J Surg Med. 2019;3(2):180-182.
DOI: 10.28982/josam.527957

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Prophylaxis for latent tuberculosis infection in liver transplant recipients

Karaciğer nakli alıcılarında latent tüberküloz enfeksiyonu proflaksisi

Gökhan Ertuğrul [1], Mustafa Düger [2]

[1] Hepatobiliary Surgery and Organ Transplantation Center, Medipol University, Faculty of Medicine, Istanbul, Turkey
[2] Department of Thoracic Medicine, Medipol University, Faculty of Medicine, Istanbul, Turkey

ORCID ID of the author(s)
GE: 0000-0002-8351-4220
MD: 0000-0002-4091-6465

Corresponding author / Sorumlu yazar:
Gökhan Ertuğrul
Address / Adres: Medipol Üniversitesi Tıp Fakültesi, Hepatobilier Cerrahisi ve Organ Nakli Merkezi, TEM Avrupa Otoyolu Göztepe Çıkışı No: 1, 34214, Bağcılar, İstanbul, Türkiye
E-mail: mdgertugrul@gmail.com

Ethics Committee Approval: Ethics committee approval was not received for this study because of the retrospective design of the study.
Etik Kurul Onayı: Etik kurul onayı çalışmanın retrospektif doğasından dolayı alınmamıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Received / Geliş Tarihi: 16.02.2019
Accepted / Kabul Tarihi: 20.02.2019
Published / Yayın Tarihi: 20.02.2019

Abstract

Aim: Immunosuppressive drugs predispose the liver transplant recipient to reactivation of latent tuberculosis infections. Prophylactic therapies given to these patients are very important for prevention of reactivation. The aim of this study was to evaluate the prophylaxis of latent tuberculosis infections in liver transplant recipients.

Methods: We designed a retrospective cohort study. We examined liver transplant recipients Between December 2014 and December 2017 with results of T Spot and prophylactic treatment.

Results: Among 143 recipients, positive T Spot results were detected in 21 (14.7%) cases. Twenty one patients received Isoniazid prophylaxis and no reactivation of tuberculosis was detected during follow-up of 48 months.

Conclusion: Isoniazid appears to be successful in prophylactic treatment of latent tuberculosis infection in liver transplant recipients.

Keywords: Liver transplantation, Latent tuberculosis infections, Prophylaxis

Öz

Amaç: İmmünsüpresif ilaçlar karaciğer nakli alıcısını latent tüberküloz enfeksiyonlarının reaktivasyonuna yatkınlaştırır. Bu hastalara verilen profilaktik tedaviler, reaktivasyonun önlenmesi için çok önemlidir. Bu çalışmanın amacı, karaciğer nakli alıcılarında latent tüberküloz enfeksiyonlarının profilaksisini değerlendirmektir.

Yöntemler: Retrospektif bir kohort çalışması tasarladık. Karaciğer nakli alıcılarını Aralık 2014 - Aralık 2017 tarihleri arasında T Spot ve profilaktik tedavi sonuçları ile inceledik.

Bulgular: 143 alıcı arasında, 21 (%14,7) vakada pozitif T Spot sonucu tespit edildi. Yirmi bir hastaya İsoniazid profilaksisi yapıldı ve 48 aylık takipte tüberkülozun herhangi bir reaktivasyonu tespit edilmedi.

Sonuç: Isoniazid, karaciğer nakli alıcılarında latent tüberküloz enfeksiyonunun profilaktik tedavisinde başarılı görünmektedir.

Anahtar kelimeler: Karaciğer nakli, Latent tüberküloz enfeksiyonu, Proflaksi

How to cite / Atıf için: Ertuğrul G, Düger M. Prophylaxis for latent tuberculosis infection in liver transplant recipients. J Surg Med. 2019;3(2):180-182.

Introduction

Tuberculosis is a serious opportunistic infection for liver transplant recipients [1–4]. Tuberculosis incidence estimated as 0.7% to 2.3% in liver transplant recipients [5,6].

Mycobacterium tuberculosis specific interferon gamma release assays; QuantiFERON ® (QI-AGEN, Gaithersburg, USA, and Australia) and T-SPOT® (Oxford Immunotec, Oxford, UK) are methods for diagnosing latent tuberculosis infections [7,8].

Isoniazid prophylaxis are used for avoid to reactivation of latent tuberculosis infection in the post-transplant period [9]. The risk of Isoniazid hepatotoxicity is higher for liver transplant recipients [6].

The aim of this study was to evaluate the prophylaxis for latent tuberculosis infections in liver transplant recipients.

