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Research article

Inhalation of Sodium Pyruvate to Reduce Hypoxemia and Dyspnea Associated with Chronic Respiratory Diseases- A Multi-Study Retrospective Analysis

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Abstract

Background: Hypoxemia is defined as low oxygen in the blood (SaO_2) which results in reduced oxygen to the whole body. Dyspnea is defined as a shortness of breath. Chronic hypoxemia symptoms in lung diseases also include and are associated with lung tightness, breathlessness, coughing, trouble breathing, fatigue, erythema, low lung capacity and volume. Hypoxemia can be caused by injury to the lungs, as a result of lung and sinus diseases and infections, like COVID-19 and long COVID, chemicals, ozone, oxygen radicals, obesity, lung cancer, and a host of other medications. In an acute context, hypoxemia can cause symptoms such as those in respiratory distress and death. Most patients with severe COPD, lung infections, lung cancer, and pulmonary fibrosis have a high incidence of hypoxemia and dyspnea. Current medications including steroids often fail to treat these severe symptoms. Design: Data were gathered from 6 human FDA clinical studies that were designed to determine the effect of a 20mM sodium pyruvate nasal spray (N115), in patients with varying lung diseases including patients with COPD, pulmonary fibrosis, allergic rhinitis, long COVID, and sinusitis patients that suffered with hypoxemia. Even though the number of patients tested for some lung diseases like pulmonary fibrosis, and long COVID, are small in comparison to the total numbers for COPD, the safety and efficacy of N115 is consistent across all lung and sinus diseases, with the short term or long-term use of N115. Patient symptoms, vital signs and respiratory function were evaluated compared to a placebo control or a no-treatment baseline control. Findings: Dosing and treatment duration varied by disease and study, but the overall results were consistent. Regardless of the etiology of the disease, (COPD, pulmonary fibrosis, allergic rhinitis, long COVID, and sinusitis) administration of N115 by nasal spray produced statistically and clinically significant improvement in FEV_1, and SaO_2 to reduce hypoxemia and dyspnea. Conclusions: The 6 clinical trials analyzed here add to the total 19 human clinical trials with over a thousand patients, and show that N115 is safe and effective regardless of the etiology of the lung disease (COPD, allergic rhinitis, CF, sinusitis, Long COVID and patients with Pulmonary Fibrosis), to reduce symptoms, increase lung functions and decrease hypoxemia and dyspnea in patients that have these symptoms.

Keywords: COVID-19, SARS-CoV-2, nonresolving pneumonia, corticosteroids, Pulmonary Fibrosis, COPD, Sinusitis, Allergic Rhinitis

Introduction

All lung and sinus diseases share the common features of hypoxemia, dyspnea, coughing, and fatigue and decreased lung functions especially in patients with interstitial lung disease (pulmonary fibrosis), Covid-19 infections, and long COVID. It is also well documented that hypoxemia is prevalent in patients with COPD [1], especially smokers and that low FEV_1 values are associated with decreased oxygen saturation levels [2]. Interstitial lung diseases encompass a large group of chronic lung disorders associated with excessive tissue remodeling, scarring, fibrosis, decreased FEV_1, FVC, PEF, FEV1/FVC, SaO_2, and nitric oxide with hypoxemia and dyspnea [3, 4]. Many of these symptoms are also found in patients with severe COPD, lung cancer and in lung infections like COVID-19 [5]. Unfortunately, available over-the-counter nasal spray products fail to provide relief from nasal or lung inflammation, and drugs containing steroids often have serious side-effects and may eventually lose

their efficacy. There have been many complaints by patients with Idiopathic Pulmonary Fibrosis regarding the efficacy of steroid-based inhalation products to treat or reduce their symptoms and improve their breathing [6]. Numerous studies have shown oxidative stress to be associated with many nasal and lung diseases and that antioxidants are effective in attenuating fibroproliferative responses in the lungs of animals and humans [7]. Sodium pyruvate (N115) is a natural antioxidant of the human body and as an antioxidant it has been shown to significantly reduce inflammatory agents throughout the human body including in the lungs and nasal passages [8, 9].

