Hyperbaric oxygenation accelerates prosthetic rehabilitation of lower limb amputees

Simanic Igor [1], Teofilovski Mirko [1], Paspalj Dalibor [2], Radotic Milutin [1], Djordjevic Dusica [3], Zivkovic Vladimir [3], Jakovljevic Vladimir [3]

[1] Specialized Hospital for Rehabilitation and Orthopedic Prosthetics, Belgrade, Serbia
[2] Institute for Gerontology, Belgrade, Serbia
[3] Department of Physiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

CORRESPONDING AUTHOR: Vladimir Jakovljevic M.D., Ph.D. – *drvladakgbg@yahoo.com*

ABSTRACT

The purpose of the study was to assess the effects of hyperbaric oxygen (HBO_2) therapy on prosthetic rehabilitation of patients with unilateral lower limb amputation. Narang's scale, the Locomotor Capabilities Index and the two-minute walk test were used to assess functional abilities of amputees on the admission and on discharge from hospital. We also kept records of some clinical parameters whose improvement enables better mobility of patients: thigh and lower leg girth, strength of amputation stump, existence of amputation stump contracture, existence of some other complications on amputation stump, blood oxygenation and pulse palpation. Our results show that hyperbaric oxygenation accelerates prosthetic rehabilitation of lower limb amputees. HBO_2-treated patients were discharged from the hospital faster than the controls (hospitalized for 133.2 ± 54.87 days *vs*. 158.36 ± 53.05 days), they had improved arterial Hb saturation (97.40 ± 3.51% *vs*. 94.74 ± 3.28 %) and pulse palpability (pulse palpable in 27 *vs*. 18 subjects), less complications of the amputation stump (complications present in 24 *vs*. 30 subjects), greater healthy leg thigh girth (50.75 ± 3.96 cm *vs*. 48.90 ± 2.59 cm), stronger amputation stump (mark 3.90 ± 0.54 *vs*. 3.33 ± 0.47) and better functional abilities as measured by adapted Narang's scale (category 3.43 ± 1.30 *vs*. 4.10 ± 1.12) and locomotor capabilities index (score 38.06 ± 10.90 *vs*. 33.16 ± 8.80). These findings highlight the increasing validity of this procedure after limb amputation, which should be confirmed by further research in multicenter studies involving a larger number of respondents.

INTRODUCTION

Hyperbaric oxygen (HBO_2) therapy is increasingly used in a number of areas of medical practice. As defined by the Undersea and Hyperbaric Medical Society, HBO_2 represents a treatment in which a patient intermittently breathes 100% oxygen while the treatment chamber is pressurized to a pressure greater than sea level [1]. So, the effects of HBO_2 are based on the physiological and biochemical effects of hyperoxia. The increment of partial oxygen pressure in blood helps enable the body to overcome hypoxia, energy metabolism collapse and consequent cell death [2].

There is extensive literature suggesting the use of HBO_2 in a range of clinical conditions [3]. A growing number of studies prove the efficacy of HBO_2 in the treatment of chronic non-healing wounds and other forms of severe soft tissue damage of lower limbs [4-6]. HBO_2 represents one of the most effective procedures in treatment of "diabetic foot" – *i.e.*, ulcerations, edema and ischemic changes that lead to necrosis and gangrene of the foot [7-14]. It has proven to be an effective adjunct to multidisciplinary therapies to improve limb salvage and help reduce the patient's hospital stay and wound care expenses [15]. In a prospective long-term follow-up of 38 patients with diabetic foot ulcers, Kalani and co-workers [12] noted that HBO_2 accelerated the rate of healing and reduced the need for amputation.

Literature suggests that HBO_2 represents one of the most effective procedures in the treatment of infected wounds and prevention of amputation, but the data about its possible positive effects on a patient's rehabilitation when, despite all applied therapeutic procedures, amputation takes place, are almost non-existent. Thus,

TABLE 1. General characteristics of population

Characteristic	Experimental group	Control group	Test
Age (X ± SD; years)	61.20±11.93	62.60±11.52	p>0.05
Gender (n; male/female)	25/5	21/9	p>0.05
Cause of amputation (n; diabetic gangrene/ vascular etiology/ trauma)	19/6/5	19/9/2	/*
Level of amputation (n; transfemoral/transtibial)	17/13	16/14	p>0.05

* χ^2 test could not be performed due to low number of frequencies in one subgroup (n<5)

the aim of our work was to assess the effects of HBO_2 on a number of parameters important for the prosthetic rehabilitation of patients with unilateral lower limb amputation.

