Multidisciplinary Biopsychosocial Program for Chronic Musculoskeletal Pain at the Dead Sea

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ABSTRACT: **Background:** Multidisciplinary biopsychosocial rehabilitation for patients presenting with rheumatic diseases has been shown to produce better results in a warm climate. Dead Sea Climatotherapy (DSC) has been successfully used for decades to treat many patients with rheumatic diseases.

Objectives: To evaluate the short-term improvement of Norwegian patients who presented with chronic pain following a multidisciplinary biopsychosocial approach to treatment combined with DSC. Both objective and subjective clinical parameters were evaluated.

Methods: This retrospective study included a statistical analysis of 938 patients presenting with rheumatoid arthritis and ankylosing spondylitis (n=105), osteoarthritis (n=342), fibromyalgia (n=374), and other orthopedic conditions (n=117). Clinical assessments were conducted before and after a 3 week treatment program at the Dead Sea.

Results: Six parameters improved significantly in the rheumatoid arthritis and ankylosing spondylitis group as well as in the osteoarthritis group. Five parameters in the fibromyalgia group improved, while two improved in the orthopedic conditions group. Overall, major significant changes occurred in the pain self-assessment, joint motility, and daily activities scores.

Conclusions: A 3-week multidisciplinary biopsychosocial program combined with DSC induced positive changes in the clinical parameters of Norwegian patients presenting with chronic musculoskeletal pain.

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KEY WORDS: Dead Sea, fibromyalgia, inflammatory joint diseases, multidisciplinary biopsychosocial rehabilitation, osteoarthritis

Multidisciplinary biopsychosocial rehabilitation, which has been used for more than a decade, has been found to improve the health-related quality of life in patients with chronic back pain [1]. A multidisciplinary approach to the problem is now widely accepted as the best method of managing chronic pain, as was demonstrated in recent meta-analyses of low back pain [2,3].

In 2004, a Dead Sea medical clinic, the Deutsches Medizinisches Zentrum (DMZ), implemented a new treatment approach for Norwegian patients with chronic pain who traveled to the clinic in groups. The patients participated in a biopsychosocial program, which included cognitive behavioral therapy (CBT), psycho-education, psychosocial activities, graded exercise therapy, sporting activities, hydrotherapy, and physiotherapy. Following the rules of evidence-based scientific methods, these treatments were combined with the environment provided by the climate at the Dead Sea.

The aim of this study was to evaluate short-term improvements in disease activity in Norwegian patients with chronic pain who simultaneously received Dead Sea Climatotherapy (DSC) and participated in a multidisciplinary biopsychosocial program.

PATIENTS AND METHODS

PATIENTS

In this retrospective study, all files of Norwegian patients presenting with chronic pain who were treated at the DMZ medical center between 2005 and 2016 were retrieved for analysis.

The patients were referred by their personal physician and organized into groups. These groups arrived at the Dead Sea and stayed for 3 weeks of treatment between February and May and between September and December. All participants signed an informed consent document, which permitted the use of their anonymized data. The inclusion criterion was the presence of chronic musculoskeletal pain of any etiology that lasted for at least 6 months. The exclusion criteria included contraindications for DSC, such as unstable heart disease, severe photosensitivity disorder, malignant melanoma, severe kidney failure, unstable epilepsy, serious mental illness, cognitive decline, and drug and alcohol abuse.

We analyzed 938 patient files. Most patients (81.7%) were female. The age of the patients ranged from 15.7 to 92.6 years (mean 63.6 ± 12.92 years). The mean duration of their stay was 20.5 ± 3.05 days, and the number of previous visits to the DMZ clinic ranged from 0 to 13 (mean 1.12 ± 2.05). The body mass

index (BMI) values ranged from 17 to 45 kg/m^2 (mean 27.00 ± 4.83 kg/m^2).