To date, N115, has demonstrated efficacy, with no known side effects, for all lung and sinus diseases tested including: COPD, Pulmonary Fibrosis, lung cancer, Cystic Fibrosis, Allergic Rhinitis, Chronic Rhinitis, Sinusitis, Flu, COVID-19 and Long COVID. In 19 human clinical trials (Phase I, II, III including animal safety data) submitted to the FDA, N115 produced statistically significant increases in all lung functions with reductions in nasal and respiratory inflammation, reduction in oxygen radicals, congestion, coughing, fatigue, a reduction in hypoxemia and dyspnea, and a reduction of inflammatory cytokines including IL-6, which is associated with the cytokine storm in COVID-19 patients. Nasal administration of N115 also increases the synthesis of nasal nitric oxide, a natural defence molecule that kills invading bacteria, fungi, and viruses to prevent and reduce the severity of infections [10]. In this summary report, we retrospectively analyze the effects of N115 in various lung diseases in patients with hypoxemia to assess its overall capacity to improve lung function and blood O_2 levels.

Study Design and Results

146 patients from 6 different clinical trials with various lung and sinus diseases (Table 1) were administered N115 and retrospectively analyzed for the effects on lung function (SaO_2 and forced expiratory volume in one second (FEV_1)). A urine pregnancy test was given to all women of child bearing age. If the patients were also on nasal sprays as part of their normal therapy, that nasal spray was eliminated.

Retrospective analysis of the data indicated that nasal saline controls had no effect on lung function measurements including FEV-1 (Table 2) and SaO2 (Table 3) over any time period in any of the trials. The data indicate that inhaled 20mM sodium pyruvate (N115) in individuals with COPD, allergic rhinitis, pulmonary fibrosis, sinusitis, and long COVID produced statistically and clinically significant improvements in lung function measurements including FEV-1 (Table 2) and SaO_2 levels (Table 3) immediately after administration of the drug, and the improved effect was maintained during the remainder of the study time.

Study I. Individuals with severe COPD (n=58), were treated with inhaled sodium pyruvate or saline placebo control. Sodium pyruvate nasal spray increased FEV_{-1} and SaO_2 values in these patients. The patients were measured on day one for FEV_{-1} and Sa02 values then treated with a saline placebo and FEV_{-1} and

Table 1. Patient Demographics

Total Number	Gender	Age	Patient's Stated Heritage	Dx	Smoker?
146	F=71 M=75	12-81	White=120	COPD=58	Cigarettes=104
			Latino=21	PF=20	Cigars=16
			Black=5	Sinusitis=30	None=26
				Allergic R =16	
				Long Covid=22	

Table 2. Percentage change in FEV_1 levels in patients treated with N115 or a control.
The data listed in table 2 were collected over multiple years and includes data from 6 Phase I/II/III clinical trials gathered from patients with hypoxemia administered N115, (submitted to the FDA), and data from consumer testing. The data are compared to either the baseline measurements (N.T.) or against a saline placebo control as indicated. FEV_1 values were not measured for Long COVID. Statistical analysis was performed using a two-tailed Student's t-test and $p<0.05$ was considered statistically significant.

	% Increase in FEV_1 (STDEV)		*P value*
	N115	*Control*	
Severe COPD (58)	13.1 (±3.26)	4.4 (±2.76) Saline	p<0.0001
Allergic Rhinitis with COPD (16)	11.9 (±3.26)	2.3 (±1.61) Saline	p<0.0001
Sinusitis (30)	13.5 (±3.26)	2.2 (±1.26) Saline	p<0.0001
Idiopathic PF on meds (6)	89.9 (±55.6)	27.2 (±38.1) N.T.	p=0.0457
PF w/COPD on meds (9)	-4.08 (±13.0)	-3.5 (±12.9) N.T.	p=0.9250
PF w/COPD off meds (5)	35.7 (±43.1)	3.98 (±3.79) N.T.	p=0.1404
long COVID (22)	-----	------	-------
Total (146)	16.4 (±22.91)	4.1 (±10.3)	p<0.0001