MATERIALS AND METHODS

The study was performed in Specialized Hospital for Rehabilitation and Orthopedic Prosthetics (Belgrade, Serbia), from March 2011 to December 2011. The study population consisted of 60 patients with unilateral amputation of lower limb due to diabetic gangrene, vascular diseases or trauma. General characteristics of the population are presented in Table 1. The study was approved by Ethical Committee of the Hospital, and all patients gave written informed consent.

Subjects were randomly assigned to either the experimental or the control group. The experimental group was, besides standard prosthetic rehabilitation, subjected to 15 one-hour HBO_2 treatments in a multiplace chamber, where they breathed 100% oxygen at a pressure of 1.7 atmospheres absolute (atm abs).

Standard prosthetic rehabilitation contains the following procedures:

1) internal and orthopedic examination and prognosis for prosthetic rehabilitation;
2) kinesitherapy treatment including: daily respiratory exercise, immobilization and bandage for amputated extremity (twice a day, two hours' treatment), postural exercise (10 minutes daily), exercise training for upper limb musculature (15 times daily), training for better flexibility in different joints (15 times daily), exercise training for the rest of lower limb musculature (above the amputation region) (15 times daily), multidisciplinary team prescription of adequate prosthesis – (responsible physician, physiotherapist, orthopedic technician and leader specialist in physical medicine and rehabilitation, education for walking with first prosthesis (twice daily, 45 minutes in duration), biomechanical evaluation;
3) permanent physical treatment: laser therapy (15 treatments), magnetotherapy (20 treatments), electrotherapy (15 treatments), thermotherapy (periodically), electrostimulation (periodically).

HBO_2 therapy was performed for 15 days: once per day for 60 minutes at the atmospheric pressure of 1.7 atm abs between 3 and 4 p.m. All treatments were applied in a multipersonal chamber ("Haux") by inhaling oxygen through an oronasal mask. Oxygen saturation in peripheral circulation was monitored continuously and consistently maintained at around 100%. The first treatment was performed after the screening at Step 1 in standard prosthetic rehabilitation.

Examination of the HBO_2 influence on prosthetic rehabilitation of amputees included monitoring clinical parameters, assessing postoperative complications, and evaluation of functional capabilities of amputees. The following measurements were performed:

1. pulse palpation on art. dorsalis pedis of healthy leg;
2. pulse oximetry (measuring the oxygen saturation of arterial blood) on a fingertip using oximeter Oxy 5 (FIMA, Italy);
3. frequency of complications on amputation stump (hematoma, dehiscence, infection, edema, phantom sensations and phantom pain, etc.);
4. frequency of amputation stump contractures;
5. measurement of thigh and lower leg girth of healthy leg (measurement was performed in the middle of the body segment, using the measurement tape);
6. estimation of amputation stump's muscle strength (manual muscle test);

TABLE 2. Clinical parameters on admission and on discharge from the hospital.

Characteristic		On admission	Test	On discharge	Test
Pulse oximetry	EG	88.23±10.43	$p>0.05$	97.40±3.51	$p<0.05$
(X±SD; %)	CG	92.60±4.66		94.74±3.28	
Pulse palpation of ADP	EG	19/11	$p>0.05$	27/3	$p<0.05$
(*n*; palpable/nonpalpable)	CG	18/12		18/12	
Complications of AS	EG	27/3	$p>0.05$	24/6	$p<0.05$
(*n*; yes/no)	CG	30/0		30/0	
Contractures of AS	EG	11/19	$p<0.05$	4/26	$p>0.05$
(*n*; yes/no)	CG	28/2		6/24	
Thigh girth of HL	EG	50.08±4.12	$p>0.05$	50.75±3.96	$p<0.05$
(X±SD; cm)	CG	48.63±2.75		48.90±2.59	
Lower leg girth of HL	EG	35.91±2.52	$p>0.05$	36.25±2.64	$p>0.05$
(X±SD; cm)	CG	36.80±2.15		37.03±2.31	
Muscle strength of AS	EG	3.06±0.44	$p>0.05$	3.90±0.54	$p<0.05$
(X±SD; grade)	CG	2.86±0.34		3.33±0.47	

EG – experimental group; CG – control group; ADP – art. dorsalis pedis; HL – healthy leg; AS – amputation stump

7. evaluation of functional capabilities of patients using the Narang's scale [16,17], Locomotor Capabilities Index test (LCI) [18] and the two-minute walk test (2MWT) [19,20];
8. Time of prosthetic rehabilitation (from admission to discharge).