Materials and methods

Between December 2014 and December 2018, liver transplant recipients at Medipol University Medical Faculty Hospital Organ Transplantation Department, Istanbul, Turkey were studied retrospectively.

Two main groups were established; positive T Spot group (Isoniazid prophylaxis) and negative T Spot group (No Isoniazid prophylaxis) group. For each of these groups the age, sex, CHILD scores, Model for End-Stage Liver Disease (MELD) scores, prophylaxis for latent tuberculosis infections, reactivation of latent tuberculosis infections and mortality due to tuberculosis were evaluated.

All patients were examined by Department of Thoracic Medicine before liver transplantation and pulmonary function test, chest graph, computed tomography of thorax and T Spot test were performed.

In our clinic, Isoniazid prophylaxis was given only in patients with latent tuberculosis infection risk factors (3 patients was diabetes mellitus, 3 patients was elderly recipient (>65 years old), 2 patients history of recent contact with a person who was diagnosed with active tuberculosis) and positive T Spot (none clinical and radiological findings in patients). Patients received 300 mg Isoniazid daily and 50 mg Pyridoxine daily, and duration of treatment was 6 months. Patients were examined by Department of Thoracic Medicine every month. We investigated Isoniazid hepatotoxicity. Alanine aminotransferase, aspartate aminotransferase and bilirubin were performed every day of the admission period, and once per fifteen days after discharge.

Statistical Analysis

Continuous variables with normal distribution presented as mean ± Standard deviation. The categorical variables were given as percent and number.

Results

Among 143 recipients, T spot test was positive in 21 cases (14.7%). All these patients were treated with Isoniazid prophylaxis. Mean age of the positive T Spot group was 56.5 (25-72) years; negative T Spot group was 58.5 (26-69) years, 17 (70%) of the 21 positive T Spot group patients were male.

Mean CHILD scores of the positive T Spot group was 9 (6 -12); negative T Spot group was 8.5 (6-15) respectively. Mean MELD scores of the positive T Spot group was 15 (9-24); negative T Spot group was 16.5 (10-30) respectively.

Sixteen (76.2%) patients underwent right lobe living donor liver transplantation and 5 (23.8%) patients underwent cadaveric liver transplantation.

In study, no reactivation of latent tuberculosis infections was detected, no hepatotoxicity occurred due to Isoniazid, and no patient died due to tuberculosis in follow up period of 48 months.

Discussion

The definitive treatment of end stage liver disease is liver transplantation. The standard immunosuppressive treatment starts immediately after liver transplantation.

The immunosuppressive drugs used of transplantation patients the reactivation of latent tuberculosis infections to increases. Immunosuppressive agents greatly enhance the risk of tuberculosis reactivation in patients with latent tuberculosis infections [10-12]. In our center, Immunosuppression regimens were based on calcineurin inhibitor (tacrolimus or cyclosporine), mycophenolate mofetil and corticosteroids in liver transplant recipient.

Latent tuberculosis infection risk factors were a history of recent contact with a person who was diagnosed with active tuberculosis, human immunodeficiency virus infection, country of origin, higher intensity immunosuppression, Diabetes mellitus, and increased recipient age [13]. Liver transplant recipients have an 18 fold increased risk of latent tuberculosis infection reactivation in comparison with the general population [13-14].

Current guidelines for transplantation recommend that all recipients be routinely screened for latent tuberculosis infection with a tuberculin skin test or Interferon-gamma release assay [15-17]. In our study, among 143 recipients, 21 cases of positive T Spot were detected (14.7 %) but not clinical and radiological findings in these patients.

Isoniazid is known to be effective for tuberculosis prevention in liver transplant recipient as well as in the general population [18]. However, Isoniazid for liver transplant recipients remains controversial be¬cause of concerns about ısoniazid hepatotoxicity [19]. The rate of Isoniazid toxicity was 29% and 42.8 % in liver transplant patients [6,13]. In our clinic, Isoniazid prophylaxis (Daily 300 mg Isoniazid and daily 50 mg Pyridoxine with duration of 6 months) was given only in patients with latent tuberculosis infection risk factors and positive T Spot. All our patients were not reactivation of latent tuberculosis infections and isoniazid hepatotoxicity.

Tuberculosis in liver transplant recipients is associated with mortality rates as high as 30% to 40% [20]. In our study none of the cases died due to tuberculosis.

Our study has several limitations. First, this study was retrospective. Second, the number of cases was small.

Conclusion

Despite the limitations, Isoniazid appears to be successful prophylactic treatment of latent tuberculosis infection in liver transplant recipients.

