Research article

The effect of Pirfenidone on pulmonary function parameters in post recovery COVID-19 patients with pulmonary fibrosis compared to placebo in a Government Medical College, West Bengal

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ABSTRACT

Introduction and Aim: The recent COVID 19 pandemic has created an unprecedented challenge to the entire global healthcare system by affecting many people worldwide. Post COVID complications are multi-systemic, but pulmonary post COVID complications are most common. Involvement of the lung parenchyma ultimately leads to pulmonary fibrosis in many of the patients. Pirfenidone is a widely used antifibrotic medication in the field of idiopathic pulmonary fibrosis (IPF) management. Our study has assessed the effect of Pirfenidone on spirometry parameters in post recovery COVID 19 patients with diagnosed pulmonary fibrosis as compared to those that received placebo.

Materials and Methods: After obtaining approval from Institutional Ethics Committee, 70 adult patients of COVID-19 with established pulmonary fibrosis in the post recovery phase were chosen and allocated into two groups by randomization in 1:1 ratio. All other factors remaining same, one group was administered the recommended dose of Pirfenidone and the other group received a placebo. Spirometry parameters such as FEV₁, FEV₁/FVC ratio, FVC, PEFR of both the groups were recorded on Day 0 and Day 90 and compared using standard statistical tests.

Results: It was found that on Day 0, PFT parameters of the two groups was comparable (P value>0.05). PFT parameters of the group receiving Pirfenidone showed significant improvement on day 90 (P value<0.05). In addition, on day 90, the PFT parameters of the group receiving Pirfenidone showed significantly better values than the group receiving placebo, P value <0.05.

Conclusion: As there is a significant improvement in the PFT parameters of post recovery COVID-19 patients suffering from pulmonary fibrosis, we conclude that Pirfenidone is helpful to improve the pulmonary function parameters in post recovery COVID-19 patients with established lung fibrosis as compared to placebo.

Keywords: Pirfenidone; post recovery patients of COVID-19, lung fibrosis.

INTRODUCTION

The present COVID 19 pandemic has affected a large population throughout the world. It has created unprecedented challenges to the global health care system and thus causing a huge socio-economic burden all over the world. Though SARS COV2 causes multi-system disorders but respiratory system remains the primary target. Lung parenchymal involvement is responsible for life threatening lung conditions and ultimately respiratory failure (1).

So far, the complications of COVID 19 diseases are concerned, pulmonary fibrosis is an alarming and devastating long-term sequela imposing great challenges to the treating physicians worldwide (2,3). It may affect functional capacity and quality of life of an individual. A considerable proportion of COVID-19 patients having underlying co-morbidities like diabetes or immunodeficiency such as malignancy, patients with advanced age or with severe COVID-19 infection may show post recovery impairment of pulmonary function parameters along with abnormal radiologic findings (4-8). Pulmonary fibrosis in COVID-19 patients is being considered to be related with abnormal and dysregulated immune mechanisms which causes lung parenchymal injury (9,10).

Pirfenidone and Nintedanib are considered as two most available and widely used disease modifying antifibrotic medications in the field of idiopathic pulmonary fibrosis (IPF) management. They might have some beneficial role to decrease lung function impairment across a wide range of pulmonary disorders including COVID-19 disease if administered in the early stage of the disease. But few studies are available especially in this part of Indian population and the results regarding impact of those two drugs on pulmonary function test parameters in COVID-19 induced lung fibrosis is still uncertain and inconclusive.
Our study has assessed the effect of Pirfenidone on spirometry parameters in post recovery COVID-19 patients with diagnosed pulmonary fibrosis compared to those that received placebo.

MATERIALS AND METHODS

Our study was conducted in the Departments of Physiology and Respiratory Medicine of a Government Medical College, West Bengal. It had been an observational longitudinal comparative study over a period of 6 months. Informed consent was collected and the approval of the Institutional Ethics Committee (IEC) was obtained. Post recovery COVID 19 patients of age > 18 years of both sexes with diagnosed pulmonary fibrosis in CT scan were recruited. After screening, 30 patients among the total 100 patients initially enrolled were excluded as they were having any of the following (i.) bronchial asthma, chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), pulmonary fibrosis, lung malignancies, connective tissue diseases, immune system disorders, (ii.) heart disease., (iii.) history of syncope, (iv.) critically ill patients who cannot perform spirometry, (v.) with chronic liver or kidney diseases and (vi.) and patients not willing to relinquish consent.

Detailed history, examination was recorded and scrutiny was done. Patients were divided into two groups. Group-A: who received recommended dose of Pirfenidone and Group-B: who received placebo. Both groups were managed conservatively as per standard COVID management protocol. Thereafter, spirometry was conducted on the patients with electronic spirometer (model: Recorders and Medicare system's RMS Helios 702) at visit-1 (Day ‘0’) and visit-2 (Day ‘90’). Spirometry parameters such as FEV1, FVC, FEV1/FVC ratio, PEFR were recorded. Data analysis was performed by SPSS version-21. Descriptive statistics, independent t-test and paired t-test were applied.

