

Research

*Corresponding author

Kazuyoshi Yagishita, MD, PhD

Clinical Center for Sports Medicine and
Sports Dentistry

Hyperbaric Medical Center

Tokyo Medical and Dental University

1-5-45 Yushima, Bunkyo-ku

Tokyo 113-8519, Japan

Tel. +81-3-5803-5341

Fax. +81-3-5803-5341

E-mail: yagishita.orth@tmd.ac.jp

Volume 3 : Issue 1

Article Ref. #: 1000SEMOJ3141

Article History

Received: July 31st, 2016

Accepted: January 16th, 2017

Published: January 17th, 2017

Citation

Yagishita K, Oyaizu T, Aizawa J, Enomoto M. The effects of hyperbaric oxygen therapy on reduction of edema and pain in athletes with ankle sprain in the acute phase: A pilot study. *Sport Exerc Med Open J*. 2017; 3(1): 10-16.

doi: [10.17140/SEMOJ-3-141](https://doi.org/10.17140/SEMOJ-3-141)

Copyright

© 2017 Yagishita K. This is an open access article distributed under the Creative Commons Attribution 4.0 International License (CC BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

The Effects of Hyperbaric Oxygen Therapy on Reduction of Edema and Pain in Athletes With Ankle Sprain in the Acute Phase: A Pilot Study

Kazuyoshi Yagishita, MD, PhD^{1,2*}; Takuya Oyaizu, MD²; Junya Aizawa, PhD¹; Mitsuhiro Enomoto, MD, PhD^{1,2}

¹Clinical Center for Sports Medicine and Sports Dentistry, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8519, Japan

²Hyperbaric Medical Center, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8519, Japan

ABSTRACT

Background: An ankle sprain is a major soft tissue injury that can occur during sports activities; an ankle sprain in the acute phase causes localized edema that increases tissue pressure, impairs micro-circulation, and causes hypoxia in the injured tissue. Hyperbaric oxygen therapy (HBO₂ therapy) reduces tissue hypoxia and tissue edema.

Objective: The purpose of this study was to investigate the short-term effects of HBO₂ therapy on edema and pain in athletes with an ankle sprain in the acute phase.

Materials and Methods: Forty-four athletes with acute ankle sprain who underwent HBO₂ therapy within seven days after injury between the years 2007 and 2015 were included in this study. The HBO₂ therapy protocol included pressure up to 2.5 atmosphere absolute (ATA) (253.3 kPa) for 60 minutes. The foot and ankle volume was measured using a water-filled volumetric gauge and a visual analog scale (VAS).

Results: Foot and ankle volume was 1569.1±219.0 cm³ just before HBO₂ therapy and 1557.8±218.1 cm³ just after HBO₂ therapy ($p<0.001$). The VAS scores were 19.5±20.1 and 17.2±19.9 points for pain at rest ($p<0.05$), 41.5±27.3 and 30.9±24.4 for pain while walking ($p<0.001$), and 44.2±23.7 and 37.1±22.5 for subjective evaluation of edema ($p<0.001$) before and after an HBO₂ therapy session, respectively.

Conclusion: Our results suggested that HBO₂ therapy may provide a short-term reduction of edema and pain in athletes with an ankle sprain in this pilot study.

KEYWORDS: Hyperbaric oxygen therapy; Foot and ankle volume; Visual analog scale; Edema reduction; Pain reduction.

INTRODUCTION

Injured athletes have a strong desire for rapid recovery from their injuries and therefore, multidisciplinary treatments are necessary to improve the healing process and to achieve an earlier return to training and competition. The goal is to establish safe procedures with low risk.

Soft tissue injuries in the acute phase are presented with localized edema and swelling, which is produced by plasma leakage from damaged blood vessels. Edema increases tissue pressure, decreases local perfusion, impairs micro-circulation, and causes hypoxia in the injured tissue.¹ Ankle sprains are frequent soft tissue injuries that occur during sports activities.

The effects of HBO₂ therapy on soft tissue injuries during sports activities, including sprains,² ligament injuries,³⁻⁵ contusions, and muscle strains,⁶⁻¹⁰ have been widely reported.