Statistical analysis was performed using SPSS 19. The data in tables and figures are presented as mean ± standard deviation or as frequencies. The differences between two independent samples were assessed using the Mann-Whitney test, while the differences between two dependent samples were assessed using the Wilcoxon Signed Rank test. When data were expressed as frequencies, an χ^2 test of independence was used. When frequencies in $2x2$ contingency tables were lower than 5, Fisher's test was used. When frequencies in contingency table belonged to the same subjects before and after experimental period, McNemar's test was used.

RESULTS

The results regarding clinical parameters are presented in Table 2, while the results regarding functional abilities are presented in Figures 1-3.

Percentage of arterial hemoglobin (Hb) saturation was not significantly different between experimental and control groups on admission to hospital (p=0.152). Both groups experienced the rise of this parameter through time (p=0.000 for both groups), but this rise was higher in the group of patients who received HBO_2 therapy, so they had a significantly higher percentage of arterial Hb saturation on discharge (p=0.009).

On admission, pulse on ADP was palpable in a similar number of patients in both groups (p=0.791). The frequency of ADP pulse palpability in the control group stayed the same until discharge, but in the group of patients treated with HBO_2 therapy ADP pulse became palpable in eight more patients. The difference in frequency of ADP pulse palpability became significantly different between the experimental and the control groups on discharge (p=0.015).

Frequency of complications on the amputation stump was similar in both groups on admission (p=0.237), but on discharge the HBO_2-treated group had a significantly lower number of patients who suffered complications (p=0.024).

Regarding the amputation stump contractures, the initial difference in frequencies of this phenomenon between groups (p=0.000) disappeared after the period of prosthetic rehabilitation (p=0.731), since in both groups, and especially in the control group, the frequency of contractures decreased.

The experimental and the control groups had similar thigh girth of the healthy leg on admission (p=0.115). Thigh girth increased in both groups during the period of rehabilitation, but the rise was more noticeable in the experimental (p=0.000) than in the control group (p=0.019), so the difference between groups became significant on discharge (p=0.017).

Regarding girth of the lower leg, although it increased in both groups during the rehabilitation period (p=0.019 for EG, p=0.020 for CG), this parameter was not significantly different between groups either on admission (p=0.279) or on discharge (p=0.374).

Groups had similar muscle strength of the amputation stump on admission (p=0.061), but although it significantly increased in both groups during the rehabilitation period (p=0.000 for both groups), this rise was more noticeable in the experimental group, who on discharge had a significantly stronger amputation stump (p=0.000).

In the beginning, groups were similarly categorized according to an adapted Narang's scale (p=0.394). After the experimental period, both groups improved (were classified as lower category), but the improvement was bigger in the group of patients who received HBO_2 treatment (p=0.000 for both groups). Thus, the experimental group was classified as a lower category of the adapted Narang's scale on discharge (p=0.038).

Regarding LCI score, the results followed the same trend as for the Narang's scale. There was no significant difference between groups on admission (p=0.376): Both groups experienced improvement during the experimental period (p=0.000 for both groups), and on discharge the HBO_2 group achieved better results than the control group (p=0.048).

Although both groups increased their walking speed and stride length over time (p=0.000 for both groups), there was no statistically significant difference in results achieved on the two-minute walking test between the experimental and the control groups either on admission (p=0.297) or on discharge (p=0.081).

Regarding the total time of prosthetic rehabilitation, the HBO_2-treated group of patients needed less time to complete the hospital's rehabilitation tasks and get discharged (p=0.047).

DISCUSSION

Hyperbaric oxygen treatment has been recommended and used for a wide range of medical conditions, with a varying evidence base [3]. HBO_2 has been described as "a therapy in search of diseases" [3], since its use in many clinical conditions has not yet been elucidated. Its use in treatment of conditions that may induce amputation is widespread, but its benefits on the rehabilitation of patients after amputation have been rarely investigated. Thus, the aim of our research was to assess the effects of HBO_2 therapy on the prosthetic rehabilitation of unilateral leg amputees.

Rehabilitation of an individual with lower limb amputation is a very complex and long-term process that requires a multidisciplinary approach and involvement of many specialists from different areas in order to achieve the maximal physical, psychosocial and professional capability of an amputee, *i.e.*, enable his/her reintegration into society and improve quality of life. The key to independence for members of this group is their walking ability and their ability to move in and around their homes [21]. Mobility is a basic physical need and its best possible restoration represents an important goal of rehabilitation programs following amputation of lower limbs, and particularly of prosthetic trials [22,23].

