Therapeutic Effect of Oral Prednisolone with Antitubercular Treatment in Pleural Effusion

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ABSTRACT

INTRODUCTION: Tuberculosis (TB) is an infectious disease caused by the bacillus Mycobacterium tuberculosis and remains one of the major public health problems in Nepal. Currently 117 thousand people are living with TB in Nepal and 69 thousand new cases were registered at the National Tuberculosis Programme in 2018/19. Though nowadays National tubercular guidelines of Nepal does not recommend the use of corticosteroids in tubercular effusion, this study was to evaluate the outcome of corticosteroids in tubercular effusion as the previous study had shown its benefit on effusion. However its effect and benefit in various forms of TB are quite different.

METHOD: The study was carried out in the Medical department of National Academy of Medical Sciences, Bir Hospital, Nepal. This was a prospective, convenience sampling method with a study period of two years with all eligible and consenting individuals. This was the study of a total of 52 patients attending outdoor patient department (OPD) and wards who fulfilled the inclusion criteria.

RESULT: The first prednisolone response was evaluated in 14 days after the initiation of ATT. It was found that the level of effusion was decreased in all patients to some extent and there was complete resolution of effusion in 28 patients (26 male and 2 female) out of 52, with the early feeling of wellbeing, and improvement in the symptoms like fever, chest pain, and dyspnea. The second prednisone response was evaluated after one month of treatment, where 49 patients (94%) showed complete resolution of effusion, and 3 (6%) of them showed some extend pleural thickening due to poor adherence to prednisolone. The correlation between smoking and alcohol intake was done during the treatment of tubercular effusion and the p-value was calculated. It was found to be less than 0.05 which was significant.

CONCLUSION: Adjunctive proper use of oral prednisolone with the standard regime of ATT in tubercular effusion, resdues the chance of pleural thickening and also reduces the symptoms of fever, pleuritic chest pain, dyspnea earlier. However, the prednisolone should be used cautiously with ATT by justifying the risk-benefit of the treatment as it has many adverse effects.

KEY WORDS: Anti tubercular treatment, Pleural effusion, Prednisolone.
remains a major cause of mortality and morbidity on a global basis. Despite the use of effective antituberculous treatment regimens, there is a risk to patients, particularly developing fibrous scar leading to lung dysfunction. Therefore, the long-term disabling effects of treated tuberculosis remain an important challenge.

The cause of effusion is due to the rupture of sub-pleural caseous foci and there is a release of mycobacterial antigens into the pleural space, which causes an immunological reaction (delayed hypersensitivity). The effusion is characteristically exudative and lymphocytic. Measurements of pleural fluid adenosine deaminase (ADA) are helpful in the diagnosis of tubercular pleural effusion (TPE).

Most of TPEs may resolve and heal spontaneously. In some cases, there may be development of pleural fibrosis, due to fibrin deposition. Pleural fibrosis can lead to pleural thickening and impairment of lung function. Some authors have mentioned pleural thickening in as many as 50% of cases.

The objective of this study was to determine the effect of adjunct therapy of oral prednisolone with the standard regime of ATT on tubercular pleural effusion concerning symptoms, size of the effusion, and pleural thickening.

METHOD

The study was carried out in the Medical Department of National Academy of Medical Sciences, Bir Hospital, Nepal. This was a prospective, convenience sampling method with a study period of two years with all eligible and consenting individuals. This was a study of a total of 52 patients attending OPD and without a history of smoking and alcoholism from March 2018 to February 2020. The collected data was stored and analyzed with statistical software (SPSS version 26.0 for windows) to get the final interpretation.

