Int Marit Health
10.5603/imh.100400
www.intmarhealth.pl

ISSN 1641-9251
eISSN 2081-3252

VIA MEDICA

ORIGINAL ARTICLE

Results of treating patients with cellulitis by hyperbaric oxygen: a case-control study

Ha Nguyen Thi Hai[1*], Tam Nguyen Van[2*], Nam Bao Nguyen[3], Chi Tran Thi Quynh[3], Son Nguyen Truong[3]

[1]Ministry of Health, Ha Noi, Vietnam
[2]Hai Phong University of Medicine and Pharmacy, Hai Phong, Vietnam
[3]Institute of Maritime Medicine, Hai Phong, Vietnam

ABSTRACT

Background: *Cellulitis is an acute bacterial infection of the skin and subcutaneous tissue. The characteristic symptoms of the disease are an area of skin that is swollen, warmth, redness, pain, unknown borderline, tends to expand, and can lead to tissue necrosis. Hyperbaric Oxygen (HBO) is a non-drug treatment, which has the effect of relieving pain, reducing edema, and accelerating the wound healing process for patients with cellulitis. This study aims to evaluate the results of treating patients with cellulitis by HBO.*

Materials and methods: *A case-control study was conducted. 89 patients were diagnosed with cellulitis and treated at VINIMAM from January 2022 to December 2023. The study group included 48 patients treated with HBO combined with intravenous antibiotics, wound care. The reference group included 41 patients who were not treated with HBO but were treated with intravenous antibiotics, wound care.*

Results: *The pain relief level of the study group was better than that of the reference group (VAS score after one day of treatment: 4.34 and 5.78, after 2 days: 2.46 and 4.17, after 3 days: 1.28 and 3.35). The time for edema to subside in the study group was shorter than in the reference group. The circumference of the cellulitis area in the study group shrunk better than in the reference group. The average days of treatment in the study group were less than the reference group (8.33 ± 2.67 days and 13.17 ± 4.78 days).*

Conclusion: *Hyperbaric Oxygen was a good method to treat cellulitis, helped to reduce pain, was anti-inflammatory, reduced edema, and shortened treatment time.*

(Int Marit Health)

Keywords: cellulitis, hyperbaric oxygen therapy (HBOT), hyperbaric oxygen (HBO) Vietnam National Institute of Maritime Medicine (VINIMAM)

INTRODUCTION

Cellulitis is defined as an infection of the skin and subcutaneous tissues caused by bacteria. The characteristic symptoms of the disease are an area of skin that is swollen, warmth, rash, pain, unknown borderline, and tends to expand and can lead to tissue necrosis. The infection can appear in any position on the body but is most common in the upper and lower limbs. Cellulitis tends to affect the superficial surface of the skin. However, it can also cause inflammation in the deep tissue under the skin. It can even spread to lymph nodes and into the bloodstream causing sepsis [1–3]. Risk factors for cellulitis include poor peripheral circulation, varicose veins, diabetes, overweight, and obesity. Cellulitis may develop as a result of skin injuries, such as burns, animals bite, or in people with weakened immune systems after surgery [4, 5]. In this day and age, the treatment of cellulitis is most of using antibiotics, anti-inflammatories, and pain relief [6].

Hyperbaric oxygen (HBO) is a treatment in which patients breathe 100% pure oxygen in a device capable

✉ Tam Nguyen Van, Hai Phong University of Medicine and Pharmacy, Vietnam, 72A Nguyen Binh Khiem, Dang Giang, Ngo Quyen, Hai Phong, Viet Nam, 18000 Hai Phong, Viet Nam, nvtam@hpmu.edu.vn

Received: 24.04.2024 Accepted: 24.06.2024 Early publication date: 6.12.2024

of withstanding high pressure called a hyperbaric chamber under pressure conditions higher than atmospheric pressure (more than 1 Amosphe) [7].

Some studies show that hyperbaric oxygen is effective in treating cellulitis, infected wounds and ulcers that are difficult to heal [8–11]. The mechanism of high-pressure oxygen in this case is anti-inflammatory, pain relief, edema reduction, neovascular proliferation, and speeding up wound healing. In addition, hyperbaric oxygen can help eliminate bacteria and their growth by promoting the killing ability of white blood cells. HBO can serve as an adjunct to antibiotic therapy because it has bactericidal properties [12, 13].