HBO₂ has been reported to be an effective therapy for edema reduction, which should improve local perfusion and improving oxygenation of the injured tissues.^{1,11} However, only Borromeo et al² have reported clinical research data providing quantitative analysis of HBO₂ therapy on ankle sprains. Their randomized control trial reported that joint function scores were more favorable in the HBO₂ group, though no significant differences were observed in ankle volume or the subjective evaluation of pain. However, detailed descriptions of the effects of HBO₂ therapy was missing, especially on the short-term effects of HBO₂ therapy in the acute phase.

The objectives of this study were to investigate the short-term effects of HBO₂ therapy on edema and to provide subjective evaluations of athletes with ankle sprains in the acute phase.

MATERIALS AND METHODS

Subjects

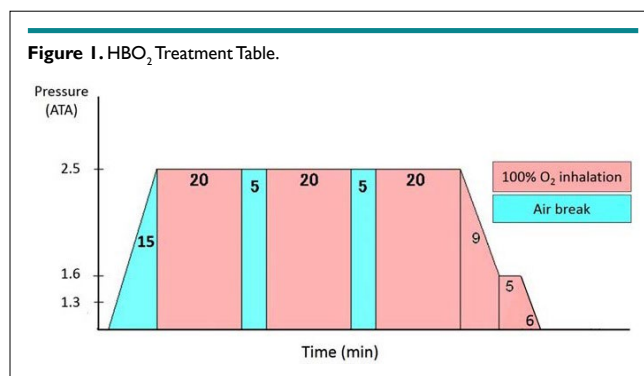
We performed a before-after analysis of patients who visited our clinic between the years of 2007 to 2015 with an acute ankle sprain sustained during sports activities within 7 days after the injury. The protocol for this study was approved by the Institutional Review Board of Tokyo Medical and Dental University, and informed consent was obtained from all subjects prior to participation. Forty-four patients (39 male, 5 female) were included in this study. Five of the subjects had a history of ankle sprain on the same side. The mean age of the patients was 23.2±3.8 years (range; 13-36 years).

The types of sports activities at the time of injury were as follows: Rugby (n=23), soccer (n=6), American football (n=4), baseball (n=3), and others (n=8). A diagnosis was made by the history of ankle sprains in sports activities and an assessment performed by a trained examiner (KY). The type of injury was classified as an inward twist (n=37), an outward twist (n=3), plantar flexion stress (n=3), or dorsal flexion stress (n=1) and by whether it affected the right (n=23) or left ankle (n=21). The severity of injury was classified into one of three grades; I: Stretched ligaments (not torn), with a stable joint and a negative anterior drawer test, II: A partially torn ligament with a lax joint and a partially positive anterior drawer test, III: Complete ligament rupture with an unstable joint and a positive anterior drawer test.¹³ In this study, the distribution of the severity of the injury was as follows: Grade 1 (n=6), grade 2 (n=35), and grade 3 (n=3). The mean number of days from injury to the first admission of HBO₂ treatment was 2.1±1.2 days (0-5 days).

HBO₂ Therapy Protocol and Treatment

The HBO₂ chamber in our university hospital was used; the maximum capacity of our multi-place HBO₂ chamber is 16 persons (NHC-412-A, Nakamura Tekko-Sho Corp., Tokyo, Japan). The HBO₂ therapy protocol included pressure up to 2.5

ATA (253.3 kPa) with treatment time of 60 minutes for inhalation of pure oxygen according to the HBO₂ therapy protocol for compartment syndrome (Figure 1).¹⁴ The HBO₂ therapy was performed within 7 days after injury, for a maximum of 5 times within a 7-day period in all cases. In total, 110 sessions of HBO₂ therapy were performed in the 44 patients (1 session (n=12), 2 sessions (n=11), 3 sessions (n=10), 4 sessions (n=9), and 5 sessions (n=2)). Other conventional treatments such as RICE (rest, ice, compression, and elevation) in the acute phase were performed concomitantly during HBO₂ therapy. RICE procedures were performed during the first week of the acute phase, range of motion exercises were applied beginning one week after injury, strength and flexibility rehabilitation was applied beginning one or two weeks after injury depending on pain and edema. The patients gradually returned to activities without any recurrence of injury.



