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Research article

Balneotherapy and health-related quality of life in individuals with Rheumatoid arthritis: An observational study under real clinical practice conditions

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Abstract: Introduction: To analyze the influence of balneotherapy applied under real clinical practice conditions on the quality of life and functionality of patients diagnosed with rheumatoid arthritis. Methods: Prospective, observational study conducted with a group of patients under real clinical practice conditions, with a 6-month follow-up. The participants were beneficiaries of the social thermalism programme of the Spanish Ministry of Health, Consumption and Social Well-being, aged 60-80 years and diagnosed with rheumatoid arthritis, who were treated at Fitero's Spa (Spain). The study excluded those individuals who had undergone another balneotherapeutic treatment in the previous 6 months, and those who had scheduled one in the following 6 months. Ten treatment sessions were applied. Each session included a bath and one or two additional techniques, which varied in each case, depending on the characteristics and preferences of the patient. The variables were gathered before initiating the treatment, and at 1, 3 and 6-months post-treatment. Results: The study included 49 individuals with an average age of 71.0 (SD 4.79) years. The variable "current health state" of EuroQol 5D-5L increased by 6.73 [-13.44 to -2.53] points and 6.26 [-12.07 to -0.46] in the first and third month, respectively. Pain was the dimension in which the largest number of participants reduced the level of their response in all the follow-up periods. Functionality showed an improvement of 0.196 [0.060 to 0.332] in the third month. Conclusions: The beneficial effects of balneotherapy on the health-related quality of life and functionality in individuals with rheumatoid arthritis can be positive..

Keywords: Balneotherapy, rheumatoid arthritis, quality of life, functionality.

1. Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease with inflammation of the peripheral joints influenced by both genetic and environmental factors [1]. RA affects 0.5%-1% of adults, it is more common in women and may occur at any age [1]. In European countries, the prevalence of this pathology has been established, with 0.5% of the Spanish population being affected by it (95% CI: 0.3 to 0.9) [1,2].

RA can affect all areas of quality of life, including work, family and leisure activities, as well as physical and mental health [2-6]. Thus, the quality of life of RA patients is reduced. To increase it, different pharmacological and non-pharmacological treatments are used. In this regard, multi-component or single exercises, physical activity interventions, balneotherapy, hydrotherapy involving resistance, strength, stretching and aerobic exercises

are effective strategies to reduce pain, functional disability, fatigue and the global impact of the disease in people with RA [2,7]. Balneotherapy or spa therapy is a multifaceted treatment that uses mineral water taken directly from a natural source and delivered rapidly to the point of use. Delivery is via diverse modalities of showers, baths, pools and mists. The water can be mixed with various types of clay, which is then applied to the skin as peloids or cataplasms. [8].

Within chronic diseases such as RA, the active participation of the patients is very important, as well as knowing their own perspectives about the intervention and the results reported by them on the variables measured (pain, physical function, limitation in daily activities..., etc.) in order to adjust the treatment to their needs and plan it within the actual clinical practice [9].

Clinical trials show great heterogeneity in the application of balneotherapy at the level of water conditions, number of sessions (2 weeks, 4 weeks, 8 weeks…), etc. [2,10,11]; however, homogeneity is seen in the measured variables, e.g., pain and quality of life [11]. Moreover, the results show clinical improvements, although it must be considered that clinical trials have been carried out in a controlled environment in which the patients had a similar history and received the same dose of prescribed treatment [2,11]. On the other hand, real clinical practice does not share these criteria, since there are patients with different medical histories, with specific needs, and that is why it is necessary to study what are the real results of the application of balneotherapy in an uncontrolled environment, aimed at patients within real clinical practice [12-14]. Thus, the main objective of this study was to analyse the influence of balneotherapy applied under real clinical practice conditions on the quality of life and functionality in patients diagnosed with RA.