Chengzi Huang, Yilian Zhong, et al. analyzed studies published on PubMed, Embase, and Web of Science study subjects including 49,152 patients with soft tissue infections (1448 patients treated by HBO combined with treatment of the underlying conditions; 47,704 patients of reference group only treated with underlying disease, not treated with HBO). The results showed that the mortality rate of the group treated by HBO was significantly lower than that of the group not treated by HBO (OR = 0.522; 95% CI: 0.403–0.677; $p < 0.05$). The rate of lesion recovery in the group treated by HBO was higher than that not treated by HBO [14].

In another study by Özer E.E et al. on patients having diabetes with soft tissue infections and secondary infection due to centipede bites treated by hyperbaric oxygen, the results showed that hyperbaric oxygen helped speed up the wound healing process, pain relief, edema reduction, and prevented the possibility of amputation while also facilitating patients return to social life in a short period [9].

Currently, in Vietnam, the Institute has applied hyperbaric oxygen in treating cellulitis, initially showing positive results. On that basis, this research was conducted with the following goal: Evaluate the results of treating patients with cellulitis by hyperbaric oxygen at the Institute of Maritime Medicine (VINIMAM) in 2022–2023.

MATERIAL AND METHODS

Study participants: 89 patients were diagnosed with cellulitis and treated at VINIMAM from January 2022 to December 2023. Study subjects were divided into 2 groups:

- Study group: treated by HBO combined with intravenous Cephalosporins antibiotics, wound care, and underlying disease control.
- Reference group: intravenous Cephalosporins antibiotics, wound care, and underlying disease control.

Criteria for selecting participants: according to AAD (American Academy of Dermatology Association) [15]. Patients were diagnosed with necrotizing cellulitis based on clinical features, such as diffuse inflammation with edema, warmth, redness of the skin, and subcutaneous tissue, accompanied by pain.

Patients agreed to participate in the study.

Patients had no contraindications to treatment with HBO.

Exclusion criteria: patients with deep thrombophlebitis, patients who did not agree to participate in the study, and had contraindications to treatment with hyperbaric oxygen.

Study design: This was a case-control study.

Sample size: 89 patients were diagnosed with cellulitis (48 patients in the study group and 41 patients in the reference group). Purposively select all patients diagnosed with cellulitis during the study period.

Data collection: Study participants were clinically examined to determine the cellulitis site on the body (upper limbs, lower limbs, head, face, neck...); Symptoms: fever, redness of the skin, warmth skin, diffuse swelling of the soft tissue, pain in the damaged skin, ulcers on the skin; measure the perimeter of the cellulitis area.

Blood test: red blood cell count (T/L), Hemoglobin (g/100 mL), Hematocrit (%), White blood cell count (G/L); blood sedimentation rate (mm/1h); quantification of fasting blood sugar (mmol/L).

TREATMENTS

Study group: Treatment with HBO according to VINIMAM 2 protocol [16], combined with intravenous Cephalosporins antibiotics, wound care, and underlying disease control if any.

Reference group: treatment with intravenous Cephalosporins antibiotics, wound care, and underlying disease control if any (Fig. 1).

EVALUATE TREATMENT RESULTS

Assessed the level of pain relief according to the VAS scale at the following times: after 1 day of treatment; after 2 days and after 3 days (no pain: 0 points; mild pain: 1–3 points; moderate pain: 4–6 points; severe pain: 7–10 points).

Assessed the level of edema reduction and the circumference of the cellulitis area by observing and measuring the size of the cellulitis area (after 3 days; 7 days and 10 days of treatment).

STATISTICAL ANALYSIS

The research data was processed using biostatistical methods, based on Statistics Package for Social Science (SPSS) for Windows 22.0 software. Frequency distributions and percentages were used to describe categorical variables, The chi^2 test was used to compare two ratios. Mean values were used to describe quantitative variables. The t-test was utilized to compare mean values.