Evaluation Procedures

Foot and ankle volume measurements were used to quantitatively evaluate ankle swelling; subjective evaluations using a VAS were also performed. In order to evaluate the short-term effects of HBO₂ therapy, all evaluations were performed immediately before and after the 105-minute HBO₂ therapy session.

To measure foot and ankle volume, the overflow water volume was measured using a water-filled volumetric edema gauge of our own making (Figure 2). This device measured 7.5 cm wide×12.5 cm long×33 cm high, and the bottom of the outflow cylinder was placed at the height of 16.5 cm from the floor so that foot and ankle volume up to 16.5 cm from the plantar face was measured. This device improves measurement accuracy compared to existing devices by reducing the water surface area. The patients were instructed to stand-bearing the same weight on both legs. The weight of the overflow water was measured and converted to volume as 1 g/cm³ specific gravity.

To evaluate the repeatability of the foot and ankle volume measurement, 5 volunteers (4 males, 1 female, mean age of 36.0±7.6 years; range 29-48 years old) were used. The volume measurements of the bilateral feet and ankles, a total of 10 feet and ankles, were performed 5 times each, and the Intraclass Correlation Coefficients (ICC_{1,5}) was evaluated. The ICC_{1,5} was 0.997 (95% CI, 0.993-0.999).

Figure 2. Measurement of Foot and Ankle. Measurement of Foot and Ankle by Water-Filled Volumetric Edema Gauge.



Eighty-five measurements of the VAS out of 110 sessions of HBO₂ therapy were fully recorded and were used for analysis in this study. The VAS evaluation included questions about pain at rest, pain while walking and a subjective evaluation of edema. The VAS consisted of a maximum of 100 points at full mark, where 100 points indicates the worst condition and 0 points indicates no complaint.

To assess the HBO₂ therapy efficacy in detail, the foot and ankle volume and VAS measurements were evaluated taking into consideration the number of HBO₂ therapy sessions and the amount of time between from the time of injury to when therapy was started.

Statistical Analysis

The data are presented as the mean±standard error of the mean (SEM). Differences were analyzed using the Paired *t*-test, and significance was accepted if the *p*-value was less than 0.05. Kruskal-Wallis one-way analysis of variance (ANOVA) tests were utilized to detect differences of foot and ankle volume in the grade of injury, the number of HBO₂ sessions and duration from injury, and differences of the VAS score in the number of HBO₂ sessions and duration from injury. Where appropriate, post hoc Bonferroni multiple comparison procedures were used. All data were analyzed using SPSS version 19.0 (SPSS Inc., 233

Wacker Dr, 11th Fl, Chicago, IL 60606, USA).

RESULTS

Foot and Ankle Volume

The foot and ankle volume in all sessions (n=110) were 1569.1±219.0 cm³ just before and 1557.8±218.1 cm³ just after HBO₂ therapy, with a reduction of 11.3±20.8 cm³ (*p*<0.001) during the 105-minute HBO₂ therapy. The foot and ankle volumes before the first session of HBO₂ therapy and after the final session of HBO₂ therapy (n=44) were 1598.1±216.8 cm³ and 1566.4±217.0 cm³, respectively, with a reduction of 31.7 cm³ (*p*<0.05). The foot and ankle volume before and after a HBO₂ therapy session depending on the severity of the injury are presented in Table 1, and there were no statistically significant differences of reduction of the foot and ankle volume in the severity of the injury.

The foot and ankle volume and reduction of volume before and after a HBO₂ therapy session depending on the number of HBO₂ therapy sessions are presented in Table 2. The foot and ankle volume and reduction of volume before and after a HBO₂ therapy session depending on the day after injury are presented in Table 3.

Table 1. Foot and Ankle Volume Depending on Severity of the Injury.

