BOLETIN LATINOAMERICANO Y DEL CARIBE DE PLANTAS MEDICINALES Y AROMÁTICAS
© / ISSN 0717 7917 / www.blacpma.ms-editions.cl

Articulo Original / Original Article

# Anti-inflammatory effects of hydrotherapy and aromatherapy in patients suffered from myocardial infarction: a pilot study from Montenegro

[Efectos antiinflamatorios de la hidroterapia y la aromaterapia en pacientes que sufrieron infarto de miocardio: Un estudio piloto de Montenegro]

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Received: 5 September 2024
Accepted: 30 November 2024
Accepted corrected: 11 December 2024
Published: 30 May 2025

**Citation:**
Pantovic S, Roganovic M, Zvizdojevic J. Anti-inflammatory effects of hydrotherapy and aromatherapy in patients suffered from myocardial infarction: a pilot study from Montenegro
**Bol Latinoam Caribe Plant Med Aromat**
24 (3): 423 - 431 (2025)
https://doi.org/10.37360/blacpma.25.24.3.31

**Abstract:** Effects of hydro- and aromatherapy on rehabilitation of patients with myocardial infarction (MI) have not yet been sufficiently investigated. This pilot study explores the anti-inflammatory effects of a combined hydro- and aromatherapy protocol in MI patients targeting inflammation. A prospective study included 22 post-MI patients undergoing 28 days of hydro- and aromatherapy at the Institute "Dr Simo Milosevic" in Montenegro. Biochemical assessments, including complete blood count and cytokine analysis, were conducted before and after treatment. Following therapy, patients exhibited increased leukocytes neutrophils, and platelets, and reduced monocytes. Fibrinogen levels significantly increased, aligning with the expected post-MI healing process. C-reactive protein (CRP) and interleukin-6 (IL-6) concentrations significantly decreased. The therapy also led to a drop in nitric oxide (NO), cortisol, dopamine, and Beclin-1 levels, highlighting potential cardiovascular benefits. These findings encourage further research with larger cohorts and extended follow-up to elucidate the long-term benefits of this protocol.

**Keywords:** Inflammation; Myocardial infarction; Hydrotherapy; Aromatherapy; Montenegro

**Resumen:** Los efectos de la hidroterapia y la aromaterapia en la rehabilitación de pacientes con infarto de miocardio (IM) aún no han sido suficientemente investigados. Este estudio piloto explora los efectos antiinflamatorios de un protocolo combinado de hidroterapia y aromaterapia en pacientes con IM, enfocándose en la inflamación. Se incluyó un estudio prospectivo con 22 pacientes post-IM que recibieron 28 días de hidroterapia y aromaterapia en el Instituto "Dr. Simo Milosevic" en Montenegro. Se realizaron evaluaciones bioquímicas, incluyendo hemograma completo y análisis de citoquinas, antes y después del tratamiento. Tras la terapia, los pacientes mostraron un aumento en los neutrófilos, leucocitos y plaquetas, así como una reducción en los monocitos. Los niveles de fibrinógeno aumentaron significativamente, alineándose con el esperado proceso de curación post-IM. Las concentraciones de proteína C-reactiva (PCR) e interleucina-6 (IL-6) disminuyeron significativamente. La terapia también condujo a una reducción en los niveles de óxido nítrico (NO), cortisol, dopamina y Beclin-1, destacando posibles beneficios cardiovasculares. Estos hallazgos fomentan investigaciones adicionales con cohortes más grandes y un seguimiento prolongado para esclarecer los beneficios a largo plazo de este protocolo.

**Palabras clave:** Inflamación; Infarto de miocardio; Hidroterapia; Aromaterapia; Montenegro.

## INTRODUCTION

Despite significant progress in prevention, diagnosis and treatment, cardiovascular diseases (CVD) are still the leading cause of mortality in Europe (Townsend *et al*., 2022). The fact that the incidence of CVD in the population younger than 50 years is increasing is particularly concerning (Andersson & Vasan, 2018). The efforts of the entire medical and scientific community are aimed at reducing the incidence of these diseases, primarily through the modification of risk factors for their development. If a cardiovascular event (for example, acute myocardial infarction - MI) arises, both primary care and secondary prevention become the focus of concern (Leong *et al*., 2017).