INFORMED CONSENT

The research was approved by the Biomedical Research Ethics Committee of the Institute of Maritime Medicine

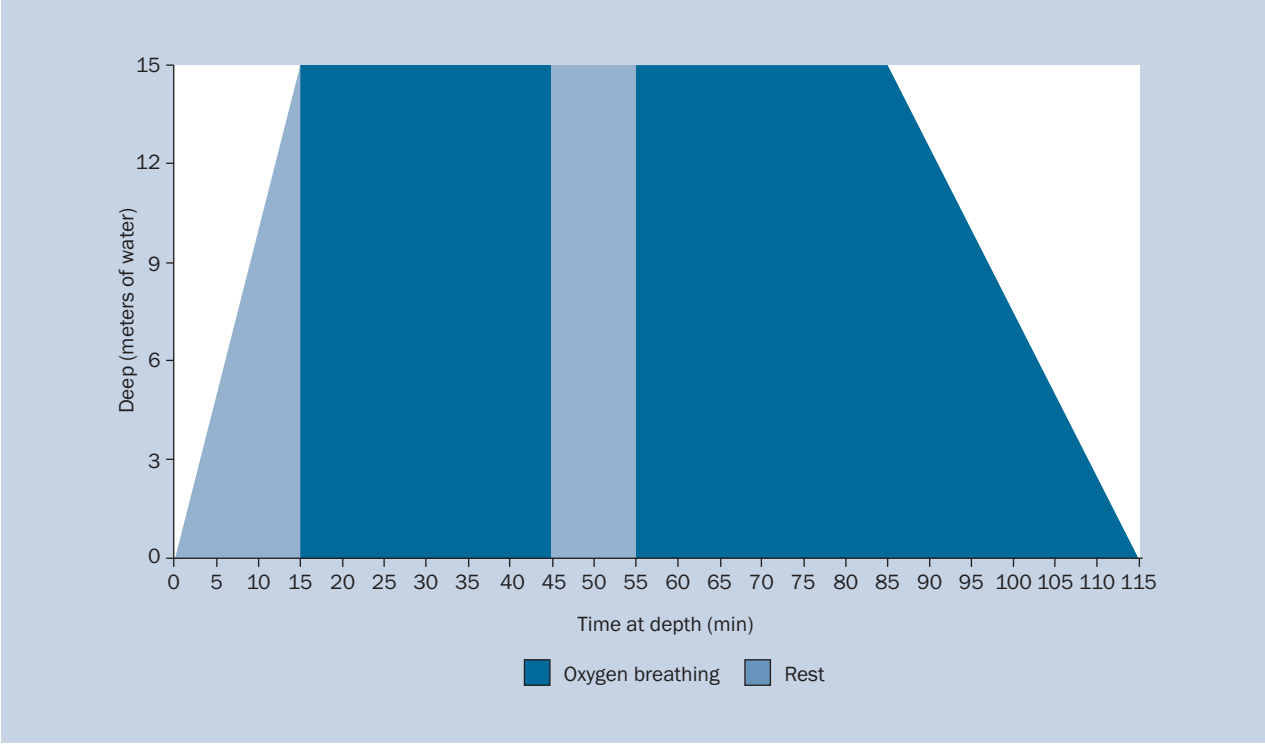

Figure 1. VINIMAM regimen 2. Patients are treated in multi-place chambers, treating pressure — 2.5 absolute atmospheric pressure; total treatment time — 115 minutes; total oxygen breathing time —90 minutes; between 2 oxygen breaths rest 10 minutes (breathe oxygen interrupt); breathing flow — free (breathe oxygen free through a mask)

according to decision 05/2022/QĐ-YHB. Subjects participating in the study were completely voluntary and signed a consent form to participate in the study.

RESULTS

Study of 48 patients with cellulitis treated by HBO combined with intravenous antibiotics, wound care, and underlying disease control compared with 41 patients with cellulitis treated only with intravenous antibiotics, wound care, and underlying condition control, the following results were obtained.

CHARACTERISTICS OF STUDY SUBJECTS

The results (Tab. 1) showed that the characteristics of gender, age, duration of illness, site of cellulitis, and co-morbidities in both groups were equivalent. 100% of patients with cellulitis in the study group and reference group had symptoms of skin redness, warmth, and edema. Symptoms of fever, pain, skin blisters, and skin ulcers did not differ between the 2 groups ($p > 0.05$). Red blood cell count, hemoglobin, hematocrit, white blood cell count, blood sedimentation, fasting, and blood sugar had no difference between the study group and the reference group ($p > 0.05$).