The grade of injury (n)	The number of HBO ₂ sessions	Pre-HBO ₂	Post-HBO ₂ (cm ³)	reduction (cm ³) [§]
Grade 1 (9)	1.5±0.8	1554.9±142.3	1552.2±137.9	2.6±13.3
Grade 2 (91)	2.6±1.2	1564.2±224.9	1552.6±223.5*	11.5±21.7
Grade 3 (10)	3.3±1.2	1626.3±230.2	1609.8±236.9*	16.5±16.7

*: Statistical differences between pre-HBO₂ and post-HBO₂ performed with Paired *t*-test (*p*<0.05).

§: No statistically significant differences in the severity of injury performed with Kruskal-Wallis one-way ANOVA.

Table 2. Foot and Ankle Volume Depending on HBO₂ Therapy Sessions.

The number of HBO ₂ sessions (n)	Pre-HBO ₂	Post-HBO ₂ (cm ³)	Reduction (cm ³) §
1 (44)	1598.1±216.8	1584.0±214.8*	14.1±23.1
2 (32)	1572.3±216.0	1562.6±214.4*	9.8±19.5
3 (21)	1553.1±196.4	1542.3±202.8*	10.8±22.3
4 (11)	1516.0 ±248.9	1510.3±249.3*	5.7±9.6

*: Statistical differences between pre-HBO₂ and post-HBO₂ performed with paired t-test ($p<0.05$).
§: No statistically significant differences in the number of HBO₂ sessions performed with Kruskal-Wallis one-way ANOVA.

Table 3. Foot and Ankle Volume Depending on Duration from Injury.

Duration from injury day (n)	Pre-HBO ₂	Post-HBO ₂ (cm ³)	Reduction (cm ³) §
1 (11)	1541.5±205.0	1521.6±206.1*	19.9±30.2
2 (23)	1638.5±213.5	1628.4±214.9*	10.2±22.1
3 (23)	1598.6±219.2	1591.2±213.7*	7.4±16.1
4 (20)	1508.2±230.2	1494.8±227.9*	13.4±21.9
5 (16)	1524.7±221.6	1518.1±225.3	6.6±15.8
6 (11)	1552.3±235.4	1540.7±229.0	11.6±24.9

*: Statistical differences between pre-HBO₂ and post-HBO₂ performed with paired t-test ($p<0.05$).
§: No statistically significant differences in the duration from injury performed with Kruskal-Wallis one-way ANOVA.

Visual Analog Scale (VAS)

VAS scores were 19.5±20.1 points and 17.2±19.9 for pain at rest ($p<0.05$), 41.5±27.3 and 30.9±24.4 for pain while walking ($p<0.05$), and 44.2±23.7 and 37.1±22.5 for subjective evaluation of edema ($p<0.05$) before and after HBO₂ therapy (Table 4).

When considering the severity of the injury, there were no statistically significant differences of improvement between groups (Table 5). When considering the number of therapy sessions, the VAS scores for pain while walking were 60.6±25.3

points and 43.2±24.6 ($p<0.05$) for the first HBO₂ therapy session (n=26) and 33.4±25.4 points and 25.8±24.6 ($p<0.05$) for the third HBO₂ therapy session (n=22) before and after an HBO₂ therapy session, respectively (Table 6). There were statistically significant differences of 1 against 2, 3 and 4 of the number of HBO₂ sessions regarding to the VAS scores for pain while walking ($p<0.05$).

With respect to the time after injury when treatment began, the VAS scores for pain while walking were 55.5±27.5 points and 36.6±23.5 (n=17) when started 2 days post injury

Table 4. VAS Scores.

Pain at rest		Pain while walking		Subjective evaluation of edema	
Pre-HBO ₂	Post-HBO ₂ (cm ³)	Pre-HBO ₂	Post-HBO ₂ (cm ³)	Pre-HBO ₂	Post-HBO ₂ (cm ³)
19.3±20.1	17.2±19.9*	41.5±27.3	30.9±24.4*	44.2±23.7	37.1±22.5*

*: Statistical differences between pre-HBO₂ and post-HBO₂ performed with paired t-test ($p<0.05$).

