

# Mud-bath therapy regulates the expression levels of microRNA in osteoarthritis. Epigenetic contribution to explain the mechanism of action of Balneotherapy

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MicroRNAs (miRNAs) play an important role in the pathogenesis of osteoarthritis (OA); they have been detected in human plasma and in synovial fluid and are considered as potential diagnostic biomarkers and therapeutic targets of OA.

Balneotherapy is a common non-pharmacological treatment for OA patients, with a beneficial effect on pain, function and quality of life and a favourable economic profile.

**Purpose:** The aim of our study was to evaluate the whole-blood levels of miR-155, miR-223, miR-181a, miR-146a and miR-let-7e in patients with bilateral knee OA after a cycle of mud-bath therapy (MBT).

**Methods:** Thirty-two patients with knee OA defined by the ACR criteria were included. Twenty-one patients (MBT Group) were daily treated with a combination of local mud-packs at 42°C and baths in mineral water, at 37°C for 15 minutes, for 12 applications over a period of 2 weeks, in addition to standard therapy; eleven patients (Control Group) continued their conventional treatment alone.

Global pain score was evaluated by Visual Analog Scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) subscores and miRNA expression were evaluated at baseline and after 2 weeks. Peripheral whole-blood was collected into PAXgene™ Blood RNA tubes, stored at -80°C and total RNA was extracted. The expression of miR-155, miR-223, miR-181a, miR-146a and miR-let-7e was determined by qRT-PCR.

**Results:** A statistically significant improvement of clinical parameters and a significant decrease of miR-155, miR-181a, miR-146a ( $p < 0.001$ ) and miR-223 ( $p < 0.01$ ) expression levels were observed after MBT. No clinical and biochemical modifications were detected in the Control Group. No significant variations of miR-let-7e were shown in both studied groups after 2 weeks.

**Conclusions:** Our data showed that MBT can modify the expression of miR-155, miR-181a, miR-146a and miR-223, that are up-regulated in OA. It could be due to the heat stress and the hydrostatic pressure, since some miRNAs were found to be temperature and mechano-responsive.

However, further studies are needed to better explain the mechanism of action of MBT and the role of miRNAs in OA.