The patient files were classified into the following four main categories according to the diagnoses given by the physicians in Norway:

- Chronic pain syndrome, which included patients with fibromyalgia
- Inflammatory joint diseases, including rheumatoid arthritis and ankylosing spondylitis
- Osteoarthritis
- Other orthopedic diseases

No control group was included in this observational study [Table 1].

SETTING

The Norwegian multidisciplinary treatment team, consisting of a psychiatrist, a psychotherapist, nursing specialists, and a physiotherapist, worked together with the multidisciplinary team at the DMZ. The multidisciplinary team included specialists in internal medicine, rheumatology, and dermatology. The patients were accommodated as regular guests at the Lot Spa Hotel in a quiet and relaxing atmosphere.

PATIENTS AND METHODS

The multimodal cognitive treatment model (MCBT) consisted of psychological interventions, including cognitive and behavioral modifications, psycho-educational, and psychosocial interventions and support. Behavioral therapies included relaxation, breathing and biofeedback techniques, and mindfulness-based stress-reduction and stress-coping strategies. Lectures and small group sessions on health issues were also integrated into the program.

A graduated physical training program and focused psychological interventions were conducted in groups. The participants spent many hours together with the others in their group, mainly outdoors. Over the course of 3 weeks, the program was regularly adjusted to the individual needs of the participants while under the supervision of the multidisciplinary team [4]. The main differences in the treatment programs were related to the number of individual psychological interventions received by each patient. All patients underwent a full DSC program and consulted with a psychiatrist, physiotherapist, or psychologist.

Table 1. The four groups of patients

Variable (unit)	Chronic pain syndrome (n=374)	Osteoarthritis (n=342)	Other orthopedic diseases (n=117)	Inflammatory joint diseases (n=105)
Female gender, %	83.2	80.7	84.6	78.1
Mean age, year	59.95 ± 13.05	69.63 ± 9.11	63.39 ± 13.49	61.24 ± 14.87
Mean body mass index, kg/cm^2	26.77 ± 4.67	27.69 ± 5.08	27.27 ± 5.25	26.00 ± 3.84
Previous visits, %	35.4	46.3	44.4	35.2

OUTCOME PARAMETERS

Objective functional assessment was not used in this study. Nevertheless, the outcomes included the following 10 variables, which were assessed at the time of arrival and at the end of the treatment:

- Objective parameters
  a. Hand grip test measured on both hands (mmHg)
  B. Six-minute walking test (6MWT, meters), measured by the same nurse at the same time of day
- Self-assessed scores for subjective parameters
  a. Sleep disturbances (0–3)
  b. Problems with daily activities and joint disability (0–3)
  c. Pain and disease activity (0–10)
  d. Duration of morning stiffness (minutes)
- Physician assessment of the disease severity on a scale from 0 to 10
- Medication variables. The medications were classified into four main categories: basic medications (disease modifying anti-rheumatic drugs [DMAR]), steroids, non-steroidal anti-inflammatory drugs (NSAIDs), and analgesics
  a. Number of medications
  b. Doses needed
- Number of hours spent under the sun for each day, reported by each patient. This parameter facilitated a more precise control over the climatotherapy protocol [5]

MacNemar tests were used to test the differences between measurements before and after treatment, and chi-square continuity was corrected. ANOVA was used for repeated measurements, while controlling for specific variables (age and BMI). In addition, the correlations between the clinical parameters and sun exposure were tested.

RESULTS

Significant differences were found after treatment in the majority of the variables in all four groups of diseases. All parameters improved but after controlling for age and BMI not all of them showed significance ($P = 0.05$) [Table 2].