In order to assess the effects of HBO_2 on amputees' prosthetic rehabilitation we evaluated their functional abilities using widely accepted tests and scales, such as the Narang's scale, the Locomotor Capabilities Index and the two-minute walk test [16-20]. We also kept records of some clinical parameters whose improvement enables better mobility of patients: thigh and lower leg girth, strength of amputation stump, the existence of amputation stump contracture, the existence of some other complications on amputation stump, blood oxygenation and pulse palpation. The results of our study show an evident positive influence of HBO_2 therapy on rehabilitation of amputees.

Peripheral vascular disease accounts for more than 90% of all amputations, and more than half occur in people diagnosed with diabetes [24]. Since most amputations take place due to vascular etiology, we explored patients' oxygen saturation of blood and peripheral vascularization through ADP pulse palpation. On admission to hospital, ADP pulse was palpable in 19 out of 30 patients from the experimental – *i.e.*, HBO_2 – group, and in 18 out of 30 controls. Since there was no change in frequency of ADP pulse palpability in the control group after the experimental period, while ADP pulse became palpable in eight patients treated with HBO_2 therapy, we can assume that HBO_2 significantly affected peripheral vascularization of our patients. Regarding hemoglobin saturation of arterial blood, both groups had a very low percentage of saturation on admission (the experimental group: $88.23 \pm 10.43\%$, control group $92.60 \pm 4.66\%$). Blood oxygenation significantly increased with time in both groups, but this increase was more noticeable in the patients treated with HBO_2, who on discharge had not only significantly higher blood oxygenation compared

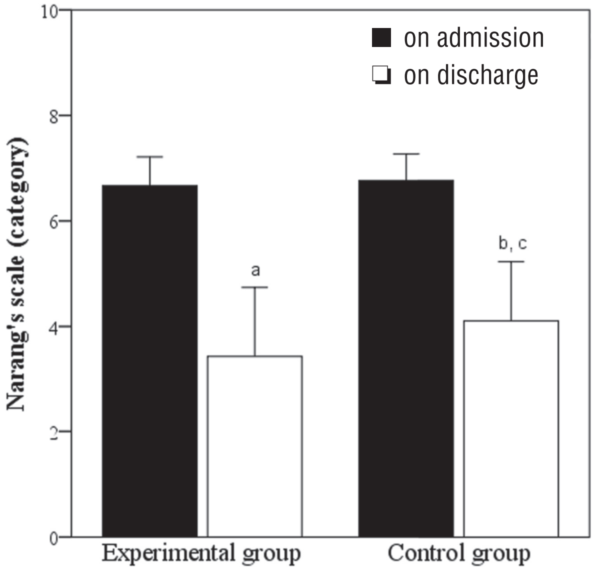

FIGURE 1. Category according to adapted Narang's scale on admission and on discharge from hospital in patients who received HBO_2 treatment and the control group (experimental group: a – p<0.01: significantly lower than on admission; control group: b – p<0.01: significantly lower than on admission, c – p>0.05: significantly higher than average category of the experimental group on discharge).

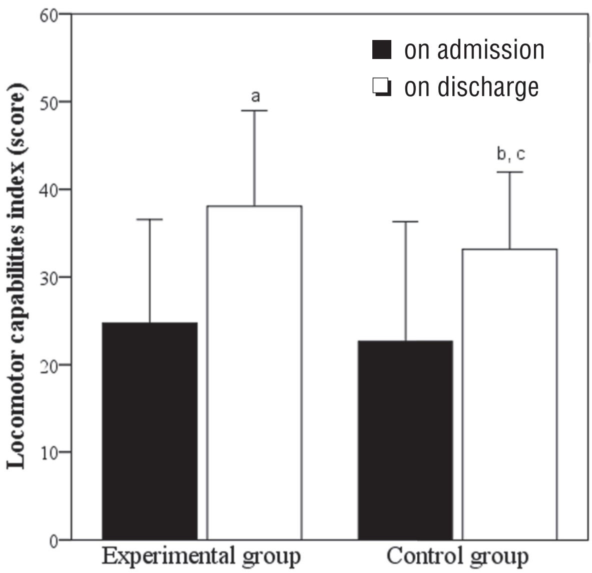

FIGURE 2. Score on Locomotor Capabilities Index test on admission and on discharge from hospital in patients who received HBO_2 treatment and the control group (experimental group: a – p<0.01: significantly higher than on admission; control group: b – p<0.01: significantly higher than on admission; c – p>0.05: significantly lower than average score of the experimental group on discharge).