Table 3. Percentage change in SaO_2 levels in patients treated with N115 or a control. The data listed in table 3 was collected over multiple years and includes data from 6 Phase I/II/III clinical trials gathered from patients with hypoxemia administered N115, (submitted to the FDA), and data from consumer testing. The data below is compared to either the baseline measurements (N.T.) or against a saline placebo control as indicated in the description above. Statistical analysis was performed using a two-tailed Student's t-test and $p<0.05$ was considered statistically significant.

	% Increase in SaO_2 (STDEV)		*P value*
	N115	Control	
Severe COPD (58)	4.5 (±2.08)	0.5 (±0.86) Saline	p<0.0001
Allergic Rhinitis with COPD (16)	2.9 (±1.5)	1.1 (±0.93) Saline	p=0.0003
Sinusitis (30)	4.1 (±1.39)	0.3 (±0.48) Saline	p<0.0001
Idiopathic PF on meds (6)	3.05 (±1.75)	0.004 (±0.67) N.T.	p=0.0026
PF w/COPD on meds (9)	1.42 (±1.41)	-0.22 (±1.45) N.T.	p=0.0267
PF w/COPD off meds (5)	5.22 (±2.17)	2.02 (±1.73) N.T.	p=0.0326
long COVID (22)	1.56 (±0.78)	0.14 (±0.49) N.T.	p<0.0001
Total (146)	3.34 (±2.29)	0.68 (±1.02)	p<0.0001

SaO_2 values were measured at one hour post inhalation. The following day, patients were again measured for lung functions including $FEV_{.1}$ and SaO_2 then given 20mM sodium pyruvate nasal spray and $FEV_{.1}$ and SaO_2 values were measured again at one hour post inhalation. Most severe COPD patients had hypoxemia (SaO_2 below 92%). These patients showed significant increases in FEV_1 values of 8.7 % ($p<0.0001$) over saline controls and significant increases in SaO_2 levels of 4.0% ($p<0.0001$) over saline controls (Table 2-3).

Study II. In our allergic rhinitis study 548 patients participated, but only 16 allergic rhinitis patients presented with hypoxemia. 92% of all patients reported that the 20mM sodium pyruvate nasal spray significantly reduced their nasal congestion and nasal inflammation. The patients were measured on day one for $FEV_{.1}$ and SaO_2 values then treated with a saline placebo and $FEV_{.1}$ and SaO_2 values were measured at one hour post inhalation. The following day, the patients were again measured for lung functions including $FEV_{.1}$ and SaO_2 then given the sodium pyruvate nasal spray and measured for $FEV_{.1}$ and SaO_2 values at one-hour post-nasal spray. These patients showed a significant improvement in FEV_1 of 9.6% over the placebo control ($p<0.0001$) and an increase in SaO_2 of 1.8 % over the placebo ($p=0.0003$) (Table 2-3).

Study III. 30 patients with sinusitis presented with hypoxemia. The patients were measured on day one for $FEV_{.1}$ and SaO_2 values then treated with a saline placebo and $FEV_{.1}$ and SaO_2 values were measured at one hour post inhalation. The following day, the patients were again measured for lung functions including $FEV_{.1}$ and SaO_2 then given the sodium pyruvate nasal spray and measured for $FEV_{.1}$ and SaO_2 values at one hour post inhalation. N115 treatment showed a significant improvement in FEV_1 of 11.3% over placebo ($p<0.0001$) and an increase in SaO_2 of 3.8 % ($p<0.0001$) when compared to the saline placebo control (Table 2-3).