The patient and their family encounter distinct challenges in coping with the aftermath of an acute cardiovascular event. Implementing a suitable rehabilitation protocol is crucial for improving the patient's quality of life, reducing associated anxiety and depression, and lowering the risks of hospital readmission and mortality (Bellmann *et al*., 2020).

Cardiovascular rehabilitation consists mostly of lifestyle changes, exercise, and psychological interventions. Hydrotherapy and aromatherapy are receiving an increasing amount of attention as complementary therapies. Hydrotherapy consists of exercises in a pool as part of treatment for many different diseases, whereas aromatherapy is characterized as the therapeutic use of essential oils (also known as volatile oils) from plants (flowers, herbs, or trees) to foster physical, mental, and spiritual well-being (Posadzki *et al*., 2013).

Hydrotherapy, as an adjunctive therapeutic approach, has the potential to effectively reduce blood pressure (Moini Jazani *et al*., 2023a), which is particularly beneficial in managing conditions related to cardiovascular health, such as MI. Its positive results on sleep quality (Moini Jazani *et al*., 2023b), as well as the potential to reduce dopamine levels (Galvez *et al*., 2024), are an additional factor that can contribute to the use of hydrotherapy in the rehabilitation of patients after MI.

Several studies published so far have proven the effectiveness of aromatherapy in patients with CVD (including MI). Some of them monitored the effectiveness of aromatherapy in patients in the acute phase of the disease (during the patient's stay in the hospital) (Haddadi *et al*., 2021; Rambod *et al*., 2020; Ebrahimi *et al*., 2022; Veiskaramian *et al*., 2021), while others (Sebastian & Kear, 2021) focused on delayed rehabilitation. Aromatherapy is useful in lowering anxiety, systolic blood pressure, heart rate, and breathing rate in patients with cardiovascular disease, according to a recently published meta-analysis (Turan Kavradim *et al*., 2021). Previous research of our group (Perovic *et al*., 2019) has demonstrated that the essential oil of Lavandula officinalis from the Mediterranean region has a significant impact on the autonomic nervous system, leading to reductions in blood pressure and heart rate, which suggests a potential for therapeutic use in post-MI rehabilitation process. β-Linalool and linalyl acetate, as major components of this essential oil, are responsible for its anti-anxiety (Donelli *et al*., 2019), anti-oxidative (Alizadeh & Aghaee, 2016) effects as well as lysosomal/mitochondrial damages in human lymphocytes (Salimi *et al*., 2022). Similar biological effects have been described for citrus essential oils, whose main components are D-limonene and cis-cinnamaldehyde (Dosoky & Setzer, 2018; Denkova-Kostova *et al*., 2020). Most of the current knowledge about the effects of citrus fruits on recovery after MI is the result of studies on experimental animals (Durço *et al*., 2019: Oliveira *et al*., 2021).

Thus, using pain and anxiety scales or altering blood pressure, heart rate, etc., the impact of the therapy regimen was assessed in the aforementioned research. Given that inflammation can both trigger and result from an acute cardiac event, the objective of our study is to investigate the effects of hydrotherapy and aromatherapy on specific inflammatory parameters in patients recovering from MI. As far as the authors know, this is the first study of this sort.

## MATERIALS & METHODS

### *Patients*

Our prospective study was conducted during 2022, after approval by Committee for Medical Ethics and Bioethics, Faculty of Medicine, University of Montenegro (No. 1113/2). We included 22 patients of both sexes, older than 18 years, who experienced acute myocardial infarction in previous 6 months, and who, according to the protocol of the Health Fund of Montenegro, were sent for rehabilitation treatment at Institute “Dr Simo Milosevic” in Igalo, Herceg Novi, Montenegro, during 28 days.