PAIN RELIEF LEVEL OF PATIENTS WITH CELLULITIS AFTER DAYS OF TREATMENT

The results (Fig. 2) showed a significant pain reduction effect in the group of patients with cellulitis treated by HBO compared to the reference group. The difference is statistically significant with $p < 0,05$.

TIME TO REDUCE EDEMA IN CELLULITIS AREA

The edema reduction time in the study group was shortened than in the reference group after 3 days, 7 days, and 10 days of treatment (Tab. 2). The difference was statistically significant with $p < 0.05$.

PERIMETER OF CELLULITIS AREA AFTER DAYS OF TREATMENT

The results (Tab. 3) showed that the circumference of the cellulitis area in the group treated with hyperbaric oxygen combined with (antibiotics + wound care) decreased significantly compared to the group treated only by antibiotics and wound care after 3 days, 7 days, and 10 days of treatment. The difference was statistically significant with $p < 0.05$.

Table 1. Characteristics of study subjects

Variable		Study group (n = 48)		Reference group (n = 41)		p-value
		No	(%)	No	(%)	
Gender	Male	29	60.4	25	61.0	0.957
	Female	19	39.6	16	39.0	
Age, Mean ± SD, (Min–Max)		59.45 ± 13.22 (23–86)		58.92 ± 13.14 (24–85)		0.851
Experience disease	< 5 days	34	70.8	30	73.2	0.807
	≥ 5 days	14	29.2	11	26.8	
Site of cellulitis	Upper limbs	9	18.8	7	17.1	0.837
	Lower limbs	32	66.7	29	70.7	0.681
	Other position	7	14.5	5	12.2	0.742
Underlying disease	Hypertension	19	39.6	15	36.6	0.772
	Diabetes	15	31.3	13	31.7	0.979
	Arthropathy	8	16.7	6	14.6	0.793
	Chronic Gout	6	12.4	7	17.0	0.694
Clinical characteristics	Fever	31	64.6	25	61.0	0.725
	Redness of the skin	48	100.0	41	100	–
	Edema	48	100.0	41	100	–
	Warmth	48	100.0	41	100	–
	Pain	46	95.6	38	92.7	0.520
	Blisters	7	14.6	7	17.0	0.829
	Skin ulcers	9	18.8	10	24.4	0.715
Paraclinical characteristics	Red blood cell (T/L), Mean ± SD	4.34 ± 0.44		4.27 ± 0.46		0.466
	Hemoglobin (mg/100 mL), Mean ± SD	130.77 ± 20.72		128.98 ± 23.11		0.701
	Hematocrit (%), Mean ± SD	0.38 ± 0.07		0.39 ± 0.08		0.531
	White blood cell (G/L), Mean ± SD	10.48 ± 3.38		10.72 ± 3.81		0.764
	Blood sedimentation [mm/1h], Mean ± SD	32.67 ± 5.21		33.87 ± 5.35		0.288
	Glucose (mmol/L), Mean ± SD	7.29 ± 2.55		6.56 ± 2.69		0.193

THE NUMBER OF DAYS OF TREATMENT FOR CELLULITIS

The results (Tab. 4) showed that the number of days of cellulitis treatment in the study group was 8.33 ± 2.67 days while in the reference group was 13.17 ± 4.78 days. The difference was statistically significant with $p < 0.001$.

