A REVIEW ABOUT THE EFFECTS OF A RESPIRATORY REHABILITATION PROGRAM IN THE DEAD SEA AREA

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ABSTRACT

Introduction: *The Dead Sea, located at 430.5 m below sea level, is characterized by higher atmospheric pressure and partial pressure of oxygen within the inspired air. Hyperbaric condition improves arterial oxygenation and may be useful in hypoxemic patients. Linked to the environmental properties of this basin, a prosperous health tourism industry has developed with the possibility of carrying out a respiratory rehabilitation.*

Methods*: Aimed to review the literature on this topic, a search query was performed consisting of various keywords related to the domains of hyperoxia, oxygen pressure, barometric pressure, Dead Sea, heart and lung diseases.*

Results*: Nine studies conducted on respiratory and cardiac patients staying in Dead Sea area were found. All agreed to show an improvement in shortness of breath, exercise capacity, quality of life and need for oxygen while staying at the Dead Sea.*

Discussion*: The hyperbaric condition typical of this region accounts for the beneficial effects documented by the studies examined. These are probably related not only to the increased partial pressure of O2 but also to the particular conditions of humidity and temperature.*

Conclusion*: Therefore, this work aims to revive the interest of the international scientific community on the beneficial effects that a stay on the Dead Sea shores can induce in patients with respiratory and cardiovascular pathologies re-examining the pathophysiological notions underlying this adaptation to the hyperbaric condition and reviewing all the literature published to date.*

Keywords: *Hyperbaric oxygen, chronic respiratory insufficiency, heart failure, respiratory rehabilitation.*

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Introduction

Why, in the history of scientific literature, has there always been a lot of interest around the conquest of the highest points on the Earth? And how come there was no similar interest in discovering the lowest ones? This remains a mystery.

There is no question that there is ample literature on the conquest of the abyss and on the resultant adaptation of the human body to this environment; in addition, thousands of papers exist on the conquest of the Himalayan peaks[1].

On the opposite hand, there is little excitement in reaching areas of the Earth's surface, strategically located below normal sea level and not entirely covered by water.

Circulatory response to acute expoure to high altitude had been well studied since the start of the modern era. It is characterized by a rise in plasma catecholamines and renin activity, with consequent increase in blood pressure and heart rate. These changes occur abruptly even at relatively lower altitudes (less than 1800 m above sea level) and most ordinarily are attributed to the effect of hypobaric hypoxemia[2]

The thought that opposite environmental conditions can induce an opposite pathophysiological response is somewhat tempting.

Not distant from Jerusalem, a few steps from the ruins of the ancient Masada, located at 430.5 m below sea level, the Dead Sea basin is located in the Jordan Rift Valley along the left-lateral transform boundary, between the Arabian and Sinai plates, and represents the lowest point on Earth (Fig. 1).

Fig. 1: The Dead Sea area.
(from Google Earth: https://earth.google.com/web/@31.38664948,35.5668598,-47.6332109a,118120.34449987d,35y,15.4774421h,0t,0r?authuser=0).

Consequently, the Dead Sea basin has the highest terrestrial atmospheric pressure. At Neve Zohar, located on the western shore of the Dead Sea, there is a meteorological observation post where the barometric pressure and temperature are monitored continuously, since January 1995.

Barometric pressure values change monthly exceeding sea level atmospheric pressure by 36 mmHg in December and 25 mmHg in July

The monthly barometric pressure changes depend on the concomitant variations in the ambient temperature that affect the density of the air, occurring the highest percentage increase above normal atmospheric pressure during the winter months and therefore the lowest during the summer months.

The higher the atmospheric pressure the higher the partial pressure of oxygen (p_iO_2) within the inspired air, with the apparent consequence of a far better oxygenation also at arterial level[3,4] (Tab. 1).

For example, people travelling from Jerusalem (located at an altitude of 800 m above sea level, with a barometric pressure of 696 mm Hg) to the Dead Sea area, undergo a change of 1230 m in altitude and of 105 mmHg in atmospheric pressure[5].

