

## Clinical effects of mud-bath therapy and oral glucosamine sulfate after 6 months of discontinuation in patients with knee osteoarthritis: results from a randomised, controlled, crossover study

Sirs,

Osteoarthritis (OA) represents the most prevalent form of chronic articular disease, leading progressively to severe physical impairment, disability and reduced quality of life in middle-age and elderly, people (1). Among OA pharmacological therapies, glucosamine crystalline sulfate (GlcN-S) has shown efficacy in the improvement of OA-related pain and functional impairment (4). Recent data show mud packs application as a therapeutic option able in improving function, perceived pain and quality of life in knee OA patients (5-7).

In a previous randomised, controlled, crossover study we reported that combined treatment providing mud-bath therapy and glucosamine crystalline sulfate (GlcN-S) has a positive and safe role in improving pain, function and quality of life in knee OA after six months (7).

The present study is an extension of the previously reported investigation on knee OA treatment (7).

At the end of this phase, all OA patients discontinued any treatment and we observed them after 6 months (T12), during which patients did not use any treatment for OA.

At T12 visit, for each patient, we collected data including personal history, physical examination with recording of measures of OA severity and activity: knee circumferential measurements, active knee extension range of motion (ROM) and active knee flexion ROM. Pain intensity, OA severity and activity were also evaluated by the use of the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index, Lequesne algo-functional Index, and visual analogue scale (VAS). The Health Assessment Questionnaire (HAQ) was used for the evaluation of functional status and the 28-item General Health Questionnaire for the evaluation of somatic symptoms (GHQ-28).

The study protocol was approved by the ethics committee of local health unit (Naples, Italy) (protocol number: 12/CE). All patients signed and approved the informed consent.

When comparing data obtained at T12 with basal examination (T0), we observed for all the study variables in the entire cohort of patients the persistence of the statistically significant improvement obtained by the initial 6 months of treatment (T0-T6) (Table I).

**Table I.** Indices of osteoarthritis activity, pain intensity, osteoarthritis severity, quality of life, psychosocial status at baseline (T0), at 6-month (T6) and at twelve-month (T12) visit of patients included in the study.

	T0	T6	T12	p*
Active knee flexion ROM (grade)	125.47 ± 22.08	137.64 ± 16.58	138.73 ± 15.47	0.001
Active knee extension ROM (grade)	3.49 ± 2.21	5.64 ± 1.86	5.22 ± 1.95	0.0002
Knee circumferential measurement (cm)	41.49 ± 6.77	38.43 ± 5.96	38.08 ± 5.96	0.013
WOMAC OA index	33.55 ± 22.08	18.50 ± 16.73	14.40 ± 11.56	0.0001
LEQUESNE algo functional index	11.24 ± 4.85	6.50 ± 4.57	6.42 ± 4.32	0.0001
VAS	42.22 ± 21.98	25.42 ± 19.85	21.89 ± 14.23	0.0001
HAQ	0.76 ± 0.61	0.54 ± 0.34	0.30 ± 0.33	0.0001
GHQ28	1.94 ± 0.48	1.57 ± 0.52	1.64 ± 0.49	0.005

ROM: range of motion; WOMAC: Western Ontario and McMaster Universities; VAS: visual analogue scales; HAQ: Health Assessment Questionnaire; GHQ-28: 28-item General Health Questionnaire.

\*p-value in the Comparison between values at T0 and T12.

When analysing separately data in the two groups of the study, no differences were found in the comparison between them at each study time.

In a recent randomised, controlled, crossover study we have reported that combined treatment providing mud-bath therapy and GlcN-S has a positive and safe role in improving pain, function and quality of life in mild/ moderate knee OA (7).

Aim of the present study has been to evaluate the persistence of this improvement after 6 months of discontinuation of all treatments for OA.

Results of the present extension study report that mud-bath therapy and oral GlcNS after 6 months of their discontinuation in patients with knee OA show sustained clinical efficacy.

In particular, when comparing basal (T0) data with results obtained at T12, for all the considered values, patients maintained the statistically significant improvement after the 6 months of treatment.

Data derived from this extended period of observation following a previous RCT suggest that the association of GlcN and mud-bath therapy has a positive role in maintaining stable improvement of pain, function and quality of life in knee OA patients.

In conclusion, the association of GlcN-S and mud-bath therapy after 6 months of their discontinuation in patients with knee OA show sustained clinical efficacy.

This beneficial effect could be related to the peculiar physicochemical properties of Ischia natural mineral water and mud. These could represent an important therapeutic opportunity for OA patients, in combination with GlcN-S, and should be taken into account in further studies.

F. CASO<sup>1\*</sup>, MD, PhD

L. COSTA<sup>1\*</sup>, MD, PhD, Assist. Prof.

A. DEL PUENTE<sup>1</sup>, MD, PhD, Assist. Prof.

D. SORBO<sup>2</sup>, MD

U. BALESTRIERI<sup>3</sup>, MD

R. PELUSO<sup>1</sup>, MD, PhD, Assist. Prof.

R. SCARPA<sup>1</sup>, MD, Assoc. Prof.

<sup>1</sup>Rheumatology Unit, Department of Clinical Medicine and Surgery, University Federico II, Naples, Italy;

<sup>2</sup>Orthopaedic Unit, Rizzoli Hospital, Ischia, Italy; <sup>3</sup>Julio Jasolino Thermal Study Centre, Ischia, Italy.

\*F. Caso and L. Costa contributed equally to this article.

Address correspondence to:

Raffaele Scarpa, MD,  
Rheumatology Unit, Department of Clinical Medicine and Surgery, University Federico II, via S. Pansini 5, 80131 Naples, Italy.  
E-mail: rscarpa@unina.it

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