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Case Report

Effects of High-Intensity Pulsed Electromagnetic Fields (HI-PEMF) in Interstitial Lung Fibrosis due to the Anti-Synthetase Syndrome Associated with Sjogren's Syndrome. A Case Report

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Abstract

In Anti-Synthetase Syndrome and Sjogren's Syndrome, pulmonary fibrosis (Interstitial Lung Disease) are a common source of lung failure, often exacerbated by the weakness of the respiratory muscles. Pulmonary rehabilitation procedures does not always improve the breathing performance and further or alternative therapeutic options would be necessary in this complaints. Pulsed Electromagnetic Fields have proven effective in various muscle-skeletal disorders and, on these bases, we report the results of their validity in the above mentioned conditions. From May to September 2019, a woman 50 years aged, in severe dyspnea due to a rare combination of both syndromes underwent a series of treatments with Diamagnetotherapy, a technology that exploits the therapeutic effects High Intensity-PEMF. During the treatments and afterwards, the patient reported the progressive improvement of dyspnea, on the oxygen saturation, muscle strength and life quality to date. This result may open suitable therapeutic chances in pulmonary fibrotic states, including in post-COVID 19.

Keywords: *Anti-Synthetase Syndrome; Sjogren's Syndrome; Interstitial Lung Disease; Pulsed Electromagnetic Fields; Diamagnetotherapy*

Abbreviations

ASS: Anti-Synthetase Syndrome; ILD: Interstitial Lung Disease; IMM: Idiopathic Inflammatory Myopathy; PM: Polymyositis; DM: Dermatomyositis; SS: Sjogren´s Syndrome; PEMF: Pulsed Electromagnetic Fields; LF-HI- PEMF: Low Frequency, High-Intensity Pulsed Electromagnetic Fields; CT: Computing Tomography

Introduction

In the ASS, a series of auto-antibodies, including anti-Jo-1, anti-PL-12, anti-PL-7, anti-OJ, anti-EJ, anti-KS, anti-Zo and Anti--YRS [1] contribute to typical clinical features of IIM (90%), PM and DM ("mechanic's hand"), non-erosive asymmetric arthritis, Raynaud's phenomenon and lung fibrosis [2,3]. SS affects the mucous membranes and causes the secretive insufficiency of the exocrine glands in the conjunctiva, oral, tracheobronchial and vaginal mucosa. Joint autoimmune diseases (overlapping syndromes) and progressive lung fibrosis (ILD), correlate with a high risk of respiratory failure [4,5]. CT scan images of lung fibrosis in the ASS, range of various degrees of interstitial fibrosis of ground-glass opacities [6,7] and in SS, non-septal linear opacities, interlobular septal thickening and single or multiple

cysts occur [5,8]. Furthermore, in SS lymphocytic infiltration of the airways triggers bronchial hyperreactivity with recurrent respiratory infections. Rarely, they are a cause of death respect to fibrosis. The treatment of lung fibrosis includes immunosuppressive, corticosteroid and anti-fibrotic drugs, non-invasive continuous oxygen therapy and the impairment of the respiratory muscles need adequate rehabilitative programs [4]. Nonetheless, they do not always supply the desired effects and subsidiary, or alternative therapeutic options, such as the biophysical stimulation of the respiratory muscles with PEMF, already effective in musculo-skeletal disorders, could be a valid choice to support the respiratory performance in lung fibrosis.

Case Presentation

We treated with an LF**-** HI-PEMF machine, in addition to the medical therapy consisting of Azatropine and Miclofenato plus continuous oxygen therapy (O_2 90% - 91% - 4l) a woman (P.E.S) aged 50, suffering from ILD in concurrent ASS and SS dated from 19 years. She was positive to antinuclear ANAs (1:160), Anti-Spliceosomal Sm (19:7) and anti-Jo antibodies (1: 23), also complained of diffuse muscle weakness and dyspnoea at rest so much to need the use of a wheelchair. The Spirometry revealed, over time, increasing restrictive-obstructive features with poor response to bronchodilator drugs, while a CT scan showed subpleural interstitial fibrosis, thickening of interlobular septa and converging pseudo-nodular images in the upper left lobe of the lung.

Once acquired the informed consent, the patient received the treatment with a self- limiting High-Intensity -Low-Frequency Pulsed Magnetic Field (up 2 Tesla) machine. The device, named CTU Mega 20® (Periso SA - Switzerland), is normally employed for the treatment of the muscle-skeletal disorders and applies the molecular and water repulsive effect of the high magnetic fields (Diamagnetic effect). Furthermore, the variable amplitude of the magnetic field provides a wide bandwidth of frequencies able to induce the selective endogenous bio-stimulation of the tissues. In the course of the treatment, the maximum energy employed was of 50 J with a repetition rate of the pulse of 6 Hz. A total of 8 treatments, with an average interval of 14 days in outpatient care were carried out at the Cell Regeneration Medical Organization (Bogotá-Colombia) from May to September 2019. The treatment area included the thorax, both shoulders and the upper part of the abdomen (intercostal muscles, serratus anterior muscle, the diaphragm) moving the handpiece or in standing position, with or without a coupling specific conductive cream.