Usually, in hypoxemic patients oxigenation is implemented by giving patients an increased fraction of inspired O_2 concentration (F_iO_2). Oxygen supplementation has been shown to extend survival but requires a tool like an oxygen tank and tubing.

An alternative approach is to increase environmental pressure, thus giving patients a higher piO2. Hyperbaric oxygenation remains fundamentally utilized in the sector of underwater medicine or civil medicine[6], for acute carbon monoxide poisoning or similar conditions that render hemoglobin transiently ineffective for O2 transport[7].

At sea level (altitude = 0 m)
P_{atm} = 1013,25 hPa = 1 atm = 760 mmHg
p_iO_2 = 159 mmHg
p_AO_2 = 100 mmHg
where $p_AO_2 = (P_{atm} - p_{H2O)}\ F_iO_2 - p_aCO_{2/}RQ$ with pH_2O at the airway level = 47 mmHg

At Jerusalem (altitude = 800 m)
P_{atm}= 927,92 hPa = 696 mmHg
p_iO_2 = 146 mmHg
p_AO_2 = 87 mmHg

At Dead Sea level (altitude = - 430.5 m)
P_{atm}= 1061,55 hPa = 800 mmHg
p_iO_2 = 168 mmHg
p_AO_2 = 108 mmHg

The p_aO_2 will depend from the patient's age and the presence of pathologies that can alter alveolar-capillary gradient and the pACO2 value.

Table 1: The Oxygen cascade.
Legend
P_{atm} = atmospherical pressure; p_iO_2 = partial pressure of oxygen in inspired air; p_AO_2= alveolar partial pressure of oxygen; p_aO_2 = partial pressure of oxygen in arterial blood; p_aCO_2 = partial pressure of carbon dioxide in arterial blood; p_ACO_2 = alveolar pressure of carbon dioxide; F_iO_2 = fraction of inspired oxygen (20.93% in the Earth's atmosphere); pH^2O = partial pressure of water vapor; RQ = the respiratory quotient (The value of the RQ can vary depending upon the type of diet and metabolic state. RQ is different for carbohydrates, fats, and proteins with an average value around 0.82 for the human diet).

Hyperbaric condition improves arterial oxygenation, mainly because of a rise in the amount of O_2 physically dissolved within the plasma. The rise in the arterial partial pressure of O_2 (paO_2) makes O_2 more readily available for diffusion in hypoxic tissues.

Unfortunately, we have no data about resident populations. There aren't studies evaluating whether the effects of this unique climate may be beneficial to permanent residents of the Dead Sea region in terms of oxygenation and exercise capacity.

The only one study comparing the Dead Sea residents with a control group of individuals who live in the same desert area of southern Israel, but at a much higher altitude, above sea level, evidenced a significantly higher Quality of Life (QOL) measures in Dead Sea residents, but we have no hematological and respiratory data from this population[8].

Though the beneficial properties of the Dead Sea were already known to the Ancient Greeks and Romans. Even King Herod visited the area and its healing waters during his reign.

In the Middle Ages this area fell into oblivion, regaining new interest only in the middle of the last century, precisely for the beneficial properties in dermatological and rheumatological fields[9].

Due to the thalasso-therapeutic properties of Dead Sea sulfur-containing waters, that are known to be beneficial for several sorts of arthritis and dermatitis, numerous luxury resorts have sprung abreast of the sides of the sea.

Nowadays, health tourism attracts numerous patients from northern Europe countries as well as from the nearby area of Jerusalem.

Both Israel and Jordan are seeking to focus on tourism to rebuild a normality made of peace and customary work.

As a results of the above pathophysiological considerations, this area could be interesting for scientists involved in respiratory rehabilitation. As the guidelines point out, a good respiratory rehabilitation program must include a whole host of strategies like secretion clearance techniques, correct management of the oxygen therapy, effective use of respiratory devices, breathing strategies, regular practice of exercise and physical activity, healthy food intake, irritant avoidance, leisure activities, etc[10].

So what better than practice respiratory rehabilitation in an elegant luxury resort, where you can eat well, you can enjoy pleasant activities, you are far from any form of air pollution?