Table 5. VAS Scores Depending on the Severity of the Injury.

(Point)

The grade of injury (n)	Pain at rest			Pain while walking			Subjective evaluation of edema		
	Pre-HBO ₂	Post-HBO ₂	Improvement §	Pre-HBO ₂	Post-HBO ₂	Improvement §	Pre-HBO ₂	Post-HBO ₂	Improvement §
Grade 1 (5)	23.2±25.1	18.8±22.1*	4.4±6.4	45.6±28.4	29.4±25.3*	16.2±12.2	36.2±27.6	26.6±23.6	9.6±12.9
Grade 2 (74)	19.6±19.9	17.4±20.3*	2.2±10.1	41.2±27.4	31.9±25.4*	9.4±10.1	44.3±22.9	38.1±22.7*	6.1±15.0
Grade 3 (8)	16.0±17.4	14.5±13.2	1.5±11.8	45.8±26.7	26.4±10.9*	19.4±24.1	53.4±28.2	35.6±17.0*	17.8±12.3

*: Statistical differences between pre-HBO₂ and post-HBO₂ performed with paired t-test ($p<0.05$).

§: No statistically significant differences in the severity of the injury performed with Kruskal-Wallis one-way ANOVA

Table 6. VAS Scores Depending on HBO₂ Therapy Sessions. (Point)

The number of HBO ₂ sessions (n)	Pain at rest			Pain while walking			Subjective evaluation of edema		
	Pre-HBO ₂	Post-HBO ₂	Improvement §	Pre-HBO ₂	Post-HBO ₂	Improvement §	Pre-HBO ₂	Post-HBO ₂	Improvement §
1 (26)	28.1±25.1	24.2±21.7*	3.9±8.0	60.6±25.3	43.2±24.6*	17.5±12.5‡	59.8±25.4	52.3±23.3	7.5±20.6
2 (24)	19.7±18.5	13.5±16.8*	6.2±7.1†	34.5±22.2	26.9±20.9*	7.6±12.2	44.1±20.3	34.6±19.7*	9.5±13.6
3 (22)	15.7±16.8	18.4±23.3	-2.7±13.6†	33.4±25.4	25.8±24.6*	7.6±10.4	36.0±20.5	30.2±20.8*	5.8±12.3
4 (11)	8.9±7.2	8.3±8.7	0.6±9.1	24.4±21.2	19.8±22.4	4.6±9.6	27.2±11.3	22.0±10.1*	5.2±7.0

*: Statistical differences between pre-HBO₂ and post-HBO₂ performed with paired t-test ($p < 0.05$).
 †: Statistical differences between 2 and 3 of the number of HBO₂ sessions performed with post hoc Bonferroni multiple comparison procedure ($p < 0.05$).
 ‡: Statistical differences of 1 against 2, 3 and 4 of the number of HBO₂ sessions performed with post hoc Bonferroni multiple comparison procedure ($p < 0.05$).
 §: No statistically significant differences in the number of HBO₂ sessions performed with Kruskal-Wallis one-way ANOVA.

Table 7. VAS Scores Depending on Duration from Injury. (Point)

Duration from injury (Day (n))	Pain at rest			Pain while walking			Subjective evaluation of edema		
	Pre-HBO ₂	Post-HBO ₂	Improvement §	Pre-HBO ₂	Post-HBO ₂	Improvement §	Pre-HBO ₂	Post-HBO ₂	Improvement §
1 (5)	21.0±18.7	16.0±14.6	5.0±7.9	60.6±25.3	48.0±19.5*	11.0±6.5	56.0±12.6	47.6±15.1	8.4±13.2
2 (17)	25.1±20.8	21.0±17.6*	4.1±7.2	55.5±27.5	36.6±23.5*	18.9±15.9†	59.5±22.2	45.9±20.9*	13.5±16.5
3 (21)	20.6±19.6	15.2±17.7*	5.3±7.9	43.6±24.1	33.5±23.4*	10.1±10.8	48.6±25.4	41.8±24.9*	6.8±8.6
4 (17)	15.5±17.1	14.0±17.2	1.5±7.6	30.1±20.7	20.9±19.1*	9.2±12.8	40.4±20.1	31.2±20.1	9.1±18.1
5 (16)	11.8±14.1	14.6±19.0	-2.8±15.3	28.8±24.9	24.0±23.4*	4.8±8.7†	27.8±17.7	24.9±19.0	2.9±8.5
6 (5)	28.8±30.1	30.8±40.0	-2.0±14.6	40.2±35.2	36.6±39.9	3.6±7.4	44.0±27.4	39.4±24.0	4.6±7.2