Methods

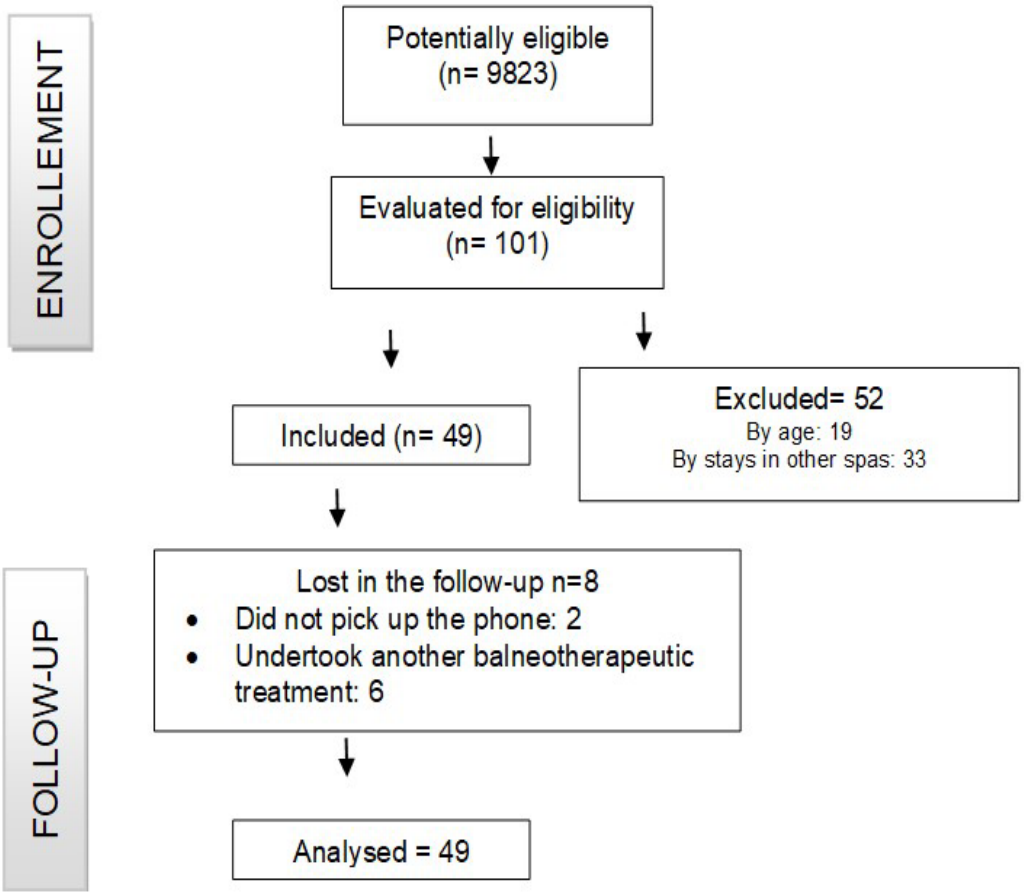
Study Design

This is a prospective, observational, single-group study conducted under real clinical practice conditions at Fitero's Spa (Navarra, Spain), with a 6–month follow-up. The study was registered in Clinical Trials.gov (NCT03952897). It was approved by the Clinical Research Committee of the Toledo Hospital (Reg. 14-07-2017) and complies with the principles of the Declaration of Helsinki, the rules of Good Clinical Practice (GCP) and the legal requirements established for this type of studies.

Participants

The sample was constituted by beneficiaries of the social thermalism programme of the Spanish Ministry of Health, Consumption and Social Well-being, who were treated at Fitero's Spa in the periods of August-November 2017 and February-June 2018.

The study included men and women aged 60-80 years, diagnosed with rheumatoid arthritis in their place of residence by their rheumatologist doctor, and with capacity to complete questionnaires and provide an informed consent. The study excluded the individuals who had undertaken a balneotherapy treatment within 6 months prior to the intervention, and those who were planning to do it within the following 6 months.



Procedures

The study was carried out at Fitero's Spa, whose water is hyperthermal, highly mineralised, chlorinated-sulfated-sodic-calcic and radioactive [15] (Table 1).

The participants were recruited in the doctor's office of Fitero's Spa, after the physician prescribed the balneotherapeutic treatment. In all cases, they were asked to participate in the study and to sign an informed consent.