RESULTS

The present study comprised of 70 post recovery COVID-19 patients with established pulmonary fibrosis and was allocated randomly into two groups. Among 35 patients in group 1, 77% were male and 23% were female (Fig.1), whereas among 35 patients in group 2, 69% were male and 31% were female (Fig.2).

Table 1: Demographic parameters in patients

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A (Pirfenidone)</th>
<th>Group B (Placebo)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>50.91±12.33</td>
<td>53.17± 8.80</td>
<td>0.41</td>
</tr>
<tr>
<td>Height (Cm)</td>
<td>155.03 ± 2.90</td>
<td>154.7± 2.37</td>
<td>0.622</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>50.89±11.95</td>
<td>47.6± 8.49</td>
<td>0.213</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>21.17± 4.90</td>
<td>19.91±3.67</td>
<td>0.253</td>
</tr>
</tbody>
</table>

Table 2: PFT parameters in patients

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A (Pirfenidone)</th>
<th>Group B (Placebo)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁ %</td>
<td>39.49±13.52</td>
<td>33.8± 11.02</td>
<td>0.06</td>
</tr>
<tr>
<td>FVC %</td>
<td>64.3±16.23</td>
<td>59.8±13.56</td>
<td>0.22</td>
</tr>
<tr>
<td>PEFR %</td>
<td>23.2±5.27</td>
<td>24.7± 10.90</td>
<td>0.45</td>
</tr>
<tr>
<td>FEV₁/FVC %</td>
<td>60.6±7.24</td>
<td>58.09±6.25</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Table 3 showed comparison of spirometry parameters in patients of Group-A during first visit (day 0) and second visit (day 90). Significant improvement was found at visit 2.

Table 4: PFT parameters in patients at visit 2 (day 90)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A (Pirfenidone)</th>
<th>Group B (Placebo)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁ %</td>
<td>62.5± 27.60</td>
<td>32.97±5.66</td>
<td>0.001</td>
</tr>
<tr>
<td>FVC %</td>
<td>76.97± 20.24</td>
<td>58.2± 9.65</td>
<td>0.002</td>
</tr>
<tr>
<td>PEFR %</td>
<td>45.9± 28.71</td>
<td>24.2± 4.99</td>
<td>0.001</td>
</tr>
<tr>
<td>FEV₁/FVC %</td>
<td>76.89± 12.81</td>
<td>60.3± 4.98</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Comparison of the spirometry parameters between Group-A and Group-B patients during second visit are

**Fig.1: Gender distribution in patients receiving Pirfenidone**

**Fig.2: Gender distribution in patients receiving placebo**
presented in Table 4. Significant improvement of FEV₁, FVC, PEFR and FEV₁/FVC (p-value<0.05) was observed in patients of Group A compared to Group B.

DISCUSSION

The demography features (Age, height, weight, body mass index) and the baseline spirometry values such as FEV₁, FVC, PEFR and FEV₁/FVC at visit-1 were comparable in two groups (Table-1, Table-2 respectively; p-value>0.05). Table 3 shows the comparison of spirometry parameters changes within the group of patients receiving Pirfenidone during first visit (day 0) and second visit (day 90). Significant improvement was found during second visit compared to first visit. Moreover, spirometric parameters showed significant improvement during second visit in patients receiving Pirfenidone. These findings agree with other studies where Pirfenidone was administered in patients with Idiopathic Pulmonary Fibrosis (11-13).

Pulmonary fibrosis in post-recovery COVID-19 patients may be a pathological consequence of diffuse alveolar damage, micro vascular thrombosis (14). On the other hand, the cytokine storm produced because of dysregulated immune function caused by SARS COV-2 may be responsible for acute lung injury, fibrosing organizing pneumonia. Formation of TGF-beta, excessive stretch on alveolar epithelium during mechanical ventilation and oxygen free radicles produced due to prolonged use of high concentration of oxygen causing oxidative stress are the other profibrotic mechanisms.

Pirfenidone acts through regulation of TGF-beta activity, TNF-α and β pathways as well as cellular oxidation and thus plays an important role to prevent inflammation and lung fibrosis. Therefore, Pirfenidone is a well-established medication indicated for the management of Idiopathic Pulmonary Fibrosis (15). The similar cytokine profile in IPF and COVID-19 disease may indicate the possible pathophysiologic mechanism. Therefore, Pirfenidone is helpful to improve the pulmonary function parameters in post recovery COVID-19 patients and may reduce the progression of fibrosis.

The number of studies is limited showing effect of Pirfenidone on spirometric parameters in post recovery COVID-19 patients especially in this part of India. Our study might be helpful in this regard. However, large sample size with multi-centric study design including advanced stage of fibrosis may be more useful to establish the impact of Pirfenidone.

CONCLUSION

Pirfenidone may be helpful to improve the pulmonary function parameters in post recovery COVID-19 patients with established lung fibrosis compared to placebo. These findings provide further evidence to suggest possible decline in disease progression and outcome.

CONFLICT OF INTEREST

Authors declare that there is no conflict of interest.

REFERENCES