DISCUSSION

Cellulitis is an acute infection of the skin and subcutaneous tissues, usually caused by Streptococcus or Staphylococcus bacteria [3]. Some risk factors for cellulitis are poor peripheral circulation, skin tears, lymphedema, athlete's foot, diabetes, and obesity. Current treatment of cellulitis

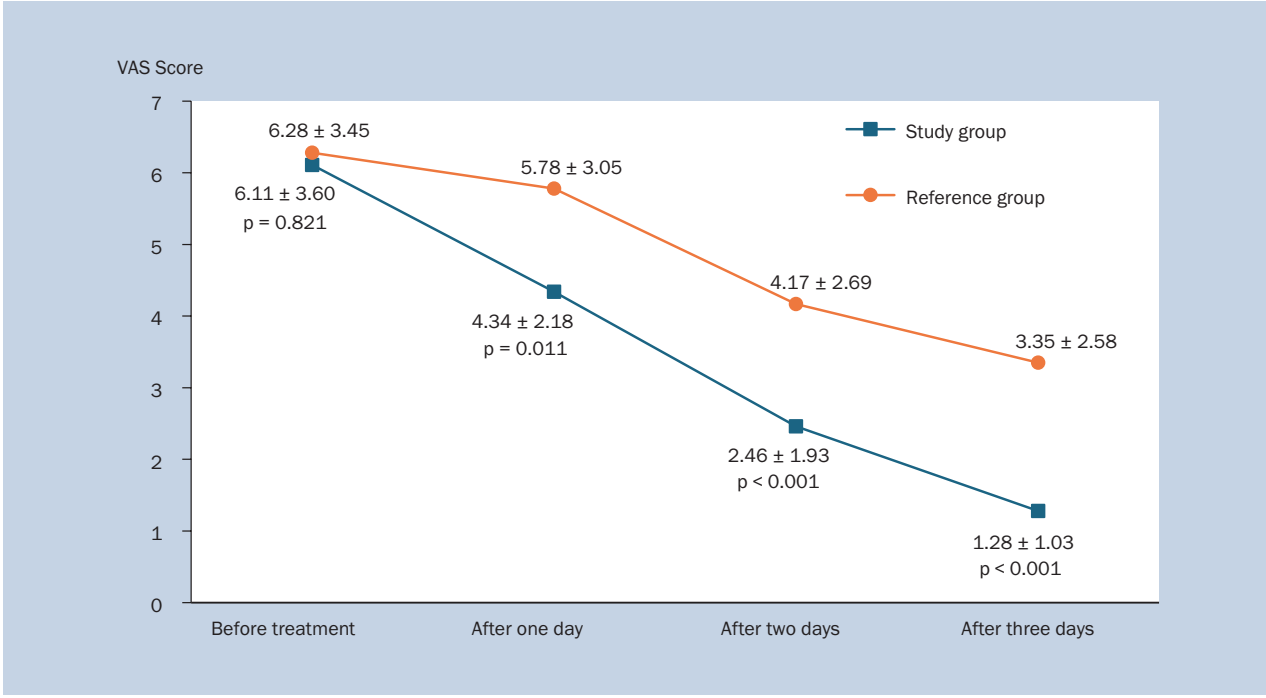

Figure 2. Pain relief level of patients with cellulitis after days of treatment

Table 2. Time to reduce edema in cellulitis area

Time to reduce edema	Study group (n = 48)		Reference group (n = 41)		p-value
	No	(%)	No	(%)	
After 3 days of treatment	26	54.2	31	75.6	0.036
After 7 days of treatment	18	37.5	26	63.4	0.015
After 10 days of treatment	4	8.3	17	41.5	< 0.001

Table 3. Perimeter of cellulitis area after days of treatment

Circumference of cellulitis area [cm]	Study group (n = 48) (Mean ± SD)	Reference group (n = 41) (Mean ± SD)	p-value
When entering hospital	22.05 ± 13.24	21.82 ± 14.17	0.910
After 3 days of treatment	13.11 ± 5.27	17.24 ± 8.49	0.006
After 7 days of treatment	5.21 ± 3.89	11.21 ± 5.98	< 0.001
After 10 days of treatment	2.36 ± 0.93	5.63 ± 3.25	< 0.001

