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Original Research Article

Effect of H1N1 Infection on Capacity of Long Term Exercise Tolerance

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Abstract:

Introduction: Swine influenza is an acute, highly contagious respiratory disease that results from infection with type-A influenza virus (H1N1). It not only causes an immediate adverse morbidity and mortality but also has been reported to have adverse impact on long term health outcome. This study was planned to assess long term consequences of H1N1 in respect of long term exercise tolerance.

Material: This was a cross sectional study conducted at tertiary care centre, Sixty patients were included, All diagnosed cases of influenza H1N1. Each patient was evaluated after around one year of illness by pulmonary function test (PFT) using standard protocol by single operator.

Results: Out of Sixty patients Group 1 included 38 patients without any chest disease and non-smoker, group-2 included 13 patients with smoking habits), and Group-3 included 9 patients with h/o asthma or with chest disease. Patient of group-1 (63.33%) were observed to have mild decrease in exercise capacity and mild restriction in PFT, Patients of group-2(21.66%) showed decrease in exercise capacity more than the patients of group-1 and mixed pattern in PFT, Patients of group-3(15%) showed marked decrease in exercise capacity as compared to pre illness exercise capacity and showed predominantly obstructive pattern in PFT, requirement of bronchodilator was significantly increased in group-3 patients.

Conclusions: H1N1 infection is associated with significant long term respiratory morbidity. Exercise tolerance is significantly reduced as evident from symptoms profile, obstructive pattern in PFT and increased need of bronchodilator.

Keywords: mMRC, Dyspnoea, Pulmonary function test, Swine influenza, ARDS.

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Introduction

Influenza A virus subtype H1N1, a pandemic in October 2009, caused widespread outbreaks of H1N1 influenza in humans. As of 17 June 2010, more than 214 countries had reported confirmed cases of infection with pandemic 2009 influenza A (H1N1) virus. [1] Patients typically presented with severe pneumonia and acute respiratory distress syndrome (ARDS), which led to severe lung damage and in some cases death. Varying degree of abnormal pulmonary function were reported, including diffusion disorder and small airway function disorder. This lung

parenchymal damage caused by H1N1 virus result in mixed pattern of pulmonary function test. After recovery from severe pneumonia and ARDS, various degrees of lung lesions occur, having an impact on patients' respiratory function and in turn his or her quality of life. This study was planned to assess long term consequences of H1N1infection in patients admitted in our hospital around one year back and treated, in respect of long term exercise tolerance by using pulmonary function test and Modified Medical Research Council scale for dyspnoea.

Materials and Methods

This was a cross sectional study conducted at tertiary care centre, Government Medical College Kota and attached group of hospitals, Rajasthan, India which included sixty patients (35 male and 25 female) after taking approval from institute ethical committee. study was conducted between 1 Jan 2019 to 31 dec 2019.All patients were diagnosed cases of influenza A virus subtype H1N1 using Real Time Polymerase Chain Reaction (PCR) at regional swine flu laboratory of Government Medical College Kota, Rajasthan, India who were treated according to standard guidelines. The Modified Medical Research Council Dyspnoea Scale was used to evaluate dyspnoea of patients for evaluation of exercise tolerance [2]. All participants answered a questionnaire detailing any complaints of dyspnoea, tiredness, cough, expectoration, medical treatment and smoking habits. Questions were framed with the help of Airway Questionnaire 20(AQ20). Patients with severe H1N1 infection requiring ventilator therapy (invasive as well as non-invasive) were excluded. Patient of CHF, Liver cirrhosis, CKD, Anaemia and recent respiratory tract infection were excluded from the study. Written and informed consent was taken from each patient. Statistical calculation were computed using Microsoft Excel.

Pulmonary Function Test [3] was assessed using standard guideline (Gold Spirometry 2010) by a single operator using Spiro excel 1.1 software, measuring- Forced expiratory volume at 1 second (FEV1), Peak expiratory flow (PEF), forced expiratory flow at 50% and 75% (FEF50, FEF75), and functional vital capacity (FVC), FEV1/FVC. Each patient was assessed for any recent infection, deformity, cough, fever, by taking history and general physical examination, routine blood test, pulse oximetry and chest radiography

Results

In order to assess the potential long term effects of mild H1N1 influenza infection on exercise tolerance patients were first assessed at approximately one year following recovery and hospital discharge. All patients were divided in 3 groups. Group-1 included 38 patient(20 male and 18 female) without any H/O chronic chest disease and smoking habits, Group-2 included 13 patients (10 male and 3 female) with smoking habits, and Group-3 included 9 patients (5 male and 4 female) with chronic chest disease e.g., -COPD, Bronchial Asthma, Seasonal allergy etc.

