

Full Length Research Paper

Prevalance of tuberculosis in patients on hemodialysis and peritoneal dialysis

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It has been shown that the incidence of tuberculosis is higher in dialysis patients than general population. We retrospectively compared herein, the prevalence, frequency, clinical features and outcome of tuberculosis in patients on chronic hemodialysis (HD) and peritoneal dialysis (PD) program for more than three months. We screened 1040 HD and 345 PD patients. The prevalence of tuberculosis was higher in HD group (n=34; 3.27%) than the PD group (n=4; 1.16%) (p=0.037). The mean age was higher in the HD group (51.5±13.3 vs. 26.7±5.9 years). The rate of extrapulmonary tuberculosis was 50% in both groups. In the HD group, treatment ended with cure in 20 patients, was still ongoing in 13 patients and one patient died of pulmonary tuberculosis. Of the four in the PD group, two were cured, one died of tuberculoma of the brain and the other has completed the first four months of treatment at the time of analysis. The lower prevalence of tuberculosis in PD population may be related with different demographic and socioeconomic factors as well as the modality of dialysis.

Key words: Hemodialysis, peritoneal dialysis, tuberculosis, prevalence.

INTRODUCTION

The risk of tuberculosis (TB) is higher (6.9- to 52.5-fold) in patients with chronic renal failure when compared to the general population (Hussein et al., 2003). There are some differences from those with competent immune system like clinical presentation, laboratory diagnostic methods and outcome. Extra pulmonary tuberculosis is more common in dialysis population; with a rate of 38 to 50% (Hussein et al., 2003; Zahiri et al., 1997; Kayabasi et al., 2008). Diagnosis is usually difficult in those patients due to nonspecific clinical presentation with fever of unknown origin, fatigue, loss of weight; tuberculin skin test (anergy) being usually negative and low probability of microbiologic evidence tuberculosis, by direct observation of acid resistant bacilli or culturing the organism (Cengiz, 1996; Woeltje et al., 1998). There is need for an effective program for prevention, screening, early diagnosis and

treatment of tuberculosis in this population, especially in countries in which tuberculosis is endemic (Woeltje et al., 1998; Smirnoff et al., 1998). Due to difficulties in diagnosis, empirical treatment may be considered when there is strong clinical suspicion, although there is not enough proof for such a protocol (Cengiz, 1996). This study aimed to retrospectively compare the prevalence and clinical characteristics of tuberculosis in patients on HD and PD treatment.

MATERIALS AND METHODS

Patients who were on chronic hemodialysis program in our city for more than 3 months in eight HD centers and five PD centers which represent different socioeconomic and cultural characteristics of the city population were chosen. Those who were diagnosed to have tuberculosis at least three months after the start of dialysis were retrospectively examined for their clinical, demographic and laboratory parameters. Hemodialysis patients who were not residents of the city but only guests, HD patients who had been switched from PD temporarily due to mechanical or metabolic reasons; and those with duration of dialysis treatment less than

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Table 1. Diagnostic methods in HD and PD groups.

Diagnostic method	HD group (number of patients)	PD group (number of patients)
Microbiological	17 (Sputum culture for tuberculosis)	1 (Culture of the peritoneal effluent)
Pathological	Lymph node biopsy (12) Pleura biopsy (1) Vertebra biopsy (2) Bone biopsy (1) Skin biopsy (1)	1 (Lymph node biopsy)
Clinical and radiological suspicion	0	2

three months and diagnosed in another city were excluded. Patients who were on chronic PD program in our city for more than three months were involved, excluding guests in the city and those who had switched from HD due to mechanical reasons. PD patients present to clinical visits regularly every month if their clinical situation does not require more frequent visits.

We examined the files of the patients retrospectively and found those who were diagnosed to have tuberculosis. Demographic parameters (age, gender, birth place, educational status, occupation) as well as primary renal disease, co-morbid diseases, duration of dialysis were noted. Diagnosis of tuberculosis was carried by microbiological and pathological examination; while some were accepted to have tuberculosis if there was strong clinical suspicion. Timing of diagnosis, previous history of anti-tuberculosis treatment, family history, site of presentation, names, dosage and durations of drugs, side effects of the treatment and outcome of the disease were recorded.