With these ideas in mind, in the late nineties and early two thousand a few research projects have been initiated; in particular they have been focused on the behaviour and possible rehabilitative treatment of patients affected by pulmonary and cardiac diseases during a stay in the Dead Sea basin.

The aim of this paper is to review the consequences of a stay in the Dead Sea area on cardiorespiratory systems.

Methods

Search strategy

We searched PubMed, EMBASE and Cochrane database for eligible original studies or review published up to March 2020. The search query consisted of various keywords related to the domains of hyperoxia, oxygen pressure, barometric pressure, Dead Sea, heart and lung diseases. These separate domains were combined with the AND operator. References of included studies were screened for publications that were not identified in the search.

Study selection

After a first screening based on title, where irrelevant articles were excluded, I carried on a selection based on the abstract and finally a selection on full text screening.

Inclusion criteria were studies that investigated the effect of hyperbaric hyperoxia induced by short-term stay in Dead Sea region in patients affected by severe lung or heart failure

We excluded studies involving the beneficial effects of Dead Sea area on a variety of skin problems and on several sorts of arthritis.

In PubMed a complete of 9 original studies was found.

In EMBASE only a book by Hanns-Christian Gunga was identified. But, if it may be useful in terms of general notions on physiological adaptations to extreme environments, it does not provide any information on the environment object of my study[1].

Into the Cochrane database, only 2 reviews on the effects of balneotherapy for arthritis treatment were found, but no reviews useful for my research.

In consideration of the numerical smallness of the collected studies and data, no meta-analysis of the same was performed.

Results

Most of the collected papers relate to advanced respiratory diseases, like cystic fibrosis (CF) or chronic obstructive pulmonary disease (COPD), in which patients need oxygen and respiratory rehabilitation.

However, a few of articles ask the likelihood of exploiting the actual properties of this earth region to rehabilitate patients suffering by heart failure.

In both populations, improvement in exercise performance at the Dead Sea was observed.

Respiratory disease

One of the foremost active groups in studying the effects of the Dead Sea on CF patients was that of Pulmonary Institute, Hadassah University Hospital in Jerusalem, directed by Professor Kramer.

In a first study in 1994, 10 patients with end-stage lung disease (4 COPD; 2 CF; 3 pulmonary fibrosis; 1 post-thromboembolic pulmonary hypertension) and receiving long-term O2 therapy, underwent blood gas analysis, spirometry, progressive exercise testing, and sleep oximetry[(11)].

The measurements were repeated at different altitudes, firstly in Jerusalem, 6 days after arrival at the Dead Sea and, finally 7 to 14 days later in Jerusalem. No change in pulmonary function was recorded.

At blood gas analysis, p_aO_2 increased from a median of 51.6 mmHg in Jerusalem to 67.0 mmHg at the Dead Sea, paCO2 from 43.2 to 45.9 mmHg, and S_aO_2 from 87.7 to 92.8%, all in a significant way. At the maximal exercise, O_2 consumption at peak exercise (VO_{2peak}) improved from a median of 0.83 to 1.06 l/min. Also at the sleep oximetry, the median S_aO_2 during sleep increased from 85 to 90%. These data explain the improvement reported by patients in terms of shortness of breath, exercise capacity and fewer need for oxygen[(11)].

In a second paper, published in 1996, Kramer et collaborators explored the behavior of arterial oxygen tension, exercise capacity, sleep oxygen saturation, and quality of life while staying at the Dead Sea. All the parameters increased during both a short stay (1 week) as well as a longer stay (3 weeks), confirming that the low altitude can be of benefit to patients with advanced lung disease. The improvement in exercise performance persisted 2-3 weeks after leaving the area[(12)].

In 1998 an other work tried to match the effects of a stay in Dead Sea area to the conventional O_2 therapy of equal intensity in term of p_iO_2[(13)].

Eleven hypoxic patients with COPD from Jerusalem were taken down to the Dead Sea area for 3 weeks. Many of these patients were on chronic O_2 supplementation in Jerusalem before the Dead Sea sojourn. The patients underwent to blood gases, spirometry, progressive exercise, 6MWT, and sleep oximetry. All tests were done in Jerusalem, at the Dead Sea area and repeated 2 weeks after returning to Jerusalem.