Six clinical parameters improved significantly in the inflammatory joint diseases and osteoarthritis groups, five parameters improved significantly in the chronic pain syndrome group, and two parameters improved in the other orthopedic diseases group. Overall, major significant changes occurred in

Table 2. Changes recorded in the 10 clinical parameters and their significance in the four groups

	Chronic pain syndrome			Osteoarthritis			Other orthopedic diseases			Inflammatory joint diseases		
Parameter (range or unit)	N	Change (%)	*P* value	N	Change (%)	*P* value	N	Change (%)	*P* value	N	Change (%)	*P* value
Sleep disturbances (0–3)	305	-42.9	0.001*	305	-41.3	0.006*	91	-40.6	0.185	96	-42.3	0.086
Problems with daily activities (0–3)	305	-44.4	0.029*	305	-41.4	0.002*	91	-43.0	0.117	97	-40.0	0.001*
Patient self-assessment (0–10)	289	46.3	0.637	298	34.8	0.134	90	45.2	0.850	96	38.6	0.001*
Joint disability (0–3)	303	36.3	0.826	304	37.2	0.001*	91	33.8	0.021*	97	32.7	0.007*
Hand grip left (mmHg)	332	10.4	0.009*	313	9.7	0.518	103	8	0.381	101	13.8	0.511
Hand grip right (mmHg)	333	9.7	0.026*	313	9.2	0.361	103	9.7	0534	101	14.3	0.951
Six-minute walk test (meters)	322	2.1	0.493	304	5.0	0.026*	95	5.2	0.946	96	4.0	0.508
Patient self-assessment (0–10)	182	-43.3	0.029*	226	-44.6	0.001*	76	-45.2	0.002*	66	-37.2	0.035*
Morning stiffness (minutes)	175	-60.8	0.936	213	-66.5	0.391	70	-60.7	0.269	66	-58.1	0.043*
Physician disease severity assessment (0–100)*	239	43.9	0.685	255	42.1	0.001*	99	40.8	0.849	70	36.8	0.002*

*$P < 0.05$

the self-assessed scores of pain, joint motility, and daily activities [Table 3].

In all four groups, significant decreases in the use of analgesics and NSAIDs were reported, but similar decreases were not observed for DMARs and steroids (data not shown).

In the chronic pain syndrome, osteoarthritis, and other orthopedic diseases groups, longer sun exposure was linked to better outcomes. The same was not true for the inflammatory joint diseases group [Table 4].

Table 3. Summary of significant changes after Dead Sea climatotherapy in the four groups

Parameter	Chronic pain syndrome	Osteoarthritis	Other orthopedic diseases	Inflammatory joint diseases
Pain self-assessment	$P < 0.05$	$P < 0.01$	$P < 0.01$	$P < 0.05$
Joint disability assessment	not significant	$P < 0.01$	$P < 0.05$	$P < 0.01$
Daily disability assessment	$P < 0.05$	$P < 0.01$	not significant	$P < 0.01$
Physician disease severity assessment	not significant	$P < 0.01$	not significant	$P < 0.01$
Six-minute walk test	not significant	$P < 0.05$	not significant	not significant

Table 4. Correlations between the variables and the intensity of sun exposure (*P* values and significance)

	Chronic pain syndrome		Osteoarthritis		Orthopedic diseases	
	Calculated UVB dose received	Maximum daily sun exposure	Calculated UVB dose received	Maximum daily sun exposure	Calculated UVB dose received	Maximum daily sun exposure
Joint disability assessment	-0.207**	-0.084	-0.143*	-0.181**	-0.254*	-0.045
Physician disease severity assessment	-0.178**	0.026	-0.121	-0.179**	-0.335**	-0.235*

*$P < 0.05$, **$P < 0.01$ (2-tailed)

DISCUSSION

For more than 2 decades, scientists have conducted clinical trials on the effectiveness of spa therapy for various inflammatory and non-inflammatory diseases such as rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, osteoarthritis, and fibromyalgia. In their review on this topic, Moses and colleagues [6] concluded that there was significant improvement in most of the assessed clinical parameters that usually did not last more than a few months. They underlined the lack of complications and the pleasant environment of such a treatment. In our study, the Dead Sea biopsychosocial model resulted in substantial improvement in the short-term outcomes in patients presenting with chronic skeletal diseases, with similar results regarding the clinical parameters evaluated in previous studies on ankylosing spondylitis [7] and osteoarthritis [8].