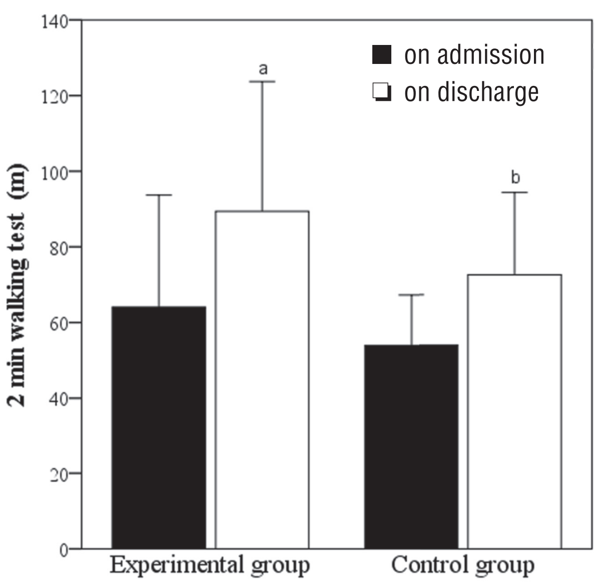

FIGURE 3. The distance that patients from the experimental and control groups covered by walking for two minutes on admission and on discharge from hospital (experimental group: a – p<0.01: significantly higher than on admission; control group: b – p<0.01: significantly higher than on admission).

with the control group (97.40±3.51% *vs.* 94.74±3.28%), but also entered the levels of blood oxygenation of a healthy person (95 - 99%). These effects of HBO_2 therapy were expected, and although they represent a temporary change, they certainly positively affected early rehabilitation of our patients and helped with improvement of other parameters important for the prosthetic rehabilitation.

Complications on the amputation stump, such as hematoma, dehiscence, infection, edema, joint contractures, etc., are very frequent phenomena in the early rehabilitation period of amputees [25]. Almost all of our patients (57 out of 60) experienced on average two to three complications when admitted to hospital. On discharge, three patients treated with HBO_2 were free of any amputation stump complication, which may be partially attributed to the effects of HBO_2 therapy on the above-mentioned peripheral vascularization and blood oxygenation.

Joint contractures usually occur between the time of amputation and prosthetic fitting. The lower limb amputee is at increased risk for developing joint contractures secondary to immobilization, poor positioning, pain and changes in agonist-antagonist muscle balance [25]. Additionally, the risk of contracture is increased in the presence of other complications, such as edema, ischemia, bleeding, flaccid paralysis, spasticity, etc. [26]. Contracture can prohibit prosthetic fitting, affect step length, and place abnormal forces on joints and increase energy expenditure during ambulation [27].

On admission, 40 out of 60 patients experienced joint contracture, and they were particularly frequent in the control group (28 out of 30 controls had contracture of the amputation stump). This problem was successfully solved by a proper exercise program – *i.e.*, an active and passive range-of-motion program with terminal stretch – so on discharge, only four HBO_2-treated patients and six controls still had AS contracture.

As previously mentioned, the goal of rehabilitation programs following the amputation of lower limbs is improvement of the mobility of amputees. A multitude of measurement scales and questionnaires are available, each differing in methods and measuring range [22]. Measuring mobility by a scale has been shown to have limitations; all measure only a number of aspects of mobility. Thus we included three mobility tests in our research: the adapted Narang's scale [16,17], the Locomotor Capabilities Index [18] and the two-minute walk test [19, 20].

The Narang's scale [16], adapted by Pohjolainen [17], ranks patients into 7 categories based on their ability to ambulate. "Ambulating with prosthesis but without other walking aids" represents the first class, while "non-ambulatory except in a wheelchair" patients are classified as the seventh class. On admission, our patients belonged mostly to the seventh or sixth class ("non-ambulatory except in a wheelchair" or "walking with aids, but without prosthesis," respectively).

After the experimental period, patients from both groups significantly improved their ability to move and use a prosthesis. However, on discharge, patients treated with HBO_2 were classified as lower grade (more mobile) than the controls. Median and average class in HBO_2-treated patients was third ("independent indoors, ambulating with a prosthesis and one crutch, but requiring two crutches outdoors and occasionally a wheelchair"), while the median class in controls was fifth ("walking indoors only short distances, ambulating mostly with a wheelchair"). On average, however, they reached the fourth class of Pohjolainen's categorization ("walking indoors with a prosthesis and two crutches or a walker, but requiring a wheelchair for outdoor activities").