### *Exclusion criteria were*

Patients with chronic heart failure stage IV according to World Health Organization (WHO) classification or cardiac arrhythmias with hemodynamic instability as well as patients with signs and symptoms of active infection, with malignancy, renal insufficiency, acute or chronic liver disease, mental illness, immunodeficiency conditions, pregnant women and

serious chronic diseases. All respondents signed an informed consent form before entering the survey.

### *Treatment*

Patients were treated daily at Institute ,,Dr Simo Milosevic'' using hydro- and aromatherapy during 20 minutes through the application of essential oils of medicinal plants in a warm pearl bath "Igaljka", at a temperature of 36 - 37°C. The protocol included the use of a pearl bath "Igaljka" in which 150 L of mineral water with a maintenance temperature of 36 - 37°C are poured, in which lavender (1 mL) and citrus (0.5 mL) essential oils are added. The participants lied in the bath prepared in this way for 20 minutes. All patients continued using their previously prescribed drugs.

### *Biochemical assessment*

Laboratory evaluation of the effects of hydro- and aromatherapy involved analysis of biochemical parameters from the serum of patients. Serum samples were taken at two intervals: before the start of therapy (T1) and at the end of treatment, i.e., after 28 days of treatment (T2). Blood samples (6 mL) were taken from the cubital vein using Vacutainer® tubes, in a supine position, in the morning, after 12 hours of sleep. Blood samples were immediately centrifuged at 2500 rpm during 10 min, and serum aliquots were stored at -80°C.

Complete blood count was done on a hematology analyzer (XE 5000 Sysmex), cortisol and dopamin concentration was measured on Cobas e601 (Roche), fibrinogen and CRP levels on Cobas c501 (Roche), while cytokines interleukin-6 (IL-6), Beclin-1, heat shock protein 72 (Hsp-72) and nitric oxide (NO), were determined by ELISA method (Rayto) according to the manufacturer's instructions (CUSABIO Human). For the specified parameters for IL-6, Hsp-72, Beclin-1 and NO Intra-assay: CV less than 8% and inter-assay: CV less than 10%.

### *Statistical analysis*

The statistical analysis for this study was performed using the Statistical Package for the Social Sciences (SPSS). Descriptive statistics were used to summarize baseline characteristics for study cohort. An Independent-Samples T-Test was conducted to compare the means of groups of patients. To explore the relationships between variables, correlation analysis was performed using Pearson's r coefficient. $p$-value<0.05 was considered statistically significant.

## RESULTS

As mentioned earlier, our study included 22 participants with an average age of 50.9 years. Table No. 1 provides a summary of the key demographic and clinical characteristics. Table No. 2 presents the mean values of the analyzed parameters before (T1) and after (T2) the combined hydro- and aromatherapy treatment, following the previously outlined protocol. The correlation analysis results are displayed in Table No. 3. Positive correlations were observed between CRP and Beclin-1 prior to treatment, CRP and dopamine post-treatment, leukocytes and platelets before treatment, and leukocytes and fibrinogen post-treatment. Additionally, correlations were found between neutrophils and IL-6, as well as neutrophils and Beclin-1 after treatment. Negative correlations were identified between leukocytes and monocytes after treatment, monocytes and fibrinogen before and after treatment, and neutrophils and monocytes before and after treatment.

## DISCUSSION

The analysis of the complete blood count parameters revealed notable changes, including increased leukocyte and platelet counts, and a decrease in monocytes. These results align with the well-established phases of MI healing - namely, inflammation, healing, and remodeling (Nunes-Silva *et al*., 2017) - where leukocytes, particularly macrophages, play a pivotal role (Vagnozzi *et al*., 2020). These effects could be attributed to the anti-inflammatory and immunomodulatory effects of essential oils used in aromatherapy, such as *Lavandula officinalis*, which has been shown to enhance immune response and modulate leukocyte activity (Silva *et al*., 2015). Similar effects have been observed in other studies examining the role of essential oils in inflammatory conditions (Zuo *et al*., 2020), supporting our findings that the combined use of hydrotherapy and aromatherapy may enhance post-MI healing.