Such results not only concur with those of previous studies, but might also confirm a substantial advantage of warm climatic conditions for patients with musculoskeletal pain [9]. A recent prospective study demonstrated that 4 weeks of rehabilitation in a warm climate improved health and body function for up to one year in 161 patients with arthritis (63% of whom were treated with biologics) [10]. Moreover, the level of rehabilitation was shown to be better than after the same program administered in Norway. A study of 182 patients with fibromyalgia who were randomized to a rehabilitation program in a warm or cold climate showed improvement of physical function regardless of the climatic setting, but those in the warm climate demonstrated better long-term effects on pain and pain distribution [11].

These two last publications confirm the possible role of warm climate and balneotherapy in the rehabilitation of chronic pain, even if a meta-analysis on rheumatoid arthritis patients who received balneotherapy found only modest benefits [12]. The policy of the National Norway Rehabilitation Regulation Center seems to confirm the superiority of a warm climate for the treatment of chronic pain, as patients are regularly sent to such climatic conditions and report substantial results [13].

INFLAMMATORY JOINT DISEASES

Among the four groups, the inflammatory joint diseases group (n=105) exhibited the most marked results. The duration of morning stiffness decreased substantially in 62.3% of the patients from 51 to 21 minutes (58.1% improvement, $P = 0.043$).

Problems with daily activities and joint disability were similarly reduced (40% and 32.7% improvement, $P = 0.001$ and $P = 0.007$, respectively). In addition, the general assessments and the pain assessments improved by 38.6 and 37.2%, respectively ($P = 0.001$ and 0.035, respectively). The use of pain killers and anti-inflammatory drugs was effectively reduced ($P < 0.001$).

These results correspond with those published previously on balneotherapy at the Dead Sea [14] or in other locations. Inflammatory joint diseases improve in a warm climate, and publications have already reported good outcomes of physiotherapy in stable and warm climates [15].

CHRONIC PAIN SYNDROME

Measurements were available for more than 300 patients included in this cohort (n=374); however, only 185 patients (48.6%) returned the double questionnaire assessing pain. We found a statistically significant difference after therapy of 2.57 points in terms of pain on a 0 to 10 cm visual analogue scale (VAS) ($P = 0.029$), which is higher than in many other publications [16]. Given that the primary efficacy parameter of many studies is often defined as approximately 30% VAS improvement or greater [17], the Dead Sea rehabilitation program seems to be a valuable option, showing an improvement of 43.3%.

Sleep disturbances, self-reported on a scale from 0 to 3, were also improved during the 3 week stay. For 305 patients (81.5%), the mean difference reached 0.78 (from 1.82 to 1.04, 42.9% improvement, $P = 0.001$). A reduction in pain and an increased level of physical activity during the day might be the reasons for this observation. Modest but significant changes after Dead Sea balneotherapy have already been described [18], but the addition of a multidisciplinary rehabilitation program seems to surpass those results.

OSTEOARTHRITIS

This group included 342 patients with knee and/or hip osteoarthritis at a moderate to severe stage. The mean VAS pain assessment was 5.7 points at arrival. In total, 226 patients (66.1%) returned the pain self-assessment questionnaire, with a significant improvement of 44.6% (2.54 points, $P < 0.001$).

The 6MWT [19] showed a modest but significant 5% improvement (470.5 meters, $P = 0.026$). The 6MWT value was only significant in the osteoarthritis group, and it correlated well with the changes in the subjective variables (pain and disability). The disability score recorded on a scale of 0 to 3 showed an improvement of almost 1 point (2.27 to 1.33, 41.4% improvement, $P = 0.002$), confirming the positive changes also found in the other five clinical parameters.