Table 4. The number of days of treatment for cellulitis

The number of days of treatment	Study group (n = 48) (Mean ± SD)	Reference group (n = 41) (Mean ± SD)	p-value
Patients without diabetes	6.50 ± 2.67	10.21 ± 4.54	< 0.001
Patients with diabetes	12.21 ± 4.62	17.68 ± 5.63	< 0.001
Total	8.33 ± 2.67	13.17 ± 4.78	< 0.001

in hospitals is mainly using antibiotics and reducing edema [3, 6]. Study on 48 patients with cellulitis treated by HBO combined with intravenous antibiotics, wound care, and underlying disease control. Assessing pain levels using the VAS scale, the results showed that the study group had better pain relief days after treatment than the reference group ($p < 0.001$). In addition, the time to reduce edema and the circumference of the cellulitis area in the group of patients treated by HBO decreased significantly than in the group of patients only treated by intravenous biotics and wound care. The mean number of days of treatment in the study group was shortened more than the reference group (8.33 ± 2.67 days and 13.17 ± 4.78 days, $p < 0.001$). To explain this, some studies believed that HBO has a mechanism that helped increase oxygen supply to tissues, had anti-inflammatory effects, reduced wound edema, and increased the synthesis of fibroblasts and collagen to help heal wounds quickly [8, 10–12, 14]. On the other hand, hyperbatic oxygen acted as a natural antibiotic which helped to eliminate bacteria and their growth by promoting the killing ability of white blood cells. HBO acted as a bactericidal/bacteriostatic agent against anaerobic bacteria by increasing the formation of free oxygen radicals. It could serve as an adjunct to antibiotic therapy because it has bactericidal properties [10, 17].

Flegg et al. suggested that hyperbaric oxygen affected the synthesis of collagen fibers, which was a factor in strengthening wounds so that it could increase wound healing speed. On the contrary, the speed of wound healing would slow down due to the lack of oxygen. The lack of oxygen in tissues significantly reduced the wound healing process and on the contrary, ischemic injuries would be clinically improved when blood oxygen was increased. Increasing blood oxygen helped speed up wound healing and reduce wound edema. When the ischemic injury area was supplied with plenty of oxygen, angiogenesis was promoted, and the wound-healing process was quickly completed. Experiments on dog skin grafts have shown that hypoxia and poor circulation increase the risk of infection [18]. The present study's results were similar to studies by some authors on the role of HBO in the treatment of wounds, difficult-to-heal ulcers, and cellulitis [8, 9, 19, 20].

Research by Elif Ebru Özer et al. on patients with cellulitis after centipede bites accompanied with diabetes, who were treated by HBO, results showed that hyperbaric oxygen helped reduce pain, accelerated the wound healing process, and prevented the possibility of amputation [9].

David Wilkinson studied patients with cellulitis, and the results showed that the group of patients treated with hyperbaric oxygen helped anti-inflammatory and reduce edema better, shortened the time of treatment, and increased the survival rate more than 8.9 times (95%CI: 1.3–58.0; $p = 0.02$), reduced amputation rate ($p = 0.05$) [19]. Another research on 617 patients with venous leg ulcers (313 patients were treated by HBO and wound care, 304 patients in the reference group were only treated by wound care). Research results showed that the group of patients treated by HBO combined with wound care helped shorten wound healing time by 13.76 times; and reduced ulcer size by 2.64 times in comparison with the group not treated by HBO. At the same time, the study group had a lower score than the reference group in assessing pain level using the VAS scale [12].

A study by Douso (2009) on patients after surgery having cellulitis treated by HBO showed that the level of pain relief, edema reduction, and the period to heal wound scars was decreased significantly than patients treated only by antibiotics and wound care [8]. Sarah Perren et al. studied patients having ulcers due to diabetes treated by HBO compared to those who were treated by internal medic wound care. Patients were monitored and evaluated weekly. The results showed that the level of granular tissue growth, depth, and area of ulcers in the group treated by HBO had a superior improvement compared to the group not treated by hyperbaric oxygen ($p < 0.001$) [20]. In another research on 341 patients with cellulitis (275 patients were treated by hyperbaric oxygen, 66 patients were not treated by hyperbaric oxygen), the results showed that the group of patients treated by HBO had better wound healing and reduced mortality compared to the group not treated by HBO (OR = 0.42, 95%CI: 0.22–0.83, $p = 0.001$) [21].

LIMITATIONS OF THE STUDY

This study evaluated the effects of hyperbaric oxygen in the treatment of cellulitis. However, patients were divided into 2 treatment groups (study group: treated by HBO combined with intravenous Cephalosporins antibiotics, wound care, and underlying disease control; reference group: intravenous Cephalosporins antibiotics, wound care, and underlying disease control), there is no group treated with hyperbaric oxygen alone. The study has not isolated bacteria in cellulitis, antibiotics should be used experience.