Fibrinogen, an acute-phase reactant and recognized risk factor for MI (Shojaie *et al*., 2009), increased significantly after the application of our therapeutic protocol. This result aligns with previous studies that have reported elevated fibrinogen levels as a natural response in post-MI patients (Surma & Banach, 2021). The increase we observed may reflect the initial inflammatory phase, and further studies could assess longer-term fibrinogen changes with extended therapy duration.

**Table No. 1**
**Demographic and clinical characteristics of patients**

| Characteristic | Value |
|---|---|
| Total number of patients | 22 |
| Female [%] | 55 |
| Age | |
| Mean value ± SD [years] | 50.9 ± 8.8 |
| Minimum; maximum [years] | 34; 64 |
| Comorbidities | |
| Hypertension [%] | 81.8 |
| Hyperlipidemia [%] | 68.2 |
| Diabetes mellitus [%] | 31.8 |
| Legend: SD – standard deviation | |

**Table No. 2**
**Laboratory results before (T1) and after (T2) hydrotherapy and aromatherapy**

| | Reference value | T1 (before treatment) | | T2 (after treatment) | | *p*-value |
|---|---|---|---|---|---|---|
| | | Mean value | SD | Mean value | SD | |
| Leucocytes number [x$10^9$/L] | 3.8-11.5 | 7.55 | 2.18 | 8.23 | 2.59 | 0.00 |
| Monocytes [%] | 1.8-3.9 | 2.75 | 0.58 | 2.54 | 0.92 | 0.01 |
| Neutrophils [%] | 41.4-82.0 | 61.64 | 9.69 | 63.69 | 11.89 | 0.00 |
| Thrombocytes number [x $10^9$/L] | 166-367 | 250.40 | 52.75 | 267.95 | 64.46 | 0.00 |
| CRP [mg/L] | 0.90-5.80 | 2.31 | 1.01 | 2.24 | 0.67 | 0.02 |
| Fibrinogen [g/L] | 2.91-7.00 | 4.68 | 1.22 | 5.30 | 1.15 | 0.00 |
| IL-6 [pg/mL] | 2.9-40.7 | 22.36 | 13.39 | 19.19 | 10.5 | 0.00 |
| Hsp-72 [ng/mL] | 31.04-821.60 | 169.47 | 208.11 | 144.80 | 198.32 | 0.00 |
| NO [IU/mL] | 102.91-7.05 | 305.47 | 97.76 | 244.45 | 95.26 | 0.00 |
| Cortisol [nmol/L] | 254.0-978.0 | 515.78 | 178.70 | 463.41 | 159.45 | 0.00 |
| Beclin 1[pg/mL] | 0.07-0.17 | 0.10 | 0.02 | 0.09 | 0.02 | 0.00 |
| Dopamin[nmol/L] | 1.2-113.4 | 13.37 | 24.02 | 10.97 | 20.4 | 0.00 |
| **Legend: CRP – C-reactive protein; g – gram; Hsp-72 – heat-shock protein 72; IL-6 – interleukin 6; IU international unit; L – liter; mg – milligram; mL – milliliter; ng – nanogram; nmol – nanomole; NO – nitric oxide; pg – picogram; SD – standard deviation** | | | | | | |

In previously published studies, several biohumoral markers were detected as predictors of survival of patients after MI (Berton *et al*., 2010). C-reactive protein (CRP) is well-established biomarker for cardiovascular inflammation. Elevated CRP levels are linked to greater myocardial damage and poorer prognosis post-MI (Reindl *et al*., 2017; Oprescu *et al*., 2021). Our study found that the combination of hydro- and aromatherapy led to a significant reduction in CRP levels, which is consistent with findings from other research. This result speaks in favor of the importance of our therapeutic protocol in the rehabilitation of patients with CVD.

Interleukin-6 (IL-6), a central player in the inflammatory response, has been increasingly recognized for its role in the development and progression of CVD (atherosclerosis, MI, heart failure, stroke) (Su *et al*., 2021). The significant decrease in IL-6 concentration in our study further supports the anti-inflammatory potential of our therapeutic protocol. Such reductions in inflammatory markers have been linked to improved outcomes in post-MI patients, as shown in studies involving similar patient populations (Ridker &

Rane, 2021; Groot *et al*., 2019). Previous research has shown that the reduction in IL-6 concentration can be attributed to the active compounds in citrus essential oils (Shen *et al*., 2017).