Study IV. For 20 PF patients, test results following N115 nasal spray at the end of one day were compared to their previous one-day screening and baseline data (there current therapies) as the control for FEV_1 and SaO_2 [11]. Pulmonary fibrosis patients with COPD (n=9) remained on their medications (steroids) while receiving the nasal spray. The $FEV_{.1}$ values for this group did not improve. They all reported that their current medication worked well for them, thus no improvements were expected. However, there was an improvement in their SaO_2 of 1.20% ($p=0.0267$) over their previous one-day screening and baseline data levels. Patients with idiopathic pulmonary fibrosis without COPD (n=6), remained on their medications (steroids) and showed a significant improvement in FEV1 of 62.7% ($p=0.0457$) over the patients previous screening and baseline measurements (Table 2) and a significant immediate and long-term average improvement was also seen in SaO_2 levels continuing from day one through the three day study period of 3.05% ($p=0.0026$) or higher over baseline measurements (Table 3) [11]. Patients with idiopathic pulmonary fibrosis without COPD have long complained that current medications have failed to significantly improve their lung functions [6]. Finally, patients with pulmonary fibrosis with COPD (n=5) were removed from their current medications (steroids) while receiving the nasal spray. This group demonstrated a trend for improvement in their $FEV_{.1}$ values by 31.7 % ($p=0.1404$) over one-day screening and baseline data (Table 2) and their SaO_2 levels significantly increased 3.2% ($p=0.0326$) over one-day screening and baseline data (Table 3) [11].Study VI. Long COVID patients treated for 1 week with N115 were compared to the previous week without treatment as a baseline. Patients were not randomized but served as their own negative controls. N115 treatment for 7 days resulted in significant 1.5% increase in SaO_2 over the control week ($p<0.0001$). FEV1 measurements were not taken for Long COVID patients [11].

Conclusions

Sodium Pyruvate is a natural antioxidant of the human body that inhibits fibrosis and received Orphan Drug Product Designations for the treatment of Cystic Fibrosis and Pulmonary Fibrosis [12-15]. The purpose of this paper was to assess data on

the efficacy of N115 from 6 human clinical trials to successfully treat hypoxemia, dyspnea, low FEV_{-1}, trouble breathing, lung tightness, congestion, erythema, coughing, and fatigue, including patients with COPD, allergic rhinitis, sinusitis, pulmonary fibrosis and long COVID. To treat the symptoms in these patients, N115 (sodium pyruvate) was chosen because of its safety and efficacy profile after treating thousands of patients with COPD, allergic rhinitis, pulmonary fibrosis, and sinusitis with no severe adverse events reported. Many of these patients were treated three times daily for up to six weeks [9]. In 19 Phase I, II, III FDA human clinical trials, compared to a saline placebo, only N115 reduced inflammation and oxygen radicals (hydrogen peroxide by 61% p=0.02) and inflammatory cytokines including IL-6, a cause of the cytokine storm in patients with an active COVID-19 infection [12]. In these clinical trials, N115, not the saline placebo, increased lung functions and SaO_2 levels to decrease hypoxemia in one hundred forty six patients with varying lung diseases suffering with hypoxemia. It may be important to note that N115 produces greater results in patients with the most severe hypoxemia as evidenced by the COPD patients in other studies [9]. This is not surprising since patients with near normal levels of SaO_2 have little room for improvement, but these patients still had improved FEV_1 levels demonstrating that N115 still improves lung function. Also, N115 did not improve SaO_2 levels compared to saline during an active COVID-19 infection, perhaps suggesting that the overactive immune response in these patients blocks any effect of sodium pyruvate [11]. However, it still improved coughing and fatigue [11]. For Long COVID patients that suffer from chronic sequelae, including low SaO_2, we observed significant improvement in trouble breathing and SaO_2 [11].

Data summarized here on the treatment of patients with hypoxemia and dyspnea demonstrates the efficacy of inhaled sodium pyruvate (N115) in these patients whether using a single dose or multiple doses over extended periods of time. Overall, treatment with N115 in patients with lung and sinus diseases increases lung function to improve their quality of life.

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