The Locomotor Capabilities Index represents one of the most comprehensive and most valuable tests for evaluation of functional abilities of amputees. Follow-up studies of lower limb amputees, interviewed six months to five years after rehabilitation, provided evidence of test-retest reliability [28,29], internal consistency [30] and construct validity [28,29,31] of the LCI. These findings suggest that the LCI is able to evaluate and detect changes in the global locomotor ability of lower leg amputees with the prosthesis both during prosthetic training and in follow-up studies [18].

Mobility improvement enables functional independence of lower limb amputees in all activities of personal care and daily living, and enhances their quality of life [23,32]. In our research, both the experimental and control groups achieved not significantly different LCI scores on admission to hospital. Just like the Narang's test, the LCI test also showed that both groups significantly improved their functional abilities during the experimental period, and proved that HBO_2-treated patients experienced more noticeable mobility improvement. Thus, on discharge, HBO_2-treated patients scored higher on the LCI test compared with controls.

Walk tests are quantitative measures of speed and distance that provide information about functional exercise capacity. An informal unpublished Canadian survey of amputee programs in 1998 reported the two-minute walk test as the second most commonly used outcome measure [20]. The primary outcome of interest is distance walked, but velocity can also be calculated. The 2MWT also showed that our patients from both groups experienced improvement of mobility during the experimental period, but, unlike the results of the adapted Narang's scale and the LCI test, there was no statistically significant difference between the experimental and the control groups on discharge (89.36 ± 34.34m *vs.* 72.53 ± 21.80m). This was due to great variations of results achieved on this test (note the SD in the previous seentence).

Brooks *et al.* has shown that this test is responsive to change with rehabilitation and that it correlates with measures of physical function and prosthetic use in this population [19], but big variations in results achieved on this test – even in the same population two days in a row (on the first day subjects performed 2MWT twice and achieved similar results of 50 meters, while on the day after they passed about 120 meters, again in both attempts) [20] – question the role of learning, motivation and training in improvements observed.

Better results on tests of functional abilities achieved by patients treated with HBO_2 compared with patients from the control group may be due in part to a higher muscle mass of healthy leg and stronger amputation stump muscles. Namely, groups had similar healthy leg thigh and lower leg girth and strength of amputation stump on admission, but during the experimental period the HBO_2 group experienced higher gains in healthy leg thigh girth and amputation stump muscle strength, which enabled their improved mobility, not only in rectilinear movement, but also in a number of transfers and other movements that amputees have to perform during everyday activities (get up from the floor, pick up an object from the floor, walk outside on uneven ground, step up/down a sidewalk curb, go up/down the stairs with a hand-rail, walk while carrying an object etc.).

The final parameter that persuades us about the positive effects of HBO_2 therapy on the prosthetic rehabilitation of lower limb amputees is the time of prosthetic rehabilitation – *i.e.*, the time from admission to hospital until discharge from hospital. Subjects treated with HBO_2 needed significantly less time from admission to finishing prosthesis and getting discharged compared to patients who were not on HBO_2 therapy.

As already emphasized, there are a very low number of studies in whose light we could discuss our results. One of the available studies is a case report of a 67-year-old aboriginal woman with severe chronic obstructive pulmonary disease (COPD) and hypercapnic respiratory failure who underwent right transtibial amputation for severe foot gangrene [24]. Patients with severe COPD are rarely offered limb prostheses, as many of these patients are limited by their ventilatory status and unlikely to achieve the high energy expenditure required for successful prosthetic ambulation [24]. This study showed that a rehabilitation program enriched with oxygen supplementation improved her strength, endurance and stump contracture, and she was able to walk for short distances with a prosthesis. The limitations of that study are surely low number of subjects and no control group, but it is obvious that its results are in consistent with ours.

Research on animal models also support the use of HBO_2 in the treatment of amputated limbs [33]. Namely, it was shown that HBO_2 treatment (100% O_2, 2.9 atm abs, 24°C, for 240 minutes) may encourage preservation of metabolic processes and delay the progression of metabolic acidosis in this amputated limb model. This is further supporting evidence for the tissue-preserving effect of oxygen when delivered in hyperbaric conditions.