**Table No. 3**
**Correlation analysis of laboratory parameters**

| | | CRP | A | B | C | D | E | IL-6 | Hsp-72 | NO | Beclin 1 | Dopamine | Cortisol |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CRP | T1 | 1 | -.203 | .081 | -.086 | .320 | -.065 | .145 | -.240 | -.127 | **.496*** | .201 | .080 |
| | T2 | 1 | -.131 | **.438*** | .226 | -.112 | .016 | -.015 | -.290 | -.288 | .235 | **.439*** | -.036 |
| Leucocytes | T1 | -.203 | 1 | **.558**** | -.167 | .072 | .313 | .017 | .096 | .023 | -.130 | .298 | -.210 |
| | T2 | -.131 | 1 | .205 | **-.457*** | .384 | **.482*** | .025 | .285 | .055 | .230 | .187 | .033 |
| Thrombocytes | T1 | .081 | .558** | 1 | .049 | -.073 | .276 | -.061 | -.360 | -.290 | -.065 | .348 | -.213 |
| | T2 | .438* | .205 | 1 | .289 | -.198 | .279 | -.070 | -.278 | -.383 | -.167 | .420 | -.065 |
| Monocytes | T1 | -.086 | -.167 | .049 | 1 | -.423 | **-.581**** | -.266 | -.297 | -.416 | -.199 | .252 | -.080 |
| | T2 | .226 | -.457* | .289 | 1 | -.699** | **-.452*** | -.048 | -.171 | -.221 | -.253 | .033 | -.134 |
| Neutophils | T1 | .320 | .072 | -.073 | **-.423** | 1 | .057 | .406 | .180 | .255 | .295 | .121 | .264 |
| | T2 | -.112 | .384 | -.198 | **-.699**** | 1 | .213 | **.429*** | .278 | .198 | **.396** | .358 | .281 |
| Fibrinogen | T1 | -.065 | .313 | .276 | -.581** | .057 | 1 | -.043 | .067 | .068 | .228 | -.196 | .014 |
| | T2 | .016 | .482* | .279 | -.452* | .213 | 1 | -.064 | -.240 | .062 | .152 | -.011 | -.060 |
| IL-6 | T1 | .145 | .017 | -.061 | -.266 | .406 | -.043 | 1 | .367 | -.023 | .083 | .315 | .207 |
| | T2 | -.015 | .025 | -.070 | -.048 | .429* | -.064 | 1 | .356 | .032 | .165 | .349 | .250 |
| Hsp-72 | T1 | -.240 | .096 | -.360 | -.297 | .180 | .067 | .367 | 1 | .315 | -.001 | .187 | -.104 |
| | T2 | -.290 | .285 | -.278 | -.171 | .278 | -.240 | .356 | 1 | .349 | .044 | .210 | -.058 |
| NO | T1 | -.127 | .023 | -.290 | -.416 | .255 | .068 | -.023 | .315 | 1 | .111 | -.007 | .005 |
| | T2 | -.288 | .055 | -.383 | -.221 | .198 | .062 | .032 | .349 | 1 | .138 | .051 | .064 |
| Beclin 1 | T1 | .496* | -.130 | -.065 | -.199 | .295 | .228 | .083 | -.001 | .111 | 1 | .078 | -.002 |
| | T2 | .235 | .230 | -.167 | -.253 | .396 | .152 | .165 | .044 | .138 | 1 | .102 | -.020 |
| Dopamine | T1 | .201 | .298 | .348 | .252 | .121 | -.196 | .315 | .187 | -.007 | .078 | 1 | -0.066 |
| | T2 | .439* | .187 | .420 | .033 | .358 | -.011 | .349 | .210 | .051 | .102 | 1 | 0.007 |
| Cortisol | T1 | .080 | -.210 | -.213 | -.080 | .264 | .014 | .207 | -.104 | .005 | -.002 | -0.066 | 1 |
| | T2 | -.036 | .033 | -.065 | -.134 | .281 | -.060 | .250 | -.058 | .064 | -.020 | 0.007 | 1 |