The balneotherapeutic treatment was established following the real clinical practice, thus the physician of the spa prescribed an individualised treatment, attending to the clinical situation and preferences of the patient. The number of therapeutic sessions was 10 in all cases, as is established by the Spanish social thermalism programme. Each session included a bath at 38ºC for 15 minutes, and another two techniques, which varied between circular shower (15 min at 38˚C), stream (10 min at 40-42 ˚C), footbath (15 min at 38º C), mobilisation in the swimming pool (20 min at 32-34˚C), and steam room (15 min at 45˚C and 100% humidity). In all cases, the individuals continued their usual pharmacological treatment.

The data were gathered through personal interview before initiating the intervention (A0), and through phone call at 1 month (A1), 3 months (A3) and 6 months (A6) after the end of the intervention. In all cases, the same member of the research team was in charge of conducting the evaluations. Moreover, when the stay at the spa finished, the completion of the prescribed treatment was verified, as well as any possible incidents.

Table 1. Physical and chemical characteristics of the mineral water of Fitero's Spa (Spain).

Temperature (˚C)			46.2
Conductivity at 25˚C (µS cm^{-1})			7200
pH			6.3
Residual dry matter at 180˚C (mg/L)			4915
ANIONS			
	mg/L	mEq/L	% meq
Cl^-	1481.6	41.797	58.17
F^-	1.0	0.052	0.07
HCO_3^-	109.8	1.800	2.50
CO_3^{2-}	0.0	0.0	0.0
NO_3^-	0.0	0.0	0.0
SH^-	0.0	0.0	0.0
SO_4^{2-}	1355.0	28.211	39.26
CATIONS			
	mg/L	mEq/L	% mEq
Na^+	955.0	41.544	58.27
K^+	31.8	0.825	1.16
Li^+	0.3	0.046	0.06
Ca^{2+}	432.7	21.593	30.29
Mg^{2+}	88.5	7.281	10.21
Sr^{2+}	0.0	0.0	0.0
Fe total	0.2	0.008	0.01
DILUTE GASES			
CO_2 (mg/L)			24.8
SH_2 (mg/L)			0.0
Rn^{222} (Bq/L)			100

Outcome measures

The main outcome variables were health-related quality of life (HRQoL), obtained through the EuroQol 5D-5L questionnaire [16], and functionality, assessed through the Health Assessment Questionnaire (HAQ) [17]. Both questionnaires had been previously validated in Spanish to be administered through interview and phone call or self-administered.

The EuroQol 5D-5L is an instrument used to evaluate HRQoL in general populations. It assesses 5 dimensions of HRQoL: mobility, self-care, the capacity to perform activities of daily living, pain/discomfort, and anxiety/depression. The score of each item has 5 response levels, from 1 (absence of problems) to 5 (presence of extreme problems). The answers to these dimensions provide a state of health from which the EuroQol index is calculated, whose values range between 0 and 1, with 0 being the worst possible result.
Furthermore, the perception of the participants toward their own health state upon completion of the questionnaire was evaluated using the EQ-5D visual analogue scale (EQ-5D-VAS), whose score ranges from 0 to 100, with 0 being the worst possible state and 100 the best. The estimated minimal important differences of the EuroQol index is 0.15 [18].

The Health Assessment Questionnaire (HAQ) has been designed for adults with rheumatoid arthritis and other musculoskeletal diseases, and it evaluates the difficulties of the individual to perform 20 activities of daily living, grouped in 8 areas: dressing and grooming, getting up, eating, walking, personal hygiene, reaching objects, pressure and other activities.
Each item is given a score between 0 and 3 according to the following scale: 0 = no difficulty, 1 = some difficulty, 2 = great difficulty, 3 = incapable. Moreover, it also has several corrective questions. The final score ranged between 0 (no incapability) and 3 (maximum incapability). The minimum relevant difference estimated was 0.250 [19].

Furthermore, sociodemographic and clinical variables were recorded, as well as variables related to the balneotherapeutic treatment. In the follow-up assessments, the participants were also asked about variations in their pharmacological treatment, the appearance of new diseases, accidents or hospitalisations and possible surgical interventions.