In pre- and post-treatment, the following parameters were analyzed

- 0^2 saturation at the pulse oximetry.
- Designed assessment scores assembling functional and vital parameters respectively:
    - Impairment: Fatigue, strength, walk, comorbidities and autonomy, in a cumulative class of values respectively: Yes (from 1 to 5 points) or No (0 points). The total scores were classified as Severe functional impairment (4 - 5 points), Moderate impairment (2 - 3 points), Slight impairment (0 - 1 points).
    - Critical parameters: Age, breathing rate, oxygen saturation, heart rate, systolic blood pressure, consciousness state and body temperature were attributed in a range from 0 points (normal vital parameters) to 3 points as worst value for each item. The total scores were classified as need of home care and periodic clinical monitoring (1 - 4 points), the need for hospital care (score 5 - 7 points), need for intensive care (score 7 points).
- Dyspnoea at mMRC questionnaire: Modified British Medical Research Council Questionnaire- (range from 4 points for severe dyspnoea to 0 points for exertional dyspnoea).

Results

Due to the persistent spread of COVID in Colombia, CT follow-up scan could not be carried out at the scheduled time (March 2020 or after). Nevertheless, clinical and paraclinical scores showed progressive improvements as follows:

- Oximetry values and oxygen addiction showed, respectively, the increase of the oxygen saturation from 90% to 4 litres at the starting time, to 98% at end of the treatments while the need of the oxygen ranged from continuous to only at night (Table 1).
- Impairment scores decreased from 5 points - severe impairment - before starting the treatments, to 3 points - moderate impairment- at the end of the treatments (Table 2a and 2b).
- Critical parameters decreased from 8 points - need of intensive care - before starting the treatments, to 6 points - need of hospital care- at the end (Table 3a and 3b).
- mMRC questionnaire showed the progressive reduction of the dyspnoea from 4 points pre-treatment, to 0 points at the first follow up, 2 months after the end of the treatments.

Date of Treatment	Pulse oximetry (Oxygen saturation)	Need for oxygen therapy
30/05/2019	90% to 4 Lt	Continuous
17/06/2019	97%	Continuous
19/06/2019	96%	Continuous
15/07/2019	96% to LT litres.	Only at night
24/07/2019	96%	Only at night
23/08/2019	93%	Only at night
24/09/2019	98% 1 Lt per cannula	Only at night
22/09/2019	98%	Only at night

Table 1: *Changes of the O_2 saturation and oxygen addiction during the treatments. Lower need of the oxygen after the third diamagnetic treatment.*

Fatigue	Daily weakness	Yes _1_ (1)/No____ (0)
Strength	Increase in a level without help or break	Yes ___ (0)/No__1__ (1)
Deambulation	Walking a distance of three or more blocks Without help or breaks	Yes ___ (0)/No__1__ (1)
Comorbidities	Three or more comorbilities	Yes__1__ (1)/No____ (0)
Class of functionality	< 4 METS > 4 METS	(1) (0)

Table 2a

Fatigue	Daily weakness	SI __ (1)/NO__0__ (0)
Strength	Increase in a level without help or break	SI _0___ (0)/NO____ (1)
Deambulation	Walking a distance of three or more blocks without help or breaks	SI ___ (0)/NO__1__ (1)
Comorbidities	Three or more comorbilities	SI __1__ (1)/NO____ (0)
Class of functionality	< 4 METS > 4 METS	(1) ( )

Table 2b

Table 2: *In the pre-treatment phase, fatigue, low strength and low walking autonomy were predominant (a). At the end of the diamagnetic treatment there an improvement in fatigue an muscle strength occurs (b).*

	0	1	2	3
Age	< 65			> 65
Breathing Rate	16 - 20	11 - 16	9 - 10 o 20 - 25	< 8 or >25
Oxygen Saturation	> 96	93 - 95	91 - 93	< 90
Systolic Blood Pressure	91-100	101-110	111 - 219	> 220 or < 90
Heart Rate	50-90	41 - 50 or 91-110	111 - 130	< 40 or > 130
Consciousness	Awareness			Lethargy - Coma- Confusion
Body Temperature	36.1 - 37 - 37.8	36.1 -36 or 37.8 - 39	>39	<35