This study confirmed previous results, with a significant improvement in blood gases exchange, 6MWT distance (from 337 ± 107 to 449 ± 73 and 507 ± 91 m, respectively; p<0.005) and VO_{2peak} (from 0.90 ± 0.26 to 1.10 ± 0.26 and 1.06 ± 0.25 l/min; p=0.01).

Many of the patients using O_2 supplementation during their normal life, were able to increase their exercise performance at the Dead Sea without requiring artificial aids. Blood gas analysis values returned to their baseline levels after returning to Jerusalem, while 6MWT distance (453 ± 47 m, p<0.02) and VO_{2peak} (1.10 ± 0.36 l/min) remained significantly high.

The Authors concluded that a conventional O_2 therapy supplementation at the rate of 1 to 2 l/min would have permitted an identical increase in p_iO_2 (± 21 mmHg) but not have yielded the same result[(13)].

How to say that under conditions of iso-piO2, the Dead Sea sojourn acts as a mini-hyperbaric O2 therapy. The higher ambient temperature of the Dead Sea area as compared to Jerusalem, in addition to the constantly higher p_iO_2, can explain the higher gas exchanges.

In 2006 Falk published data about 14 CF patients (6 females, 8 males), aged 15-45 years, suffering from a moderate to severe lung disease, who performed spirometry, a graded sub-maximal and a maximal exercise test on a treadmill, and a 6 minute walking test (6MWT).(10) Patients were tested twice: at sea level, and at the Dead Sea, in a randomized crossover design[(14)].

Both VO_{2peak} at the maximal exercise (1.68±0.73 vs. 1.57±0.74 l/min, respectively, p=0.05), and arterial saturation for O_2 (S_aO_2) at all sub-maximal exercise intensities were significantly improved at the Dead Sea in comparison with sea level. Indeed no differences were observed in lung function at rest[(14)].

Moreover, the improvement in exercise capacity was achieved in the face of a lower need for artificial oxygen.

In a similar way, Goldbart retrospectively collected data about 94 CF patients coming from Europe and participating in rehabilitation camps at the Dead Sea, during the winter months (November to March) from 1997 to 2000. Each camp ran for 3 weeks[(15)]. The barometric pressure changes due to altitude descent caused a 10 mmHg increase in p_iO_2 and a subsequent increase of 4-6 mmHg in p_aO_2.

The study assessed three major parameters: pulmonary function, weight gain, and daily symptoms. The program included chest physiotherapy for 1 hour daily. Outdoor physical activities included various ball games, horse riding, cycling and bi-weekly walking tours in the Dead Sea area. All participants enjoyed a high caloric diet with daily nutritional supplements while at camp. Only 35 patients were included for the ultimate analysis of lung function tests and S_aO_2.

A significant increase in FEV_1 (+ 8.2 ± 2.3 % of the predicted value) was measured, but not in FVC. FEV1 values began to enhance during camp but were significantly better only several weeks after the camp ended. Authors suggested that the improvement in the patients' pulmonary and nutritional status following these camps was due to the combined effect of physical activity with the distinctive environmental setting that affected the patients for an extended time, as the environmental atmospheric pressure or the bronchodilating effect of the encompassing magnesium[15].

In 2010 Griese also reached similar conclusions with his retrospective analysis of 142 CF patients aged 2-46 years who participated in rehabilitation programs taking place in Germany/Switzerland or in Israel. Overall lung function and weight improved in 97 patients during 172 stays at the Dead Sea. Outcome did not differ between Israel and German/Swiss sites. Interestingly, lung function improved during the initial phase of the stay, whereas weight gain was sustained throughout[16].

Cardiac diseases

Other authors focused their attention on the possible effects of a stay on Dead Sea area on the cardiovascular system.