On the other hand, a retrospective study by Zgonis *et al.* [15] showed that there was no significant difference in the number of HBO_2 treatments received by patients with a successful *vs.* a failed partial foot amputation, although a trend was present. Patients with a successful post-surgical outcome tended to have a greater number of HBO_2 treatments than patients who had a failed surgical outcome. The lack of a significant relationship between HBO_2 treatment and healing outcome was in agreement with Ciaravino *et al.* [34], who noted that an average of 30 HBO_2 sessions had no effect on improving the outcome of their patients with non-healing amputations and other lower extremity wounds. But it should be noted that in that study, only 13 out of 54 patients were amputees: Others were subjected to HBO_2 therapy in order to heal diabetic ulcerations, ulcerations due to arterial insufficiency or gangrene lesions. However, at present, because of the limited data available from studies using a blinded, randomized design, a definitive statement regarding the effect of HBO_2 on healing in patients post-amputation cannot be made [34,35].

In summary, the results of our study point out to the usefulness of HBO_2 therapy in prosthetic rehabilitation of lower limb amputees. HBO_2 is a relatively safe, non-invasive means of improving healing by enhancing oxygenation, decreasing edema, and modifying healing and immune responses. Although it is expensive, not universally available, and not without risks, limb preservation and speedier healing make this a cost-effective method of wound care, but further research is needed to establish its efficacy and safety in other conditions, such as after amputation.

Acknowledgement
This work was partially financed by junior project 09/11, Faculty of Medical Sciences, Kragujevac, Serbia.
No conflicts exist with this submission. ■

REFERENCES

1. Hampson NB, ed. Hyperbaric Oxygen Therapy: 1999 Committee report. Kensington MD, Undersea and Hyperbaric Medical Society, 1999.

2. Yager JY, Brucklacher RM, Vannucci RC. Cerebral energy metabolism during hypoxia-ischemia and early recovery in immature rats. Am J Physiol 1992; 262: H672-H677.

3. Gill AL, Bell CN. Hyperbaric oxygen: its uses, mechanisms of action and outcomes. QJM 2004; 97(7): 385-395.

4. Lebel D, Gortzak Y, Nyska M, Katz T, Atar D, Etzion Y. Hyperbaric oxygen therapy for chronic diabetic wounds of the lower limbs-a review of the literature. Harefuah 2007; 146(3): 223-227, 244-245.

5. Bishop AJ, Mudge E. A retrospective study of diabetic foot ulcers treated with hyperbaric oxygen therapy. Int Wound J. 2012; doi: 10.1111/j.1742-481X.2011.00936.x.

6. Escobar SJ, Slade JB Jr, Hunt TK, Cianci P. Adjuvant hyperbaric oxygen therapy (HBO_2) for treatment of necrotizing fasciitis reduces mortality and amputation rate. Undersea Hyperb Med 2005; 32(6): 437-443.

7. Bakker DJ. Hyperbaric oxygen therapy and the diabetic foot. Diabetes Metab Res Rev 2000; 16: S55–S58.

8. Kessler L, Bilbault P, Ortega F, et al. Hyperbaric oxygenation accelerates the healing rate of nonischemic chronic diabetic foot ulcers: a prospective randomized study. Diabetes Care 2003; 26: 2378–2382.

9. Thackham JA, McElwain DL, Long RJ. The use of hyperbaric oxygen therapy to treat chronic wounds: A review. Wound Repair Regen 2008; 16(3): 321-330.

10. Tiaka EK, Papanas N, Manolakis AC, Maltezos E. The role of hyperbaric oxygen in the treatment of diabetic foot ulcers. Angiology 2012; 63(4): 302-314.

11. Löndahl M. Hyperbaric oxygen therapy as treatment of diabetic foot ulcers. Diabetes Metab Res Rev 2012; 1: 78-84.

12. Kalani M, Jorneskog G, Naderi N, Lind F, Brismar K. Hyperbaric oxygen (HBO) therapy in the treatment of diabetic foot ulcers. Longterm follow-up. J Diabetes Complications 2002; 16: 153–158.

13. Fife CE, Buyukcakir C, Otto G, Sheffield P, Love T, Warriner R 3rd. Factors influencing the outcome of lower-extremity diabetic ulcers treated with hyperbaric oxygen therapy. Wound Repair Regen 2007; 15(3): 322-331.

