential for consequent adverse events.[7, 8]A total of 400 subjects, 200 staff and 200 school going children (within the age group of 14 to 16 years) were enrolled. The 210 cases in the PT group all underwent PT. A total of 190 cases who did not receive PT made up the control group. Active pulmonary tuberculosis was seen in one student and two staff members. However; PT suggested absence of LTBI.Huang, H et al investigated the effects of PT and identify factors related to PT abandonment during the school TB epidemic. Subjects (n=362) with a reactive PPD induration ≥15 mm, or with papules, blisters, and a normal chest X-ray image were recommended for PT. The subjects were assigned to a PT group (n=156) and control group (n=206), respectively, on a voluntary basis. Two cases in the PT group and 20 cases in the control group developed TB. The protective rate of PT for reducing TB was 86.8%. In the PT group, 69 cases finished PT, with a completion rate of 44.2%, and the incidence rates of adverse events and hepatotoxicity were 12.2% and 1.9%, respectively. Among 362 LTBI cases, a total of 293 cases abandoned PT. Discrimination (OR =7.173, 95% CI, 3.361–15.307), worry about adverse drug reactions (OR =2.752, 95% CI, 1.459–5.192), a low parental education level, and accepting the opinion of a non-TB specialist were identified as high-risk factors for abandoning PT.A PT regimen consisting of INH combined with RFP for 3 consecutive months is reasonable for use in schools.[9] While evaluating the risk factors with PT abandonment, it was seen that occurrence of PT adverse effects, illiterate parental education and rural residence were significant risk factors associated with PT abandonment. In another similar study, Yuan, Y et al, authors described the acceptance of LTBI treatment among college students in an eastern province of China to explore the association between perceived stigma toward TB and acceptance of LTBI treatment. In total, 1547 college students were included in the analysis. The acceptance rate of LTBI treatment among the diagnosed college students was 46.7% (n=723). The proportion of female students (n=361, 51.5%) accepting LTBI treatment was higher than that of male students. There was an interaction between perceived stigma toward TB and gender. Among college students with LTBI, perceived stigma toward TB was positively associated with acceptance of preventive treatment. Perceived stigma toward TB was positively associated with accepting LTBI treatment only among male students. The acceptance rate of preventive treatment among college students with LTBI was low.[10]

CONCLUSION

The authors inferred that PT adoption for LTBI populations at high risk is advantageous based on the aforementioned findings. But PT must begin concurrently with "source of infection" control efforts.

REFERENCES

1. World Health Organization. Global tuberculosis report 2016. Geneva: WHO; 2016. Available from: http://www.who.int/tb/publications/global_report/en/.
2. Barry CE, 3rd, Boshoff HI, Dartois V, Dick T, Ehrt S, Flynn J, Schnappinger D, Wilkinson RJ, Young D. The spectrum of latent tuberculosis: rethinking the biology and intervention strategies. Nat Rev Microbiol. 2009;7:845-55.
3. World Health Organization. The End TB Strategy. Geneva: WHO; 2014.
4. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management [Internet]. Geneva: World Health Organization; 2018. Definitions. Available from: https://www.ncbi.nlm.nih.gov/books/NBK531242/
5. Global TB report. World Health Organization. Geneva, Switzerland: WHO; 2015.
6. Mack U, Migliori GB, Sester M, Rieder HL, Ehlers S, Goletti D, et al. TBNET LTBI: latent tuberculosis infection or lasting immune responses to M. tuberculosis? A TBNET consensus statement. Eur Respir J. 2009;33:956–73.
7. Berry MP, Graham CM, McNab FW, Xu Z, Bloch SA, Oni T, Wilkinson KA, Banchereau R, Skinner J, Wilkinson RJ, et al. 2010. An interferon-inducible neutrophil-driven blood transcriptional signature in human tuberculosis. Nature 466: 973–977.
8. Calmette A. 1931. Preventive vaccination against tuberculosis with BCG. Proc R Soc Med 24: 1481–1490.
9. Huang, H., Yuan, G., Du, Y., Cai, X., Liu, J., Hu, C., Liang, B., Hu, G., Tang, X., & Zhou, Y. (2018). Effects of preventive therapy for latent tuberculosis infection and factors associated with treatment abandonment: a cross-sectional study. Journal of thoracic disease, 10(7), 4377–4386.
10. Yuan, Y., Jin, J., Bi, X., Geng, H., Li, S., & Zhou, C. (2023). Gender-Specific Association Between Perceived Stigma Toward Tuberculosis and Acceptance of Preventive Treatment Among College Students with Latent Tuberculosis Infection: Cross-Sectional Analysis. JMIR Public Health Surveill. 2023; 9: e43972.