Table 3a

	0	1	2	3
Age	< 65			> 65
Breathing Rate	16 - 20	11 - 16	9 - 10 or 20 - 25	< 8 or > 25
Oxygen Saturation	> 96	93 - 95	91 - 93	< 90
Systolic Blood Pressure	91 - 100	101 - 110	111 - 219	> 220 or < 90
Heart Rate	50 - 90	41 - 50 91 - 110	111 - 130	< 40 or > 130
Consciousness	Awareness			Lethargy-Coma Confusion
Body Temperature	36.1 - 37 - 37.8	36.1 -36 or 37.8 - 39	> 39	<35

Table 3b

Table 3: *Critical parameters. The score ameliorated from 8 points - need of intensive care (a) to 6 points - need of hospital care, respectively pre and post treatments (b). The main improvement concerned the breathing rate and the oxygen saturation.*

No pain during and after the treatments, no side effects or recrudescence of the symptoms have been reported by the patient.

Discussion

The simultaneity of the Anti-synthetase and Sjogren Syndrome is rare [9] and different etiopathogenetic factors imply an immune dysregulation in both conditions. In ASS, the clinical features of IIM and PM are at the origin of the weakness of the respiratory muscles which could impact on the morbidity and mortality of ILD [10-12]. In SS, in addition to Sicca Syndrome, asthenia, arthralgia and vasculitis are risk factors for ILD [4,5]. In such conditions, oxygen therapy and respiratory rehabilitation aim to support the lung functionality and to ameliorate the patient's health-related quality of life (HRQL). Furthermore, lower exercise capacity is a serious aspect of ILD and this limitation may be a prognostic predictor [13,14] and the necessity of additional or alternative therapeutic supports is a real perspective.

In muscle-skeletal disorders, the association between the biophysical stimulation originated from PEMF and rehabilitative programs have drowned a certain interest in terms of positive functional achievements [15]. The anti-inflammatory effects of the cytokine modulation, the regenerative ones mediated by growth factors, neo-angiogenesis [16,17], mesenchymal stem cell differentiation and muscle cell proliferation [18,19] are at the origins of this potentiality.

To compensate for the difficulties related to the impossibility of rehabilitative therapies, we treated the respiratory muscles of the patient with an original technology delivering LF-HI-PEMF. The CTU Mega 20® machine provides a low rise-time of the pulse, variable amplitudes and a broad spectrum of electromagnetic frequencies. This affects the voltage of the cell membrane, changing the electrical properties of the cells, able to induce metabolic responses according to the Intensity and the Magnetic Field Gradient [20]. On its own, the Diamagnetic effect has shown vasoactive properties in chronic limb lymphoedema [21].

Our experience reports that, in ILD, the non-invasive Diamagnetic treatment ameliorated the respiratory function and the quality of life of the patient in terms of reduced oxygen addiction and this is a significant outcome. At the beginning of the treatments, the woman was in continuous oxygen therapy with peripheral oxygen saturation values at 90% to 4 Lt/min and dyspnoea at rest. At the end of the treatments, she required oxygen therapy only at night, the peripheral oxygen saturation was at 98% and the patient complained only exertional dyspnoea. Today, the woman is currently stable and lives the usual daily activities without oxygen addiction and non-desaturation in day life efforts occurs. Besides, clinical and para-clinical scale evidence post-treatment changes from a high-risk class to a lower one and the functional impairment from severe to moderate. This is noteworthy if we consider that for a type of patients whose peripheral oxygen saturation lower than 95%, and the protracted duration of the fibrosis, 19 years, in this case, life expectancy is poor [22]. No pain, no side effects or recurrence of the symptoms occurred during and post the treatments that were well tolerated.

To our knowledge, this is the first description of the successful use of the LF-HI-PEMF in the treatment of the consequences of lung fibrosis (ILD). Owed to the worldwide current health contingencies, we couldn't yet subject the patient for a CT scan follow-up, thus we can't elucidate if the successful outcomes of the diamagnetic treatment may be due only to a direct effect of the biophysical stimuli on the musculature of the chest or to structural changes in the lung. To better understand the cause, further studies, with an adequate statistical population are necessary. Not least is the fact that the functional outcomes of the treatment refer to a patient with two concomitant autoimmune diseases (overlapping syndromes) both characterized by interstitial and airway involvement, initially refractory to conventional treatments.

Conclusion

This is a single case report and, therefore, the level of evidence cannot be signed and further RCT studies are necessary to support these results. Since this improvement doesn't happen spontaneously, we must underline that these results mean something. Hence, the possibility to employ the non-invasive and safe Diamagnetotherapy in lung fibrosis of different origin, like in a post- COVID 2 pneumonia, would be advisable.

Conflict of Interest

Dr. Pietro Romeo declares to have a scientific collaboration with Periso SA.

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