*: Statistical differences between pre-HBO₂ and post-HBO₂ performed with paired t-test ($p < 0.05$).
 †: Statistical difference between 2 days and 5 days of the duration from injury performed with post hoc Bonferroni multiple comparison procedure ($p < 0.05$).
 §: No statistically significant differences in the number of HBO₂ sessions performed with Kruskal-Wallis one-way ANOVA.

($p < 0.05$) and 28.8±24.9 points and 24.0±23.4 (n=16) 5 days post injury ($p < 0.05$) just before and after HBO₂ therapy, respectively (Table 7). There was a statistically significant difference between 2 days and 5 days of the duration from injury regarding to the VAS scores for pain while walking ($p < 0.05$).

DISCUSSION

In the present study, we administrated HBO₂ therapy to athletes with acute ankle sprains and quantitatively evaluated the short-term effects of HBO₂ therapy in the acute phase, though the RICE treatment is also effective in the acute phase, and HBO₂ therapy and the RICE treatment are confounding factors correlating to the outcomes.

The results of this pilot study revealed significant edema reduction of 11.3 cm³ and significant improvement in the VAS scores for pain at rest, pain while walking and subjective evaluation of edema after HBO₂ therapy.

We also evaluated the effectiveness of HBO₂ therapy as it relates to the severity of the injury, the number of HBO₂ therapy sessions and the duration of time from injury to the start of treatment. HBO₂ therapy was most effective at the first application with an average reduction of 14 cm³ in foot and ankle volume, and with an improvement of 17.5±12.5 points in the VAS scores for pain while walking, which was statistically sig-

nificant differences against the second, third and fourth application. Edema reduction of more than 10 cm³ was observed within 3 sessions, and the significant reductions in the VAS scores were observed within 4 sessions. Edema reduction of more than 10 cm³ was observed within 4 days from injury and significant reductions in the VAS scores were observed when treatment started within 5 days from injury. Too long HBO₂ therapy per session should be avoided due to the possibility of the manifestation of oxygen toxicity, even though the possibility is very low.¹⁵

Basic and clinical studies of HBO₂ therapy for soft tissue injuries, mainly for sprains,² ligament injuries³⁻⁵ and muscle injuries⁶⁻¹⁰ that occurred during sports activities, have been reported. Regarding to the effects of HBO₂ therapy on edema in the acute phase, Skyhar et al¹¹ examined the effects of HBO₂ therapy using a dog hemorrhagic model for acute compartment syndrome and reported that it significantly reduced edema and occurrence of muscle necrotic tissue. They speculated that those findings might be the result of hyper-oxygenation and vasoconstriction. Hyper-oxygenation increases the amount of oxygen in the peripheral tissue without hemoglobin involvement, and vasoconstriction reduces blood flow by 20% while outflow is maintained.¹² This resulted in an increase of resorption of the extra-vascular solution, and the net effect was edema reduction. Strauss et al¹¹ induced compartment syndrome in the hind limbs of 12 dogs and revealed a reduction of muscle necrosis and edema in the experimental compartment. According to these

past reports, it is expected that HBO₂ therapy will accelerate the reduction of edema by oxygenation of the localized hypoxic environment and that HBO₂ therapy can result in an earlier withdrawal from the vicious circle of localized hypoxia and edema in the acute phase.

In patients with ankle sprains, ankle edema increases the sensation of pain and restricts the ankle range of motion leading to delayed rehabilitation.¹⁶ Multidisciplinary treatments including RICE are required for rapid reduction of ankle edema, especially for high-performance athletes who need accelerated healing in order to return to competition as soon as possible.