Patients with signs and symptoms of pleural effusion supported by plain chest x-ray posterior-anterior (PA) view were included in this study. Then it was confirmed by ultrasound of chest. Diagnostic and therapeutic aspiration were done. Pleural fluid was sent for analysis including total count (TC), differential count (DC), protein, sugar, ADA, lactate dehydrogenase (LDH) and malignant cells. Sputum for AFB (Acid-fast bacilli) 3 samples were sent. Lymphocytic dominant and high ADA more than 60 IU/L were included in this study, after taking informed consent. Detail clinical examinations were done for screening from other diseases including chronic kidney disease (CKD), chronic liver disease (CLD), and congestive cardiac failure (CCF). Basic investigations were carried out according to the need. Non-consenting patients, patients with renal failure (uremia), active hepatic disease, and cardiac failure were excluded because the coexisting illness may affect the outcome. All enrolled patients were given prednisolone 1 mg/kg body weight along with a standard regime of anti tubercular treatment (ATT) for 14 days and thereafter dose was tapered in the next 16 days. The standard regime of HRZE for 2 months plus HR for 4 months was considered. Repeat chest X-ray PA view and ultrasound of chest were done at 14 days, 1 month, and were compared with previous findings. The outcome was measured in terms of the decreased amount of effusion, absence of effusion or pleural adhesion, thickening with symptomatic relief of chest pain, dyspnea cough, and fever.

RESULT

52 patients with tubercular pleural effusion were enrolled in this study. No one had a history of TB before and TB contact. Table 1 shows the baseline characteristics of participants.

Table 1: Baseline characteristics of participants

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Values</th>
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<tbody>
<tr>
<td>Male</td>
<td>39 (75%)</td>
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<tr>
<td>Female</td>
<td>13 (25%)</td>
</tr>
<tr>
<td>Smoker</td>
<td>31 (59.6%)</td>
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<tr>
<td>Alcohol consumer</td>
<td>25 (48.1%)</td>
</tr>
<tr>
<td>Age mean +/- SD</td>
<td>31.11 +/- 10.67 (19-59)</td>
</tr>
<tr>
<td>Age of male +/- SD</td>
<td>32.51 +/- 6.61 (21-49)</td>
</tr>
<tr>
<td>Age of female +/- SD</td>
<td>31.24 +/- 9.34 (19-59)</td>
</tr>
</tbody>
</table>

Tubercular effusion was mostly seen in 15 to 25 years of age group. The youngest patient was 19 years old and oldest was 59 years old with the mean age of 31.11 year and standard deviation of 10.67 years.

Figure 1: Response of steroid in 14 days
The first steroid response was evaluated in 14 days after the initiation of ATT. It was found that level of effusion was decreased in all patients to some extent and there was complete resolution of effusion in 28 patients (26 male and 2 female) out of 52 without any scarring and pleural thickening. There was also improvement in clinical symptoms of fever, pleuritic chest pain, and dyspnea in all patients within a period of 2 weeks.

Figure 2: Response of steroid in one month

The second steroid response was evaluated after one month of starting ATT. There was complete resolution of effusion without pleural scarring and pleural thickening in 49 (96%) patients. Three (6%) of them (all female) had pleural scarring and thickening. Probably this was due to the loss of adherence to corticosteroids. Out of 52 enrolled patients only three patients left corticosteroid as they were lost in their first and second follow up.

<table>
<thead>
<tr>
<th>EF level_14</th>
<th>Smoking</th>
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<tbody>
<tr>
<td>Pearson Correlation</td>
<td>.290*</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.037</td>
</tr>
<tr>
<td>N</td>
<td>52</td>
</tr>
<tr>
<td>Smoking</td>
<td>Pearson Correlation</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.290*</td>
</tr>
<tr>
<td>N</td>
<td>52</td>
</tr>
</tbody>
</table>

*Correlation was significant at the 0.05 level (2-tailed)

TABLE 3: Correlation with alcohol consumption

<table>
<thead>
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<th>Alcohol</th>
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<tr>
<td>Pearson Correlation</td>
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</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.039</td>
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<td>N</td>
<td>52</td>
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<tr>
<td>Alcohol</td>
<td>Pearson Correlation</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.287*</td>
</tr>
<tr>
<td>N</td>
<td>52</td>
</tr>
</tbody>
</table>

*Correlation was significant at the 0.05 level (2-tailed)

It was found (as shown in tables 1,2) that smoking and alcohol consumption were significantly correlated with the pleural effusion and P-value was less than 0.05.

DISCUSSION

However, It is not recommended to use corticosteroid in tubercular effusion as per guideline of National Tuberculosis Programme of Nepal, this study is to evaluate the outcome of corticosteroids in tubercular effusion as a previous study has shown its benefit on effusion. In this study, the use of oral prednisolone along with ATT, reduced the size of effusion rapidly, decreased the symptoms of fever, chest pain, and dyspnea. It also prevented pleural thickening. In this study 6 % of total treated patients developed pleural thickening due to loss of follow up and not adherent to the prednisolone.