Statistical analysis was carried out by SPSS (Statistical package for social sciences) for Windows ver. 15.0. Numeric parameters were expressed as mean \pm standard deviation. Pearson chi-square test and Fisher's exact test were used for comparison between categorical variables. Baseline numeric parameters of the groups were compared with analysis of variance (ANOVA), if the distribution of parameter is normal, or with Kruskal Wallis-H test, if the distribution of parameter is abnormal. $P < 0.05$ was accepted as significant.

RESULTS

1040 patients from eight different HD centers and 345 patients from five different PD units have been screened. Thirty four (3.27%) patients from the HD group and four patients (1.16%) from the PD group were detected to have tuberculosis [$P = 0.037$; odds ratio:0.347; confidence interval: 95% (0.122 to 0.985)]. None of the patients with tuberculosis had history of immunosuppressive medication or any disease other than chronic renal failure that may cause immune suppression. All patients in the HD group had microbiological or pathological evidence of tuberculosis, while this was true for only two patients (microbiological in one and pathological in one patient) in the PD group with the remaining two diagnosed by strong clinical and radiological suspicion (Table 1). The mean age in the HD group was higher than the PD group (51.5 \pm 13.3 vs. 26.7 \pm 5.9 years; $P < 0.05$). Male/female

ratios in the HD and the PD group were not different significantly (19/15 and 3/1, respectively). The time period between the onset of dialysis and the diagnosis of tuberculosis was 20.9 \pm 24.5 months in the HD and 10.2 \pm 8.1 months in the PD patients ($P < 0.05$).

Extra pulmonary involvement was reported to be 50% in both groups. There was no statistically significant difference between the groups regarding this data. In the HD group; 30 patients received isoniazid + rifampicin + ethambutol + pyrazinamide; one had isoniazid + rifampicin + ethambutol + a quinolone antibiotic; while in three patients, drugs other than isoniazid and rifampicin were unknown. Treatment ended with cure in 20 (58.05%) patients; was still ongoing in 13 (38.70%) patients and one patient (2.94%) died of pulmonary tuberculosis. In the PD group; three patients had isoniazid + rifampicin + ethambutol + pyrazinamide, one had isoniazid + rifampicin + pyrazinamide treatment. The disease was cured in two patients, one died of tuberculoma of the brain and the other patient completed four months of treatment at the time of analysis. The adverse effects related to anti-tuberculosis treatment in both groups are presented in Table 2.

DISCUSSION

Both incidence and prevalence of tuberculosis seem to decrease in recent years all over the world, which is true for our country also (World Health Organization, 2009). According to the reports of the Ministry of Health of Turkey; the prevalence of tuberculosis in 2006 and 2007 were 20.526 (28.1 patients per 100000 population) and 19.694 (27.9 patients per 100000 population) respectively (Ministry of Health of Turkish Republic, 2010). Rates of tuberculosis in dialysis patients have declined along with the national rates. But the rates in dialysis patients are still higher than the general population, so screening remains important. There have been different reports about the incidence and prevalence of tuberculosis in patients on dialysis treatment (Zahiri et al., 1997; Kayabasi et al., 2008; Taskapan et al., 2000), but there is

Table 2. Adverse effects of the treatment.

Adverse effects	HD group (number and percentage of patients)	PD group (number and percentage of patients)
Related to skin*	11 (32.3%)	0 (0%)
Decreased visual acuity	1 (2.9%)	0 (0%)
Color blindness	1 (2.9%)	0 (0%)
Elevated transaminase levels	0 (0%)	2 (50%)

*: Pruritus, red and dry skin.

no literature which compared the modalities of dialysis regarding the prevalence and incidence of tuberculosis. There were 9976 HD and 677 PD patients in Istanbul in 2009, according to the statistical reports of the local health authorities. This study is the largest scale study with the 10.43% of the HD and 50.96% of the PD population in the city screened. But due to the dynamic nature of these patients and presence of acute cases, it is difficult to determine the exact number of patients that fulfill the criteria for inclusion to the study at the time of analysis. Peritoneal dialysis patients have an increased incidence of peritoneal involvement compared to HD population, although it may be noted in the literature as case reports (Kayabasi et al., 2008; Aydogan et al., 2009; Canbakan et al., 2007).