Patients of group-1 (63.33%) were observed to have mild decrease in exercise capacity and mild to moderate restriction in PFT. Mean hospital stay around one year back was 5.7±1.2 days. The mean values of PFT in group-1was FEV1- 2.37±0.41, FVC- 2.71±0.52, FEV1/ FVC-89.63±4.62, PEF- 6.23±0.98, and PEF- 25%-75%-4.25±1.02 (values are in litre). Females were reported to have more deterioration in exercise capacity than males, 10 out of 38(16%) patients who suffered mild to moderate disease and required inhalational oxygen and nebulisation during admission one year back had more decrease in exercise capacity than patients who didn't require inhalational oxygen and nebulisation (n=28).

Group 1 (nonsmoker)	FVC	FEV1	FEV1/FVC	PEF	PEF 25-75
Mean Value (% of pred.)	2.71(69.97)	2.37(72.85)	89.63(109.90)	6.23(78.77)	4.25(98.19)
Standard Deviation (% of pred.)	0.52(7.29)	0.41(8.80)	4.61(6.15)	0.986(20.14)	1.02(26.90)

Patients of group-2(21.66%) showed decrease in exercise capacity more than the patients of group-1 and mixed pattern in PFT. Mean hospital stay around one year back was 6.9±1.5 days. Mean values of PFT was FEV1-2.33±0.59, FVC-2.8±0.73, FEV1/FVC-86.66±5.14, PEF-4.6±1.11, PEF25%-75%-3.2±0.9 (values are in litre). 3 patients out of 13 (23.07% all male) with more smoking habits or chain smoker had grade 3 dyspnoea for up to 3 month after discharge and have grade 1 dyspnoea at 1 year even after abstinence from smoking. Rest 10 patient in group-2 suffered grade 2 dyspnoea after discharge up to around 3 month post discharge and after one year recovered to grade 1 or 0.

Smoker	FVC	FEV1	FEV1/FVC	PEF	PEF 25-75
Mean Value (% of pred.)	2.8(67.5)	2.33(69.51)	86,66(107)	4.6(57.38)	3.2(85.37)
Standard Deviation (% of pred.)	0.73(9.85)	0.59(13.15)	5.14(6.10)	1.11(12.21)	0.9(26.70)

Patients of group-3(15%) showed marked decrease in exercise capacity and predominantly obstructive pattern in PFT was observed. Mean hospital stay around one year back was 7.2±1.33 days. Mean values of PFT was FEV-1.60±0.07, FVC-2.48±0.06, FEV1/FVC-64.63±2.17, PEF-3.80±0.28, PEF25%-75%-1.94±0.20 (values are in litre). They reported 50% or more decrease in exercise tolerance after one year as compared to pre-illness tolerance, requirement of bronchodilator was significantly increased in group-3 patients. Patients of group -3were reported to have suffered greater morbidity and longer hospital stay one year back than patients without chronic chest disease.

Group-3 (Asthmatic COPD)	FVC	FEV1	FEV1/FVC	PEF	PEF 25-75
Mean Value (% of pred.)	2.48(67.5)	1.60(43.73)	64.63(63.42)	3.80(43.32)	1.94(52.40)
Standard Deviation (% of pred.)	0.06(1.80)	0.07(3.36)	2,17(1.88)	0.28(3.29)	0.20(5.01)

Patient with BMI >30 kg/mt^2 3 out of 60 (5% of total patient) and sedentary life style irrespective of previous lung disease were reported to have greater impairment of pulmonary function as compared to patients with BMI within normal range.

Pulmonary functions were assessed at the time of examination only and no data of pre-illness pulmonary function was available. All patients were categorised based on history and clinical examination. Grades of dyspnoea were determined by retrospective questionnaire and were compared with on the spot exercise capacity.

Discussion

We conducted a cross sectional study including 60 patients at the tertiary care centre GMC Kota and attached group of hospitals Rajasthan, India and we found that the abnormal pulmonary function test and decrease in exercise capacity was associated with multiple factors both of patients and disease itself. We noted that derangement in pulmonary function and exercise capacity was more in patient with smoking habits and was severe in patient with pre-existing chronic lung disease as compared to patients without these factors, and patients with no smoking habits and no chronic lung disease with increased BMI suffered more as compared to patients with normal BMI.

