Long-term use of Vitamin-C in chronic obstructive pulmonary disease: Early pilot observation

Chronic obstructive pulmonary disease (COPD) is a disease of chronic, progressive airflow limitation with increasing prevalence globally.[1] Cigarette smoke is a common cause of COPD. It contains >4000 chemicals out of which para-benzoquinone (p-BQ), a compound isolated recently is thought to be a major causative factor.[2] This is produced from oxidation and disproportionation of para-benzosemiquinone, a pyro-product of cigarette smoke in the lungs. This p-BQ forms adduct with protein and cause oxidative damage leading to COPD.[3] The research on animal model has shown that p-BQ is responsible for inducing emphysematous change in guinea pig lungs.[3]

The p-BQ is neutralized by the formation of anti-p-BQ antibody in the system. However, for unknown reasons in some smokers, deficiency of the neutralizing antibody develops at or after the middle age and the unabated oxidative damage from the active p-BQ leads to the development of COPD. This fact has been supported by the observation of significantly lower anti-p-BQ antibody levels in smoker COPD patients compared to smoker non-COPD patients.[4] Another substance that protects against p-BQ is ascorbic acid (Vitamin C), a well-known antioxidant. It is observed that pretreatment of the guinea pigs with Vitamin C can prevent the p-BQ induced emphysema.[3] Since guinea pigs, such as human beings, are devoid of the enzymes to produce Vitamin C in their body and depend on dietary supplementation of the Vitamin, the prevention of p-BQ induced emphysema with Vitamin C raises the possibility of the same prospect in human beings too. The preventive dose of Vitamin C (30 mg Vitamin C/kg body weight) in guineapigs[3,5] may be effective in human beings also. p BQ induced continued oxidative damage may be active in the progression of COPD in humans and the treatment with a high dose of Vitamin C may help the natural course of COPD.

We have, therefore, decided to test the role of long-term high dose Vitamin C (2 g/day, 500 mg four times orally) in a small cohort of our COPD patients (n = 26) who were randomized to receive either a standard COPD therapy or the same with add-on high dose Vitamin C. They were followed up longitudinally every 3 months for 6 months with spirometry and clinical examination with intermittent telephonic enquiry to ensure compliance. The basic demographic data of these patients are summarized in Table 1. It has been found that on longitudinal follow-up there is hardly any difference in lung function. However, at 6 months, there is a drop in exacerbation rate in patients receiving add-on Vitamin C. Exacerbation rates were found to be higher (odds ratio 5.26 [2.44–11.31], P value < 0.0001) in standard therapy alone.

Table 1: Differences in age, BMI, Spirometry parameters and exacerbation rates in patients receiving COPD standard therapy and patients receiving standard therapy with add-on Vitamin C

	Standard therapy (n=12)	Standard therapy with add-on Vitamin C (2 g/day) (n=14)	P value
Age (years)	63.40±8.44	66.18±8.29	0.45
BMI (kg/m^2)	22.00±3.33	21.47±2.66	0.91
At randomization			
FEV_1% predicted	47.14±20.70	41.29±8.57	0.45
FEV_1/FVC	0.50±0.10	0.50±0.14	0.79
FVC% predicted	69.58±20.65	60.50±15.22	0.20
$FEF_{25\%-75\%}$ predicted	15.83±8.28	14.93±9.85	0.8
At 6 months	n=8	n=8	
FEV_1% predicted	50.5±2.82	47.17±20.70	0.69
FEV_1/FVC	0.54±0.15	0.50±0.10	0.42
FVC% predicted	67.38±28.13	69.58±20.65	0.80
$FEF_{25\%-75\%}$ predicted	16.25±8.17	15.83±8.28	0.88
Exacerbation rates (%)			
At randomisation	35.71	41.66	<0.0001
At 6 months	57.14	12.5	OR: 5.6

The difference between the two groups of patients of COPD with their lung function at randomization and after 6 months. The OR: 5.26 (2.44- 11.31) for exacerbation rate in the group without add-on Vitamin C suggests a higher risk of exacerbation [relative risk: 3.02 (1.73-5.27)] in them. COPD: Chronic obstructive pulmonary disease, BMI: Body mass index, OR: Odds ratio, FEV_1: Forced expiratory volume in 1 sec, FVC: Forced vital capacity, FEF_{25-75}: Forced expiratory flow at 25-75%

The reduction in exacerbation rate appears to be a significant finding despite obvious limitations of the observation. The number of patients recruited is too small to make a definitive inference and the follow-up also needs to be for a longer duration. Since exacerbations are related to faster decline of lung function, poor functional capacity, health-related quality of life, and survival prospects, a reduction in exacerbation rate would mean a lot for COPD patients. This small observation demands attention from that point of view to be validated with further research work.

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Conflicts of interest
There are no conflicts of interest.

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