In our country, incidence and prevalence of tuberculosis in the general population in 2007 was 25.2/100000 and 27.9/100000 respectively according to the registry reports of the Ministry of Health Turkish Republic (2010). Although the prevalence that we have found is lower than the previous reports of 5.7 and 23.6% with the highest number of patients screened as 296 (Cengiz, 1996; Taskapan et al., 2000; Ekim et al., 1999; Sen et al., 2008; Erkoc et al., 2004), it was much higher than the general population. We have found the prevalence of tuberculosis in HD patients as 3.35% in one of our previous studies (Kazancioglu et al., 2010). Although criteria for diagnosis were more stringent in the HD group, prevalence was higher. This may be related with immunological differences and the higher mean age in this group (Schollmeyer and Bozkurt, 1988; Hesselink et al., 2005). Another factor may be higher intellectual capabilities of PD patients and more attention about their health. The difference between the groups may be predicted considering lower educational and socioeconomic status, higher co-morbidity rates, more frequent malnutrition and inconsistency with treatment in HD population in our country. Another factor that may explain the lower prevalence of tuberculosis in PD patients may be lower rates of infection acquired in the hospital as they perform the dialysis procedure at home.

Additionally, in our study group, we observed that HD patients with tuberculosis were older and had longer duration dialysis than PD patients with tuberculosis. These factors may be operating as a cause of higher incidence in HD population. Because of the difficulties in

diagnosis of tuberculosis in dialysis patients caused by atypical clinical presentation with nonspecific symptoms like fever, fatigue, loss of weight; and frequently negative microbiological tests (skin anergy due to blunted lymphocyte functions and cytokine expression in uremia); those patients are checked annually by chest X-ray. All dialysis patients have a chest X-ray annually in our country. If there is clinical or radiological suspicion of either pulmonary or extra pulmonary tuberculosis, then further radiological and microbiological examinations are performed. Presentation of tuberculosis may be different in dialysis patients compared with the general population; pulmonary involvement being still the most frequent (Kayabasi et al., 2008). In Turkey, the percentage of extra pulmonary tuberculosis in 2007 is 30.5% according to the report of the Ministry of Health. Extra pulmonary involvement has been reported to be high in both Turkey (38 to 77%) and other countries (up to 50%) among dialysis population (Zahiri et al., 1997; Cengiz, 1996; Woeltje et al., 1998; Smirnov et al., 1998; Ekim et al., 1999; Sen et al., 2008; Erkoc et al., 2004; Hesselink et al., 2005; Kürsat and Özgür, 2001; Kaul, 2001; Nagesh et al., 2001).

This rate was 50% in both groups in our study. Sen et al. (2008) reported 18 patients (5.2%) among 343 dialysis (both HD and PD) patients screened; and 14 patients (4.9%) among 285 HD patients to have active tuberculosis infection. They involved patients who had empiric anti tuberculosis treatment without prompt evidence in contrary to our study. Another relatively large scaled study from our country again performed by Erkoc et al. (2004) reported the number of patients having tuberculosis (with/without microbiological or histopathological evidence) as 30 (10.5%) among 287 dialysis patients screened (223 HD, 64 PD). 57% of these cases had extra pulmonary disease.

The disease has different characteristics in dialysis patients regarding the drugs used. It is well known that they have more side effects in this population. We reported the rate of side effects other than skin reactions as 17.6%, which prompts more frequent visits in the HD group. In the PD group, the only side effect reported was elevated transaminase levels which were recorded in two patients (50%) in the present study. Both recovered with stopping the drugs temporarily; and starting again with gradually increasing dosage.

Conclusion

The prevalence of tuberculosis remains high when compared with the general population, although there have been improvements. Peritoneal dialysis seems advantageous with lower rates of tuberculosis compared to HD. The diagnosis of tuberculosis is difficult due to nonspecific symptoms and more frequent extra pulmonary involvement in both HD and PD patients. So we recommend routine screening of these patients in countries where tuberculosis is endemic; and with these data we can conclude that PD is superior to HD regarding risk of tuberculosis.

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