The correlation between the mechanisms and the impact that viruses have on the respiratory system has been established in many studies [4-7]. It might be anticipated that decrease in respiratory functions was due to inflammatory effect of virus on respiratory tract. The differentiation of respiratory capacity also varied between the measurements taken upon discharge and the three-month follow-up, but it was observed that the variation was smaller in comparison to the sixth-month visit, which is possibly due to the time needed for the resolution of the inflammatory effects. Recent studies have shown that the high mortality rate of influenza virus infections is a consequence of an overactive inflammatory response and the severity of infection is closely related with virus-induced cytokine dys-regulation. The most important feature of influenza A immune-pathogenesis is the appearance of "cytokine storm", which is characterized by the extreme production and secretion of numerous pro-inflammatory cytokines. This is responsible for the development of lethal clinical symptoms, such as massive pulmonary oedema, acute bronchopneumonia, alveolar haemorrhage, reactive hemophagocytosis, and acute respiratory distress syndrome, associated with necrosis and tissue destruction. [8]

During recovery pulmonary fibrosis is the major pathological change observed during recovery [9]. In addition, abnormal pulmonary function is manifested as decreased diffusion function and restrictive ventilatory disorder [10]. There is precedence for long term negative effects from pulmonary infection, as viral pneumonia-caused ARDS is a typical manifestation of severe acute respiratory syndrome (SARS) infections. Specifically, SARS patients presented with decreased pulmonary diffusion function during recovery [11-14] Furthermore, a study by Neff et al [15] revealed that among 16 survivors of severe ARDS, 9 had abnormal pulmonary function, while four presented with obstructive ventilatory disorder and four with restrictive ventilatory disorder. In addition, a study by Li et al [16] found the incidence of obstructive ventilatory disorder and restrictive ventilatory disorder was approximately 30% following infection. In 2012 Charles-Edouard Luyt MD, PhD a et all found that one year post-ICU discharge, a majority of survivors of A(H1N1)-associated ARDS had minor lung disabilities with diminished diffusion capacities across the blood-gas barrier, and most had psychological impairment and poorer HRQoL than a sex- and age-matched general population group [17]. In 2009 V. B. Lindén M. K. Lidegran at all found that ECMO-treated ARDS patients have good physical and social functioning. However, lung parenchymal changes on HRCT suggestive of fibrosis and minor pulmonary function abnormalities remain common and can be detected more than 1 year after ECMO [18]. Similar finding also found in a study conducted in china on SARS survivor by D S Hui, G M Joynt at all. They found that exercise capacity and health status of SARS survivors was considerably lower than that of a normal population at 6 months [19]. In 2017 a study conducted by Jiajia Chen, Jie Wu on H7N9

survivors also found similar airways modifications that interstitial change and fibrosis on pulmonary imaging remained 6 months after hospital discharge. Both ventilation and diffusion dysfunction improved, but restrictive and obstructive patterns on ventilation function test persisted throughout the follow-up period [20].

Inflammatory effect was more on previously damaged respiratory tract by chronic lung disease (Asthma, COPD, pulmonary fibrosis), smoking and chronically ill [21] evidenced by that increased need of bronchodilator and 50% or more reduction in exercise capacity in chronic patients. Extreme of ages was associated with more morbidity and derangement in pulmonary function [22]. Chest radiograph after one year was essentially normal without any opacities in non-smoker group and smoker group. Patient with COPD and asthma observed to have hyper-inflation of both lung fields consistent with chronicity of their illness. Auscultation of chest was normal with vesicular character in non-smoker and occasional wheezing in heavy smoker. Asthmatic and COPD patient noted to have ronchi and fixed crepitations consistent with chronic disease they have.

From above description it is evident that H1N1infection poses a great threat to normal as well as diseased lung and it is also evident that resolution of inflammation was early in non-smoker as compared to smoker and chronic patients. With time, improvement in PFT and exercise capacity was associated with resolution of inflammation of airways and changing habits with increased awareness toward healthy life style. [23]

Conclusion

H1N1 infection is associated with significant long term respiratory morbidity. Exercise tolerance is significantly reduced as evident from symptoms profile, obstructive pattern in PFT and increased need of bronchodilator. Long term pulmonary rehabilitation even after discharge or recovery from H1N1 infection is very much required to prevent long term morbidity, limitation of exercise tolerance and residual pulmonary deficit. Role of yoga, Structured breathing exercise, Chest physiotherapy needs systematic evaluation on a larger scale.

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