The complexity of a comprehensive rehabilitation program makes it difficult to demonstrate any correlation between improvements and a particular component of the program. Increased serum levels of vitamin D after 3 weeks of climatotherapy were previously found to be associated with an amelioration of chronic musculoskeletal pain and disease severity, leading to some speculation on the mechanism underlying the benefits of DSC [20]. Moreover, the immunosuppressive effect of ultraviolet radiation exposure, largely demonstrated at the Dead Sea, might be one of the reasons leading to improved physical activity. In our study, the exact impact of the biopsychosocial program could not be easily confirmed, and we cannot draw conclusions about its advantages. Similar results were recorded as seen in previous studies. For example, the overall VAS pain score for osteoarthritis patients was 2.54 points in our study compared to 2.38 in a previous study. It is possible that a long-term evaluation could show some differences in the positive outcomes reported. Finally, our patients reported that the main factor for the improvement was the hot, stable and dry climatic conditions present throughout the program.

STUDY LIMITATIONS

The lack of randomization and controls might be seen as major drawbacks when interpreting the results. Difficulties in conducting a double-blind study in our specific setting led us to carefully consider retrospective data and draw some conclusions. In this study, the large number of patients in each group, as well as the strict statistical analysis, suggests that this program has a substantial positive effect on patient health.

CONCLUSIONS

A multidisciplinary biopsychosocial program combined with DSC induced positive changes in patients with chronic musculoskeletal pain. The findings, which were recorded in nearly 1000 patients, should promote more interest in this method of treatment. Used as a complementary treatment to medical and surgical treatments, this combination therapy might lead to significant improvements in many chronic patients. Further well-designed long-term studies are warranted to confirm these findings.

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References

1. Lang E, Liebig K, Kastner S, Neundörfer B, Heuschmann P. Multidisciplinary rehabilitation versus usual care for chronic low back pain in the community: effects on quality of life. *Spine J* 2003; 3 (4): 270-6.
2. Kamper SJ, Apeldoorn AT, Chiarotto A, et al. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. *Cochrane Database Syst Rev* 2014; (9): CD000963.
3. Kamper SJ, Apeldoorn AT, Chiarotto A, et al. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain: Cochrane systematic review and meta-analysis. *BMJ* 2015; 350: h444.
4. Harari M, Dramsdahl E. Multidisiplinær behandling og rehabilitering ved Dødehavet. Indremedisineren (Multidisciplinary treatment and rehabilitation at the Dead Sea). *Internal Medicine* 2011, 2: 39-41. [Norwegian].
5. Kudish AI, Harari M, Evseev EG. The measurement and analysis of normal incidence solar UVB radiation and its application to the photoclimatherapy protocol for psoriasis at the Dead Sea, Israel. *Photochem Photobiol* 2011; 87 (1): 215-22.
6. Moses SW, David M, Goldhammer E, Tal A, Sukenik S. The Dead Sea, a unique natural health resort. *IMAJ* 2006; 8: 483-8.
7. Codish S, Dobrovinsky S, Abu Shakra M, Flusser D, Sukenik S. Spa therapy for ankylosing spondylitis at the Dead Sea. *IMAJ* 2005; 7: 443-6.
8. Sherman G, Zeller L, Avriel A, Friger M, Harari M, Sukenik S. Intermittent balneotherapy at the Dead Sea area for patients with knee osteoarthritis. *IMAJ* 2005; 11: 88-93.
9. Staalesen Strumse YA, Nordvag BY, Stanghelle JK, et al. The efficacy of rehabilitation for patients with rheumatoid arthritis: comparison between a 4-week rehabilitation programme in a warm and cold climate. *Scand J Rheumatol* 2009; 38 (1): 28-37.
10. Ajeganova S, Wörnert M, Hafström I. A four-week team-rehabilitation programme in a warm climate decreases disability and improves health and body function for up to one year: a prospective study in Swedish patients with inflammatory joint diseases. *J Rehabil Med* 2016; 48 (8): 711-18.
11. Clarke-Jenssen AC, Mengshoel AM, Strumse YS, Forseth KO. Effect of a fibromyalgia rehabilitation programme in warm versus cold climate: a randomized controlled study. *J Rehabil Med* 2014; 46 (7): 676-83.
12. Verhagen AP, Bierma-Zeinstra SM, Boers M, et al. Balneotherapy (or spa therapy) for rheumatoid arthritis. An abridged version of Cochrane Systematic Review. *Eur J Phys Rehabil Med* 2015; 51 (6): 833-47.
13. Oslo University Hospital. Treatment packages. [Available from https://oslo-universitetssykehus.no/avdelinger/direktorens-stab/stab-fag-pasientsikkerhet-og-samhandling/avdeling-for-samhandling/behandlingsreiser]. [Accessed September 2018]. [Norwegian].
14. Sukenik S. Balneotherapy for rheumatic diseases at the Dead Sea. *Int J Dermatol* 1998; 37 (9): 717-8.
15. Hafström I, Hallengren M. Physiotherapy in subtropic climate improves functional capacity and health-related quality of life in Swedish patients with rheumatoid arthritis and spondylarthropathies still after 6 months. *Scand J Rheumatol* 2003; 32 (2): 108-13.
16. Yong WC, Sanguankeo A, Upala S. Effect of vitamin D supplementation in chronic widespread pain: a systematic review and meta-analysis. *Clin Rheumatol* 2017; 36 (12): 2825-33.
17. Derry S, Cording M, Wiffen PJ, Law S, Phillips T, Moore RA. Pregabalin for pain in fibromyalgia in adults. *Cochrane Database Syst Rev* 2016; 9: CD011790.
18. Buskila D, Abu-Shakra M, Neumann L, et al. Balneotherapy for fibromyalgia at the Dead Sea. *Rheumatol Int* 2001; 20 (3): 105-8.
19. Zeni J Jr, Pozzi F, Abujaber S, Miller L. Relationship between physical impairments and movement patterns during gait in patients with end-stage hip osteoarthritis. *J Orthop Res* 2015; 33 (3): 382-9.
20. Harari M, Dramsdahl E, Shany S, et al. Increased vitamin D serum levels correlate with clinical improvement of rheumatic diseases after Dead Sea climatotherapy. *IMAJ* 2011; 13: 212-15.

