

## Abstract

Different therapeutic approaches with hydrogen (H<sub>2</sub>) have been recently put forward in sports medicine, yet the effectiveness of specific experimental treatments with H<sub>2</sub> was rarely compared with standard clinical procedures. **PURPOSE:** To analyze the effects of intensive hydrotherapy with hydrogen-rich water (HRW) on injury recovery in athletic men who suffered an acute ankle sprain and compare it with RICE protocol (rest, ice, compression, elevation), a universally accepted as best practice immediately after acute ankle sprains. **METHODS:** Eighteen healthy male professional athletes who incurred an acute ankle sprain during a sport-related activity were randomly assigned immediately after the injury to either hydrogen group (*n* = 9) or the conventional RICE treatment group (*n* = 9). Hydrogen group received six 30-min ankle baths with HRW throughout the first 24 h post-injury, with hydrotherapy administered every 4 hours during the intervention period. RICE group stood off the injured leg, with ice packs administered for 20 min every 3 hours (total of 8 sessions), with the injured ankle compressed with an elastic bandage for 24 hours and elevated at all possible times above the level of the heart. The trial was registered at ClinicalTrials.gov (NCT04167202). **RESULTS:** Hydrotherapy with hydrogen-rich water was equivalent to RICE protocol to reduce ankle swelling (2.1 ± 0.9% vs. 1.6 ± 0.8%; *P* = 0.26), range of motion (2.4 ± 1.3 cm vs. 2.7 ± 0.8 cm; *P* = 0.60), and single-leg balance with eyes opened (18.4 ± 8.2 sec vs. 10.7 ± 8.0 sec; *P* = 0.06) and closed (5.6 ± 8.4 sec vs. 3.9 ± 4.2 sec; *P* = 0.59). Neither intervention affected serum CRP, TNF-α and IL-1β (*P* > 0.05), although hydrogen treatment tended to reduce circulating IL-1β levels at 24-h follow up (10.8% on average; 95% confidence interval from 6.0 to 27.6; *P* = 0.07). **CONCLUSION:** HRW appeared to be equally effective to RICE for improving recovery after an acute ankle sprain in professional athletes, therefore advancing this innovative approach as an effective alternative in the field of sports medicine. However, more studies are needed to corroborate these findings in other soft tissue injuries.

## Background

A recent case report by our group indicated that **multi-session hydrotherapy with hydrogen-rich water** (HRW) might be a helpful intervention in terms of pain, swelling reduction and regaining range of motion after acute ankle sprain (AAS) in a professional athlete (**F1000 Research, 2020;9:245**). Nevertheless, no studies so far validated the effectiveness and safety of a novel experimental treatment with hydrogen against the standard clinical procedure of RICE for AAS management in a randomized clinical trial. This preliminary study thus aimed to monitor the impact of **intensive ankle baths with HRW** administered throughout **the first 24 h post-injury** on tissue recovery and inflammatory biomarkers in athletic men who suffered AAS and **compare it with the RICE regimen** in a randomized controlled trial.

## Methods

Randomized controlled non-inferiority parallel-group interventional study

Male **professional athletes who incurred AAS during a sport-related activity**

Hydrogen group (*n* = 9): **Six 30-min ankle baths with HRW** (HRW Natural Health Products Inc., New Westminister, BC, Canada) received throughout the first 24 h post-injury

RICE group (*n* = 9): stood off the injured leg, ice packs administered for 20 min every 3 hours, injured ankle compressed with an elastic bandage for 24 hours and elevated at all possible times above the level of the heart

Primary outcome = **change in ankle joint swelling** assessed at baseline and 24-h post-injury

Secondary outcomes = VAS for pain, ankle circumference, weight-bearing lunge test, CRP, TNF-α, IL-1β, etc.

## Results

All participants completed the trial, with no patient reported any relevant side effects of either intervention. The study outcomes during the trial were depicted in Table 1. **Hydrotherapy with hydrogen-rich water is non-inferior to RICE protocol** in terms of reducing joint swelling and pain while regaining range of motion and balance when administered intensively during the first 24 hours after AAS in professional athletes (*P* > 0.05).

**Table 1** Changes in injury outcomes and serum inflammatory markers during the trial. Values are mean ± SD.

	Baseline	24 h follow-up	<i>P</i> *
<b>Ankle swelling (cm)</b>			
HRW ( <i>n</i> = 9)	55.4 ± 3.0	54.2 ± 2.7 †	0.26
RICE ( <i>n</i> = 9)	55.3 ± 3.3	54.5 ± 3.4 †	
<b>Pain at rest (score)</b>			
HRW	48.9 ± 10.7	29.9 ± 8.1 †	0.12
RICE	47.6 ± 11.4	37.1 ± 9.1 †	
<b>Pain at movement (score)</b>			
HRW	69.3 ± 16.8	44.7 ± 14.9 †	0.13
RICE	70.2 ± 13.1	54.4 ± 13.3 †	
<b>WBLT (cm)</b>			
HRW	4.1 ± 1.7	6.5 ± 1.9 †	0.60
RICE	4.1 ± 2.0	6.7 ± 2.0 †	
<b>SLBT with eyes open (s)</b>			
HRW	24.6 ± 10.3	43.0 ± 14.4 †	0.06
RICE	31.4 ± 13.0	42.1 ± 11.9 †	
<b>SLBT with eyes closed (s)</b>			
HRW	8.8 ± 6.2	14.3 ± 7.5	0.59
RICE	8.7 ± 5.6	12.6 ± 6.8 †	
<b>CRP (mg/dL)</b>			
HRW	7.1 ± 3.9	6.8 ± 2.5	0.55
RICE	6.8 ± 3.6	6.0 ± 2.6	
<b>TNF-α (pg/mL)</b>			
HRW	27.1 ± 14.6	23.3 ± 13.7	0.45
RICE	25.8 ± 7.2	23.8 ± 9.7	
<b>IL-1β (pg/mL)</b>			
HRW	0.6 ± 0.4	0.5 ± 0.3	0.17
RICE	0.4 ± 0.2	0.4 ± 0.2	

**Abbreviations:** HRW, hydrogen-rich water; RICE, rest, ice, compression, elevation; WBLT, weight-bearing lunge test; SLBT, single-leg balance test; CRP, C-reactive protein; TNF-α, tumor necrosis factor-alpha; IL-1β, interleukin-1 beta. † Indicates significant difference baseline vs. follow-up at *P* ≤ 0.05 for each intervention. \* *P* values from independent samples two-way ANOVA time x intervention for repeated measures (HRW vs. RICE).

## Conclusion

This pilot RCT brings forward **intensive ankle bathing with HRW as an effective, safe and convenient approach to tackle AAS** in sports medicine. However, more studies are highly warranted to corroborate these findings in other soft tissue injuries and non-athletic populations.