14. Szabad G. Diabetic foot syndrome. Orv Hetil 2011; 152(29): 1171-1177.

15. Zgonis T, Garbalosa JC, Burns P, Vidt L, Lowery C. A retrospective study of patients with diabetes mellitus after partial foot amputation and hyperbaric oxygen treatment. J Foot Ankle Surg 2005; 44(4): 276-280.

16. Narang IC, Mathur BP, Singh P, Jape VS. Functional capabilities of lower limb amputees. Prosthet Orthot Int 1984; 8: 43-51.

17. Pohjolainen T, Alaranta H, Karkkainen M. Prosthetic use and functional and social outcome following major lower limb amputation. Prosthet Orthot Int 1990; 14: 75-79.

18. Franchignoni F, Orlandini D, Ferriero G, Moscato TA. Reliability, validity, and responsiveness of the locomotor capabilities index in adults with lower-limb amputation undergoing prosthetic training. Archiv Phys Med Rehab 2004, 85: 743-748.

19. Brooks D, Parsons J, Hunter JP, Devlin M, Walker J. The 2-minute walk test as a measure of functional improvement in persons with lower limb amputation. Arch Phys Med Rehabil 2001; 82(10): 1478-1483.

20. Brooks D, Hunter JP, Parsons J, Livsey E, Quirt J, Devlin M. Reliability of the two-minute walk test in individuals with transtibial amputation. Arch Phys Med Rehabil 2002; 83(11): 1562-1565.

21. Collin C, Collin J. Mobility after lower limb amputation. Br J Surg 1995; 82: 1010–1011.

22. Rommers GM, Vos LD, Groothoff JW, Eisma WH. Mobility of people with lower limb amputations: scales and questionnaires: a review. Clin Rehabil 2001; 15: 92-102.

23. Geertzen JH, Martina JD, Rietman HS. Lower limb amputation. Part 2: Rehabilitation - a 10 year literature review. Prosthet Orthot Int 2001; 25: 14-20.

24. Sohal J, Arneja A, Sharma S. Oxygen supplementation facilitating successful prosthetic fitting and rehabilitation of a patient with severe chronic obstructive pulmonary disease following trans-tibial amputation: a case report. J Med Case Reports 2010; 4: 410.

25. Huston C, Dillingham TR, Esquenazi A. Rehabilitation of the lower limb amputee. In: Zajtchuk R, ed. Rehabilitation of the injured combatant. Volume 1. Washington (DC): Office of the Surgeon General, 1998:79-159.

26. Halar EM, Bell KR. Contracture and other deleterious effects of immobility. In: Delisa JA, Currie DM, Gans BM, Gatens PF Jr, Leonard JA Jr, McPhee MC, eds. Rehabilitation Medicine: Principles and Practice. Philadelphia: JB Lippincott; 1988: 448–462.

27. Pinzur MS, Gold J, Schwartz D, Gross N. Energy demands for walking in dysvascular amputees as related to the level of amputation. Orthopedics 1992; 15: 1033-1037.

28. Gauthier-Gagnon C, Grise MC. Prosthetic profile of the amputee questionnaire: validity and reliability. Arch Phys Med Rehabil 1994; 75: 1309-1314.

29. Miller WC, Deathe AB, Speechley M. Lower extremity prosthetic mobility: a comparison of 3 self-report scales. Arch Phys Med Rehabil 2001; 82: 1432-1440.

30. Gauthier-Gagnon C, Grise MC, Lepage Y. The Locomotor Capabilities Index: content validity. J Rehabil Outcomes Meas 1998; 2: 40-46.

31. Gauthier-Gagnon C, Grise MC, Potvin D. Enabling factors related to prosthetic use by people with transtibial and transfemoral amputation. Arch Phys Med Rehabil 1999; 80: 706-713.

32. Pernot HF, de Witte LP, Lindeman E, Cluitmans J. Daily functioning of the lower extremity amputee: an overview of the literature. Clin Rehabil 1997; 11: 93-106.

33. Zemmel NJ, Amis LR, Sheppard FR, Drake DB. A temporal analysis of the effects of pressurized oxygen (HBO) on the pH of amputated muscle tissue. Ann Plast Surg 1998; 40(6): 624-629.

34. Ciaravino ME, Friedell ML, Kammerlocher TC. Is hyperbaric oxygen a useful adjunct in the management of problem lower extremity wounds? Ann Vasc Surg 1996; 10: 558-562.

35. Wang C, Schwaitzberg S, Berliner E, Zarin DA, Lau J. Hyperbaric oxygen for treating wounds: a systematic review of the literature. Arch Surg 2003;138: 272–279.

✦