One of the studies found that corticosteroid might be beneficial as it reduced the time for the resolution of pleural effusion. The risk of residual pleural effusion on chest X-ray was reduced by 45% at eight weeks and by 65% at 24 weeks compared with control. In one randomized, double-blind, placebo-controlled trial of prednisolone with ATT of 197 patients with HIV associated TPE, there was rapid improvement in signs and symptoms of pleural effusion in the prednisolone group but there was increased risk of Kaposi Sarcoma.

Cochrane review found that there were insufficient data to recommend the use of corticosteroids in tubercular pleural effusion.

Though studies have shown that the use of corticosteroid in TB is conflicting, in the study performed by Mathur, an intra-pleural installation of hydrocortisone in the cases of tubercular pleural effusion showed a response in the general wellbeing of the patients in comparison to the control group. Reduction of the pleural fluid was also faster in the hydrocortisone group as compared to the control group. Similarly, good outcomes were shown by other studies that used intrapleural corticosteroids for tubercular pleural effusion, though not used in present.

In another study by Grewal, 102 patients with pleural TB were treated with chemotherapy INH and streptomycin, chemotherapy plus systemic corticosteroids, chemotherapy plus repeated thoracocentesis, and chemotherapy plus repeated
Therapeutic Effect of Oral Prednisolone with Antitubercular Treatment in Pleural Effusion

Thoracocentesis and intrapleural corticosteroids. In this study, treatment with prednisolone, followed by a tapering off along with an ATT, was better than the treatment with intrapleural instillation of steroid.

Lee found corticosteroid with ATT reduced the clinical symptoms more quickly and enhanced absorption of pleural effusion. However, the effect was found on pleural thicking by using corticosteroids in a small cohort. But Galarza found that use of oral corticosteroids along with ATT did not affect the clinical outcome or the development of long-term pleural sequelae in tubercular effusion.

A double-blind, placebo-controlled, randomized study was done by Wyser. Thoracocentesis was done in all cases and corticosteroid was used in tubercular pleural effusion. An improvement in symptoms in the prednisolone group was found as compared to the placebo group. Residual thickening was seen in 53.3% of the patients on prednisolone as compared to 60.5% of patients in the placebo group, and this difference was not significant. Similar finding was seen in the study done by Bang which showed a more rapid improvement in clinical features in the corticosteroid group, but the absorption of pleural effusion and occurrence of pleural adhesion was not significant.

Most tubercular pleural effusions resolve spontaneously even without specific ATT. However, the resolution is often incomplete leading to loculated collections and pleural thickening, and corticosteroids might reduce these fibrotic sequelae and enhance the resolution of pleural effusion as well as clinical symptoms.

The efficacy and safety of corticosteroids on tubercular pleurisy should be judged clearly. Two non-randomized controlled trials showed that corticosteroids could promote pleural fluid absorption and reduce pleural thickening but can lead to adverse effects. Thus, corticosteroid treatment might not be necessary in all cases of tuberculous pleurisy, and clinicians should decide for use by justifying the risk-benefit of the treatment.

Adjunct therapy with corticosteroids or pleural fluid aspiration until dryness has been recommended by some researchers. Corticosteroids with anti-TB drugs may be appropriate in particular forms of TB such as tubercular meningitis and pericardial and pleural disease. Cohen, however, do not recommend routine use of corticosteroids in tubercular pleural effusion unless there are acute symptoms such as fever, chest pain, or dyspnea that are disturbing to the patient.

CONCLUSION

Adjunctive proper use of prednisolone with the standard regime of ATT, reduces the chances of pleural thickening and the symptoms of fever, pleuritic chest pain, dyspnea earlier leading to the feeling of wellbeing physically, socially and mentally. However, the prednisolone should be used cautiously with ATT by justifying the risk-benefit of the treatment as it has many adverse effects.

LIMITATION

The limitation of this study is that the sample size is very small and limited in only one Hospital. Further large sample studies should be considered. Besides this, in this study there are no control cases to compare the outcome of the study. It would have been better if there were cases and control groups. Similarly it would have been better if CT chest was done to measure the degree of pleural thicking.

REFERENCES