A: Leucocytes; B: Leucocytes; C: Monocytes; D: Neutrophils; E: Fibrinogen
* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).
T1 – before treatment; T2 – after treatment
Legend: CRP – C-reactive protein; Hsp-72 – heat-shock protein 72; IL-6 – interleukin 6; NO – nitric oxide

In contrast to expectations based on previous research (Staib *et al*., 2009), our study found a statistically significant decrease in heat-shock protein 72 (hsp72) levels. This outcome may be linked to factors such as sample size and the intensity of the hydrotherapy protocol, as sufficient thermal exposure is known to induce hsp72 expression (Amorim *et al*., 2015). Future research could investigate the precise conditions needed to optimize hsp72 activation in response to combined hydro- and aromatherapy.

The role of NO in myocardial ischemia remains complex, with studies suggesting both protective and damaging effects, depending on the context (Yu *et al*., 2018). Our study observed a significant decrease in NO levels, which could reflect a reduction in oxidative stress mediated by our therapeutic protocol. Certain essential oils, particularly those rich in antioxidant compounds, have been shown to modulate NO levels and counteract oxidative stress (Pérez-Rosés *et al*., 2016; Shen *et al*., 2017).

Several previously published reports showed that high cortisol serum level is connected with higher incidence of CVD, including MI (Tenerz *et al*., 2003). Additionally, a number of studies (Jutla *et al*., 2014) have proven that the treatment outcomes of patients with MI are worse in those with higher cortisolemia, and that in this population there is a higher risk of developing complications, including death from MI (Braukyliene *et al*., 2021). In our cohort, the initial serum concentration of cortisol was within the reference range, which we explain by the fact that the study was conducted in subjects in whom up to 6 months had passed since the acute cardiovascular event. On the other hand, the application of the therapeutic protocol in our subjects led to a statistically significant drop in serum cortisol concentration. Therefore, applying this therapeutic

protocol, from the aspect of cortisolemia, reduces the risk of unwanted outcomes in patients with MI.

Beclin-1 is a possible diagnostic of cardiac injury because it is an autophagy marker (Wang *et al*., 2018). Furthermore, there is evidence from animal models that suggests beclin-1 signaling activation could be a useful therapeutic target for microvascular damage caused by cardiac reperfusion (Sun *et al*., 2021). In our subjects, after applying the therapeutic protocol, a small but still statistically significant drop in beclin-1 serum concentration was recorded.

Numerous earlier research publications (Neumann *et al*., 2023) demonstrated that dopamine functions in the human heart as an indirect sympathomimetic, contributing to the development of myocardial ischemia injury. In our cohort, there was a statistically significant decrease in dopamine concentration after the application of the therapeutic protocol.

The correlation analyses demonstrated synchronized reductions in neutrophil, monocyte, and fibrinogen levels following the therapeutic protocol, which strongly suggests an overall anti-inflammatory effect. These findings align with prior studies that have emphasized the importance of reducing systemic inflammation, definitely involved in MI pathogenesis (Zhang *et al*., 2022).

Although our study provides important insights into the effects of hydro- and aromatherapy in post-MI patients, we recognize the limitations related to the small sample size and short follow-up period. Future studies with larger patient populations and longer follow-up durations are necessary to validate these findings and further investigate the active ingredients responsible for the therapeutic effects observed.

## CONCLUSION

Our pilot study shows that combining hydrotherapy and aromatherapy has a significant influence on inflammatory markers in patients recuperating from MI. The therapy resulted in a substantial drop in key inflammatory indicators such as CRP, IL-6 and NO, indicating that the procedure may have an anti-inflammatory impact. Furthermore, the study discovered connections between certain biochemical markers, further supporting the synchronized anti-inflammatory action of hydro- and aromatherapy. Despite the small sample size, our findings highlight the promise of this unique therapy strategy, calling for bigger populations and longer follow-up periods to gain a more thorough grasp of its long-term effects.

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