The stay at the Dead Sea was showed to work out a little but significant decrease in both systolic and diastolic blood pressure values, indicating that there is no contraindication for hypertensive patients to be exposed to climatic variations at the Dead Sea. (17)

But it had been Abinader, from Heart Institute, Bnai Zion Medical Center (Haifa, Israel), who first took on interest within the potential of hyperbaria in the management of patients suffering from heart failure or ischaemic heart disease, with the publication in 1999 of two works shortly after each other.

In his first work he described the improvement observed in a group of 12 patients with coronary artery disease (CAD) and 6 normal controls, who underwent stress test and exercise echocardiography study in Haifa (130 meters above sea level) and at the Dead Sea. Exercise duration significantly increased at the Dead Sea by 15% in both groups indicating that descent to the Dead Sea in patients with CAD is safe, improves exercise performance and reduces ischaemia[18].

Similar conclusions were drawn by the authors after the evaluation of 12 patients affected by chronic heart failure and 4 matched controls, which performed a CPET on treadmill, again in Haifa and Dead Sea level[19].

Significant changes in parameters at the Dead Sea compared with Haifa were observed, with a reduction of the Borg scale and a simultaneous improvement of exercise duration, S_aO_2 during exercise, cardiac output at rest and VO_{2peak} (+ 0.126 l/min; $p < 0.05$). Patients with a basally more severe exercise-induced oxygen desaturation were those with the best improvement in VO_{2peak} and the greatest reduction in the ventilation/carbon dioxide production slope (VE/VCO_2) values.

Authors explained the improved myocardial work with the higher ambiental oxygenation and, maybe, with the high magnesium content present within the Dead Sea brine, which may contribute to the observed reduction of blood pressure and therefore the left ventricular afterload.

In 2011 Gabizon, from The Soroka University Medical Center (Beer Sheva, Israel) published a work on the effects of a stay in a Dead Sea Resort on 19 patients with congestive heart failure and a severe impairment of systolic function (ejection fraction = 23.4 ± 10.7 %) after a recent implant of an Implantable Cardioverter Defibrillator (ICD)[20].

Despite the absence of significant changes in blood pressure, heart rate, O_2 saturation if compared with the same values before and after the stay, the study showed a significant improvement in the 6MWT that increased by a mean of 63 m, and in the QOL score that improved by a mean of 11 points, with a ICD activity index decreased.

Discussion

All studies agree on an improvement in arterial oxygenation (both when expressed in terms of paO2 and in terms of S_aO_2) during a descent to the Dead Sea. This translates into a beneficial effect in all pathophysiological situations characterized by hypoxemia such as respiratory and cardiac failure. This is the main reason for the reduction of the dyspnoea perceived by the patients and for the ability to train better even without supplemental O_2.

All this is at the origin of an improvement in the quality of life and exercise capacity. There is no doubt that numerous data are lacking for the study of this pathophysiological model. First of all, the reported studies were conducted in resorts and not in hospital centers. Many doubts remain about the possibility of carefully monitoring patients and daring to undertake a more intensive rehabilitation program. In spite of a greater risk of collateral events, this would allow even more encouraging results.

Furthermore, the effects of a longer stay in this area should be assessed. None of the examined studies evaluated permanent residents of the Dead Sea region to determine whether the effects of this unique climate may be beneficial to them in terms of oxygenation and exercise capacity. The only one study comparing the Dead Sea residents with a control group of individuals who live in the same desert area of southern Israel, but at a much higher altitude above sea level, evidenced a significantly higher QOL measures in Dead Sea residents, but without the support of some hematological and respiratory data[8].

Conclusions

The Dead Sea area is characterized by a modest increase in atmospheric pressure and consequently in the partial pressure of oxygen; it is a kind of mini-hyperbaric hospital ward. This natural model of hyperbaric hyperoxia is not comparable, in terms of achievable pressures, to hyperbaric chambers. However, the beauty of the place and its undeniable positive psychological effect, as well as its availability at a limited cost, make it an option to be considered. This work, with the reanalysis of the few data available in scientific literature, reconfirms the beneficial effects on respiratory function and exercise capacity in patients affected by severe sorts of respiratory and cardiac insufficiency. Therefore, new research on this topic would definitely be worthwile.

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