Statistical Analysis
To minimise the possible bias from loss of patients in the follow-up, we performed an intention-to-treat analysis, giving the worse value obtained in each measurement to the participants that abandoned the follow-up.
The continuous variables were described using the mean and standard deviation, after verifying that they had a normal distribution, according to the Kolmogorov-Smirnov test. The dichotomous or polychotomous variables were described by their percentage with respect to the group.
The variations in the scores of VAS-EQ, EQ Index and HAQ along time were evaluated through ANOVA of repeated measures, using the Bonferroni correction for multiple comparisons. The results are presented as mean difference, confidence interval and p-value.
The changes in the level of response in the five dimensions of the EQ-5D-5L throughout the study were conducted with Wilcoxon's signed-rank test.

All those values with p-value <0.05 were considered statistically significant. The statistical analysis of the data was performed using IBM® SPSS® Statistics 23 software.

RESULTS
Of the 9,823 potentially eligible participants, a total of 49 were finally included. Initially, 101 individuals had been diagnosed with rheumatoid arthritis, of whom 52 were excluded for not meeting the inclusion criteria. A total of 8 participants were lost in the follow-up: 4 in the third month and the other 4 in the sixth month.

All individuals included in the study completed the intervention.

Baseline characteristics
The baseline characteristics of the 49 participants of this study are shown in Table 2.

Table 2: Baseline characteristics of the individuals included in the study.

VARIABLES	Total (n=49)
Age, mean (SD)	71.0 (4.79)
Sex, n (%)	Men: 12 (24.5%) Women: 37(75.5%)
Marital status, n (%)	Single: 0 Married: 42 (85.7) Widow: 6 (12.2) Divorced: 1(2.0)
Employment situation, n (%)	Retired: 47 (95.5) Unemployed: 2 (4.1)
Social class, n (%)	II- 3 (6.1) III- 8 (16.3) IV- 9 (18.4) V- 8 (16.3) VI- 14 (28.6) Missing data: 7 (14.3)
Education level, n (%)	Primary incomplete: 6 (12.2) Primary complete: 23 (46.9) Secondary first stage: 5 (10.2) A level/VT: 9 (18.4) University degree: 4 (8.2) Missing data: 2 (4.1)
BMI (Kg/m^2), mean (SD)	27.65 (5.14)
RA diagnosis date, (years) n (%)	< 5: 10 (20.4) >5: 38 (77.6) Missing data: 1 (2.0)
Pharmacological treatment of RA, n (%)	Yes: 49 (100%) No: 0 (0%)

The average age of the participants was 71.0 (SD 4.79) years, and 37 (75.5%) of them were women. "Married" was the predominating marital status (85.7%), and almost all participants were retired (95.5%). A total of 46.9% had primary education studies, and the predominating social class was VI, i.e., unqualified worker (28.6%). The average BMI was 27.65 (5.14). In 77.6% of cases, the diagnosis of rheumatoid arthritis had been established over 5 years before the intervention and all participants followed some type of pharmacological treatment for the disease.

All participants completed the balneotherapeutic treatment, reporting no adverse effects.

Analysis of HRQoL and functionality

The scores obtained in the variable "current health state" of EuroQol 5D-5L increased by 6.73 points in the first month and by 6.26 points in the third month. The EuroQol index decreased by 0.121 and 0.098 points in the first and third months, respectively. In all cases, the differences were statistically significant (Table 3).

Table 3: Comparison of the results of the VAS-EuroQol EQ Index and HAQ.

	A0	**A0-A1**	**A0-A3**	**A0-A**
	Mean	**Mean dif. [CI95%]**	**Mean dif. [CI95%]**	**Mean dif. [**
	(SD)	**p**	**p**	**p**
EQ-VAS	63.26	-6.73 [-13.44 to -2.53]	-6.26[-12.07 to -0.46]	1.22[-6.79
	(14.98)	0.049	0.026	1.00
EQ-Index	0.660	-0.121 [-1.94 to -	-0.098 [-0.180 to -0.017]	-0.015 [-0.118
	(0.214)	0.047]	0.008	1.00
		0.000		
HAQ	0.964	0.151 [0.0084 to	0.196 [0.060 to 0.332]	0.086 [-0.105
	(0.644)	0.293]	0.005	0.36
		0.38		

Statistical significance when p value is < 0.05; EQ-VAS: EuroQol *Visual Analogue Scale; EQ-Index:* EuroQol index *value; HAQ: Health Assessment Questionnaire; SD: standard deviation; Mean dif.: mean difference;* A_0*: baseline assessment;* A_1*: assessment at 1 month;* A_3*: assessment at 3 months;* A_6*: assessment at 6 months.*