Capsule

Stressed gut epithelium gets some relief

Immunoglobulin A (IgA) is the most abundantly expressed antibody isotype and can be found at various mucosal surfaces in the body, including the gastrointestinal (GI) tract. IgA is polyreactive and can coat and restrain both commensal bacteria and enteric pathogens. **Grootjans** et al. found that endoplasmic reticulum (ER) stress in the intestinal epithelial cells of mice induced the T cell- and microbiota-independent expansion of peritoneal B1b cells, which secrete IgA. Similarly, human subjects homozygous for a variant of an autophagy gene (*ATG16L1*) known to cause ER stress showed increased numbers of GI IgA+ cells compared with controls. Thus, epithelial ER stress serves as an advantageous "eustress" response that can functionally antagonize its well-characterized role in promoting inflammation.

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Eitan Israeli

Capsule

Bacterial warhead targets DNA

The bacterial toxin colibactin causes double-stranded DNA breaks and is associated with the occurrence of bacterially induced colorectal cancer in humans. However, isolation of colibactin is difficult, and its mode of action is poorly understood. **Wilson** et al. studied *Escherichia coli* that contain the biosynthetic gene island called *pks*, which is associated with colibactin production. They identified the DNA adducts that resulted from incubating *pks+ E. coli* in human cells. To overcome the lack of colibactin for direct analysis, mimics of the *pks* product were synthesized. From the resulting synthetic adenine-colibactin adducts, it became evident that alkylation via a cyclopropane "warhead" breaks the DNA strands. Similar DNA adducts were then identified in the gut epithelia of mice infected with *pks+ E. coli*.

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