References

1. Benito N, García-Vázquez E, Horcajada JP, González J, Oppenheimer F, Cofán F, et al. Clinical features and outcomes of tuberculosis in transplant recipients as compared with the general population: A retrospective matched cohort study. Clin Microbiol Infect. 2015;21:651–8.
2. Meije Y, Piersimoni C, Torre-Cisneros J, Dilektasli AG, Aguado JM. ESCMID Study Group of Infection in Compromised Hosts Mycobacterial infections in solid organ transplant recipients. Clin Microbiol Infect. 2014;20:89–101.
3. Holty JE, Gould MK, Meinke L, Keeffe EB, Ruoss SJ. Tuberculosis in liver transplant recipients: A systematic review and meta analysis of individual patient data. Liver Transpl. 2009;15:894–906.
4. Bodro M1, SabéN, Santín M, Cruzado JM, L ladóL, González-Costello J, et al. Clinical features and outcomes of tuberculosis in solid organ transplant recipients. Transpl Proc. 2012;44:2686–9.
5. Meyers BR, Papanicolaou GA, Sheiner P, Emre S, Miller C. Tuberculosis in orthotopic liver transplant patients: Increased toxicity of recommended agents; cure of disseminated infection with nonconventional regimens. Transplantation. 2000;69:64-9.
6. Benito N, Sued O, Moreno A, Horcajada JP, González J, Navasa M, et al. Diagnosis and treatment of latent tuberculosis infection in liver transplant recipients in an endemic area. Transplantation. 2002;74:1381-6.
7. Mazurek GH, Jereb J, Vernon A, LoBue P, Goldberg S, Castro K, et al. Updated guidelines for using Interferon Gamma Release Assays to detect Mycobacterium tuberculosis infection United States, 2010. MMWR Recomm Rep. 2010;59:1–25.
8. Ferguson TW, Tangri N, Macdonald K, Hiebert B, Rigatto C, Sood MM, et al. The diagnostic accuracy of tests for latent tuberculosis infection in hemodialysis patients: A systematic review and meta-analysis. Transplantation. 2015;99:1084–91.
9. Higgins RSD, Kusne S, Reyes J, Yousem S, Gordon R, Van Thiel D, et al. Mycobacterium tuberculosis after liver transplantation: Management and guidelines for prevention. Clin Transplant. 1992;6:81-90.
10. Kiuchi T. Liver transplantation and tuberculosis in Japanese. Kekkaku. 2000;75:685-90.
11. Kobashi Y, Matsushima T. Clinical analysis of pulmonary tuberculosis in association with corticosteroid therapy. Intern Med. 2002;41:1103-10.
12. Jick SS, Lieberman ES, Rahman MU, Choi HK. Glucocorticoid use other associated factors, and the risk of tuberculosis. Arthritis Rheum. 2006;55:19-26.
13. Meyers BR, Halpern M, Sheiner P, Mendelson MH, Neibart E, Miller C. Tuberculosis in liver transplant patients. Transplantation. 1994;58:301-6.
14. Nishizaki T, Yanaga K, Soejima Y, Kishikawa K, Kajiyama K, Uchiyama H, et al. Tuberculosis following liver transplantation: Report of a case and review of the literature. Transpl Int. 1996;9:589-92.
15. Sester M, Van Leth F, Bruchfeld J, Bumbacea D, Cirillo DM, Dilektasli AG.TB-NET Risk assessment of tuberculosis in immunocompromised patients. A TB-NET study. Am J Respir Crit Care Med. 2014;190:1168–76.
16. Subramanian AK, Morris MI. Mycobacterium tuberculosis infections in solid organ transplantation. Am J Transpl. 2013;13:68–76.
17. Bumbacea D, Arend SM, Eyuboglu F, Fishman JA, Goletti D, Ison MG, et al. The risk of tuberculosis in transplant candidates and recipients: A TBNET consensus statement. Eur Respir J. 2012;40:990–1013.
18. Agarwal SK, Gupta S, Dash SC, Bhowmik D, Tiwari SC. Prospective randomized trial of isoni-azid prophylaxis in renal transplant recipient. Int Urol Nephrol. 2004;36:425–31.
19. Aguayo JM, Torre-Cisneros J, Fortun J. Tuberculosis in solid-organ trans¬plant recipients: Consensus statement of the group for the study of infec¬tion in transplant recipients (GESITRA) of the Spanish Society of Infectious Diseases and Clinical Microbiology. Clin Infect Dis. 2009;48:1276–84.
20. Mun˜oz P, Rodriguez C, Bouza E. Mycobacterium tuberculosis infection in recipients of solid organ transplants. Clin Infect Dis. 2005;40:581-7.