The responses obtained in the 5 dimensions of EQ-5D-5L are gathered in Table 4. After analysing the number of individuals who modified their answers in the 5 dimensions throughout the follow-up, it was found that pain was the dimension in which the largest number of participants reduced their level in all the follow-up periods, with a statistically significant variation. The same was observed for activities of daily living and anxiety/depression, although, in these cases, statistical significance was only maintained up to the third month (Table 5). The number of individuals who increased their response level throughout the study was not statistically significant in any dimension.

Regarding functionality, the mean scores obtained in the HAQ decreased in all the follow-up periods, although statistical significance was only reached at 3 months after the end of the balneotherapeutic treatment (Table 3).

The pharmacological treatment remained stable throughout the study, except for 2 participants, for whom methotrexate was suspended, and another 2 participants, for whom the dose of corticoids was increased. Regarding surgical interventions, one participant underwent meniscectomy in the right knee, and another participant underwent infiltration, also in the knee. In the rest of the cases, there were no variations in terms of new diseases, hospital admissions, accidents or emergencies that could have influenced the HRQoL.

Table 4: Responses by dimensions of the EuroQol 5D-5L questionnaire.

	Level	A0	A1	A3	A6
MOBILITY n (%)	**1**	17(34.7%)	22(44.9%)	20(40.8%)	14(28.6%)
	2	15(30.6%)	17(34.7%)	17(34.7%)	19(38.8%)
	3	14(28y.6%)	9(18.4%)	6(12.2%)	7(14.3%)
	4	3(6.1%)	1(2.0%)	2(4.1%)	1(2.0%)
	5	-	-	-	-
	Total	49(100%)	49(100%)	45(91.8%)	41(83.7%)
	Missing	-		4(8.2%)	8(16.3%)
SELF-CARE n (%)	**1**	30(61.2%)	39(79.6%)	33(67.3%)	29(59.2%)
	2	12(24.5%)	4(8.2%)	8(16.3%)	10(20.4%)
	3	5(10.2%)	4(8.2%)	4(8.2%)	1(2.0%)
	4	2(4.1%)	2(4.1%)	0	1(2.0%)
	5	-	-	-	-
	Total	49(100%)	49(100%)	45(91.8%)	41(83.7%)
	Missing	0	0	4(8.2%)	8(16.3%)
ACTIVITIES OF DAILY LIVING n (%)	**1**	18(36.7%)	28(57.1%)	27(55.1%)	20(40.8%)
	2	17(34.7%)	13(26.5%)	13(26.5%)	12(24.5%)
	3	12(24.5%)	6(12.2%)	4(8.2%)	8(16.3%)
	4	2(4.1%)	2(4.1%)	1(2.0%)	0
	5	-	-	-	1(2.0%)
	Total	49(100%)	49(100%)	45(91.8%)	41(83.7%)
	Missing	0	0	4(8.2%)	8(16.3%)
PAIN n (%)	**1**	2(4.1%)	12(24.5%)	9(18.4%)	7(14.3%)
	2	15(30.6%)	20(40.8%)	21(42.9%)	18(36.7%)
	3	19(38.8%)	12(24.5%)	11(22.4%)	11(22.4%)
	4	13(26.5%)	5(10.2%)	4(8.2%)	5(10.2%)
	5	-	-	-	-
	Total	49(100%)	49(100%)	45(91.8%)	41(83.7%)
	Missing	0	0	4(8.2%)	8(16.3%)
ANXIETY/ DEPRESSION n (%)	**1**	29(59.2%)	40(81.6%)	38(77.6%)	29(59.2%)
	2	12(24.5%)	7(14.3%)	5(10.2%)	6(12.2%)
	3	5(10.2%)	2(4.1%)	1(2.0%)	5(10.2%)
	4	-	-	-	-
	5	3(6.1%)	-	1(2.0%)	1(2.0%)
	Total	49(100%)	49(100%)	45(91.8%)	41(83.7%)
	Missing	0	0	4(8.2%)	8(16.3%)

A_0: baseline assessment; A_1: assessment at 1 month; A_3: assessment at 3 months; A_6: assessment at 6 months.