In a previous clinical study of HBO₂ therapy for acute ankle sprains, Borromeo et al² reported a randomized control trial for patients with acute ankle sprain, and HBO₂ treated group receiving oxygen at 2.0 ATA (202.7 kPa) compared to a control group who received air at 1.1 ATA (111.5 kPa). They reported that joint function scores were more favorable in the HBO₂ group, although no significant differences were observed for ankle volume, subjective evaluation of pain, or range of ankle movement. As we applied an HBO₂ therapy protocol of 2.5 ATA (253.3 kPa), a slightly higher pressure than that used by Borromeo² we expected to see significant effects of HBO₂ therapy.

We recognize that a fundamental limitation of this study is the lack of a control group and therefore we could not definitively conclude the superiority of HBO₂ treatment over the conventional treatment including RICE therapy without HBO₂. Thus, we reported this study as a pilot study. The second limitation of this study was the absence of evaluation of the long-term effects of HBO₂ therapy on ankle sprains. Time to return to competition was not measured and was not compared to a control group or past reports. Additionally, the VAS evaluation is highly subjective and the placebo effects cannot be discounted; this limitation is also related to the lack of a control group. Lastly, a potential limitation of this study is an incomplete collection of VAS measurements from all subjects.

Future studies should determine whether HBO₂ therapy can accelerate healing processes and reduce the period for return to competition.

CONCLUSION

This pilot and observational study in athletes with ankle sprains in the acute phase found that a reduction of foot and ankle volume was measured with 11.3±20.8 cm³ during the 105-minute HBO₂ therapy, and the VAS scores were measured with 19.5±20.1 points and 17.2±19.9 for pain at rest ($p<0.05$), 41.5±27.3 and 30.9±24.4 for pain while walking ($p<0.05$), and 44.2± 23.7 and 37.1±22.5 for subjective evaluation of edema ($p<0.05$) before and after HBO₂ therapy.

ACKNOWLEDGEMENTS

We specially thank Dr. Takashi Hirai, Dr. Yasushi Kojima, Dr.

Takashi Taniyama, and all the medical engineers of Hyperbaric Medical Center in Tokyo Medical and Dental University for supporting this study. This work was partially funded by the Yamaha Foundation for Sports.

CONFLICTS OF INTEREST

The authors have declared that no conflict of interest exists with this submission.

ETHICAL CONSIDERATIONS

This study was approved by the Institutional Review Board of Tokyo Medical and Dental University in 2005, and all patients signed an informed consent form before participation. This study was undertaken in full accordance with the ethical standards in the Helsinki Declaration.

REFERENCES

1. Skyhar MJ, Hargens AR, Strauss MB, Gershuni DH, Hart GB, Akeson WH. Hyperbaric oxygen reduces edema and necrosis of skeletal muscle in compartment syndromes associated with hemorrhagic hypotension. *J Bone Joint Surg Am.* 1986; 68(8): 1218-1224. Web site. <http://jbjs.org/content/68/8/1218.abstract>. Accessed December 6, 2016.
2. Borromeo CN, Ryan JL, Marchetto PA, Peterson R, Bove AA. Hyperbaric oxygen therapy for acute ankle sprains. *Am J Sports Med.* 1997; 25(5): 619-625.
3. Horn PC, Webster DA, Amin HM, Mascia MF, Werner FW, Fortino MD. The effect of hyperbaric oxygen on medial collateral ligament healing in a rat model. *Clin Orthop Relat Res.* 1999; 360: 238-242. Web site. http://journals.lww.com/corr/Abstract/1999/03000/The_Effect_of_Hyperbaric_Oxygen_on_Medial.28.aspx. Accessed December 6, 2016.
4. Mashitori H, Sakai H, Koibuchi N, et al. Effect of hyperbaric oxygen on the ligament healing process in rats. *Clin Orthop Relat Res.* 2004; 423: 268-274. doi: [10.1097/01.blo.0000128970.27390.f5](https://doi.org/10.1097/01.blo.0000128970.27390.f5)
5. Ishii Y, Ushida T, Tateishi T, Shimojo H, Miyanaga Y. Effects of different exposures of hyperbaric oxygen on ligament healing in rats. *J Orthop Res.* 2002; 20(2): 353-356. doi: [10.1016/S0736-0266\(01\)00094-8](https://doi.org/10.1016/S0736-0266(01)00094-8)
6. Haapaniemi T, Nylander G, Sirsjo A, Larsson J. Hyperbaric oxygen reduces ischemia-induced skeletal muscle injury. *Plast Reconstr Surg.* 1996; 97(3): 602-607. Web site. http://journals.lww.com/plasreconsurg/Abstract/1996/03000/Hyperbaric_Oxygen_Reduces_Ischemia_Induced.17.aspx. Accessed December 6, 2016.
7. Best TM, Loitz-Ramage B, Corr DT, Vanderby R. Hyperbaric oxygen in the treatment of acute muscle stretch injuries: Results