Table 5: Number of individuals who modified their response level in the EQ-5D-5L throughout the follow-up.

DIMENSIONS of the EQ-5D-5L		A1	A3	A6
MOBILITY (n)	Improved‡	19*	13	16
	Worsened‡	9	9	13
	Unaltered‡	21	27	20
SELF-CARE (n)	Improved	12	9	11
	Worsened	4	5	10
	Unaltered	33	35	28
ACTIVITIES OF DAILY LIVING (n)	Improved	17*	18*	10
	Worsened	5	3	12
	Unaltered	27	28	27
PAIN (n)	Improved	24*	29*	21*
	Worsened	2	7	7
	Unaltered	23	13	21
ANXIETY/ DEPRESSION (n)	Improved	18*	15*	12
	Worsened	3	2	8
	Unaltered	28	32	29

*$p < 0.05$; *A_1: assessment at 1 month; A_3: assessment at 3 months; A_6: assessment at 6 months.*

‡*Improved: participants who gave a lower response level with respect to the baseline level in each dimension and during the follow-up.*

‡*Worsened: participants who gave a higher response level with respect to the baseline level in each dimension and during the follow-up.*

‡*Unaltered: participants who gave a response level equal to the baseline level in each dimension and during the follow-up.*

DISCUSSION

This study presents the results of HRQoL and functionality after carrying out a balneotherapeutic treatment under real clinical practice conditions in individuals with rheumatoid arthritis. With a statistical power of over 80%, our results showed that both HRQoL and functionality improved after the balneotherapeutic treatment, and the improvement was maintained for 3 months.

Patient-reported outcomes (PROs) are currently considered as important as other physical or biochemical results for the evaluation of the state of diseases or the results of interventions, including pain and physical function [20]. In our case, pain was the dimension with the largest number of individuals who reported improvement even up to 6 months after the end of the intervention, followed by the state of anxiety/depression and the capacity to perform activities of daily living. Therefore, these could be the dimensions with the greatest influence on the improvement of QoL, which can be correlated with the improvement in functionality [21].

No adverse effect was reported during the application of the balneotherapeutic treatment or during the follow-up period, thus it can be considered that balneotherapy is a safe treatment for patients with rheumatoid arthritis.

The characteristics of the Spanish social thermalism programme have conditioned the sociodemographic profile of the sample, since this programme is aimed at retired, independent people. Thus, the age and number of retired individuals in this study are higher than those reported in other studies that use balneotherapy [22-24]. However, the HRQoL and functionality at the beginning of the study were similar to those of other studies for individuals with this pathology [25-29]. Nevertheless, our sample presented better functionality at the beginning of the study with respect to that found in RCTs that used balneotherapy [22,23,30]. This could be due to the fact that the samples of RCTs are selected according to closed criteria, which do not always correspond to the characteristics in the context of real clinical practice. In fact, the baseline values of HAQ found in this study are

similar to those reported in another study conducted under real clinical practice conditions with balneotherapy [30].

The effect size observed in both the quality of life and functionality was statistically significant, although it did not reach the minimum relevant clinical difference, which has been reached in RCTs [23,24]. This could be due to the fact that the number of sessions of balneotherapy applied in these studies was larger with respect to our study. The only study found in the literature to use balneotherapy under real clinical practice conditions in individuals with rheumatoid arthritis [30] reported a difference of 0.21 in HAQ, which was not statistically significant, probably due to the small sample size. This could indicate that the effect of balneotherapy under real clinical practice conditions is slightly better than that observed in RCTs.

The losses in the follow-up are one of the limitations of this study. To control this bias, an intention-to-treat analysis was performed, applying the worst possible score in each case to the missing data. Moreover, due to the lack of a control group, it is not possible to know the real effect size.

CONCLUSIONS

The beneficial effects of balneotherapy on health-related quality of life and functionality in individuals with rheumatoid arthritis can be positive, although the effect size seems to be slightly lower than that found in RCTs.

Balneotherapy seems to be a safe practice in individuals with rheumatoid arthritis and it would be of interest to carry out studies that determine the most effective guideline of balneotherapy in individuals with this pathology.

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