- in an animal model. *Am J Sports Med.* 1998; 26(3): 367-372.
8. Gregorevic P, Lynch GS, Williams DA. Hyperbaric oxygen improves contractile function of regenerating rat skeletal muscle after myotoxic injury. *J Appl Physiol.* 2000; 89(4): 1477-1482. Web site. <http://jap.physiology.org/content/89/4/1477.short>. Accessed December 6, 2016.
9. Horie M, Enomoto M, Shimoda M, Okawa A, Miyakawa S, Yagishita K. Enhancement of satellite cell differentiation and functional recovery in injured skeletal muscle by hyperbaric oxygen treatment. *J Appl Physiol.* 2014; 116(2): 149-155. doi: [10.1152/jappphysiol.00235.2013](https://doi.org/10.1152/jappphysiol.00235.2013)
10. Bennett MH, Best TM, Babul S, Taunton J, Lepawsky M. Hyperbaric oxygen therapy for delayed onset muscle soreness and closed soft tissue injury. *Cochrane Database Syst Rev.* 2005; 19(4): 1-39. doi: [10.1002/14651858.CD004713.pub2](https://doi.org/10.1002/14651858.CD004713.pub2)
11. Strauss MB, Hargens AR, Gershuni DH, et al. Reduction of skeletal muscle necrosis using intermittent hyperbaric oxygen in a model compartment syndrome. *J Bone Joint Surg Am.* 1983; 65(5): 656-662. Web site. <http://jbjs.org/content/65/5/656.abstract>. Accessed December 6, 2016.
12. Bird AD, Telfer AB. Effect of hyperbaric oxygen on limb circulation. *Lancet.* 1965; 1(7381): 355-356. doi: [10.1016/S0140-6736\(65\)91783-6](https://doi.org/10.1016/S0140-6736(65)91783-6)
13. Lamb SE, Nakash RA, Withers EJ, et al. Clinical and cost effectiveness of mechanical support for severe ankle sprains: Design of a randomised controlled trial in the emergency department. *BMC Musculoskelet Disord.* 2005; 6: 1. doi: [10.1186/1471-2474-6-1](https://doi.org/10.1186/1471-2474-6-1)
14. Strauss MD. Crush injuries and skeletal muscle-compartment syndromes. *Hyperbaric Oxygen Therapy Indications.* 13th Ed. North Carolina, USA: Undersea and Hyperbaric Medical Society, Inc Best Publishing; 2014: 91-101.
15. Hadanny A, Meir O, Bechor Y, Fishlev G, Bergan J, Efrati S. Seizures during hyperbaric oxygen therapy: Retrospective analysis of 62,614 treatment sessions. *Undersea Hyperb Med.* 2016; 43(1): 21-28.
16. Ogilvie-Harris DJ, Gilbert M. Treatment modalities for soft tissue injuries of the ankle: A critical review. *Clin J Sport Med.* 1995; 5(3): 175-186. Web site. http://journals.lww.com/cjsportsmed/Abstract/1995/07000/Treatment_Modalities_for_Soft_Tissue_Injuries_of.8.aspx. Accessed December 6, 2016.