CONCLUSIONS

Study on 48 patients with cellulitis treated by HBO combined with antibiotics and wound care compared to 41 patients with cellulitis receiving only antibiotics and wound care, there are some following conclusions: The pain relief level of the study group was better than the reference group (VAS scale after 1 day of treatment were 4.34 and 5.78; after 2 days of treatment were 2.46 and 4.17; after 3 days of treatment were 1.28 and 3.35). The period to reduce edema in the study group was shortened more than

the reference group after 3 days, 7 days, and 10 days of treatment. The circumference of the cellulitis area in the study group shrank better than the reference group after 3 days, 7 days, and 10 days of treatment. The average days of treatment in the study group were less than the reference group (8.33 ± 2.67 days and 13.17 ± 4.78 days). HBO should be used in treating cellulitis because it has pain-relieving, anti-inflammatory, and edema-reducing effects and reduces the number of days of treatment.

ARTICLE INFORMATION AND DECLARATIONS

Data availability statement: The data is highly reliable.

Ethics statement: The research was approved by the Biomedical Research Ethics Committee of the Institute of Maritime Medicine according to decision 05/2022/QĐ-YHB. Subjects participating in the study were completely voluntary and signed a consent form to participate in the study.

Author contributions: All authors contributed to the paper.

Funding: The research project received financial support from the Institute of Marine Medicine

Acknowledgments: The research team would like to express their deep appreciation to the study participants and Vietnam National Institute of Maritime Medicine for their unwavering support throughout this project.

Conflict of interest: The authors have no conflicts of interest to declare.

Supplementary material: None.

REFERENCES

1. Montravers P, Snauwaert A, Welsch C. Current guidelines and recommendations for the management of skin and soft tissue infections. Curr Opin Infect Dis. 2016; 29(2): 131–138, doi: 10.1097/QCO.0000000000000242, indexed in Pubmed: 26779771.
2. Esposito S, Bassetti M, Concia E, et al. Italian Society of Infectious and Tropical Diseases. Diagnosis and management of skin and soft-tissue infections (SSTI). A literature review and consensus statement: an update. J Chemother. 2017; 29(4): 197–214, doi: 10.1080/1120009X.2017.1311398, indexed in Pubmed: 28378613.
3. Sullivan T, de Barra E. Diagnosis and management of cellulitis. Clin Med (Lond). 2018; 18(2): 160–163, doi: 10.7861/clinmedicine.18-2-160, indexed in Pubmed: 29626022.
4. Halilovic J, Heintz BH, Brown J. Risk factors for clinical failure in patients hospitalized with cellulitis and cutaneous abscess. J Infect. 2012; 65(2): 128–134, doi: 10.1016/j.jinf.2012.03.013, indexed in Pubmed: 22445732.
5. Rrapi R, Chand S, Kroshinsky D. Cellulitis: A Review of Pathogenesis, Diagnosis, and Management. Med Clin North Am. 2021; 105(4): 723–735, doi: 10.1016/j.mcna.2021.04.009, indexed in Pubmed: 34059247.
6. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the infectious diseases society of America. Clin Infect Dis. 2014; 59(2): 147–159, doi: 10.1093/cid/ciu296, indexed in Pubmed: 24947530.
7. Cleveland Clinic; Hyperbaric Oxygen Therapy: What It Is & Benefits, Side Effects. https://my.clevelandclinic.org/health/treatments/17811-hyperbaric-oxygen-therapy (17.04.2024).
8. Douso ML. Hyperbaric oxygen therapy as adjunctive treatment for postoperative cellulitis involving intrapelvic mesh. J Minim Invasive Gynecol. 2009; 16(2): 222–223, doi: 10.1016/j.jmig.2008.12.007, indexed in Pubmed: 19249714.
9. Özer EE, Aksam B, Sönmez U, et al. Hyperbaric oxygen therapy of soft tissue necrosis due to centipede bite in a patient with diabetes. J Wound Care. 2022; 31(7): 586–588, doi: 10.12968/jowc.2022.31.7.586, indexed in Pubmed: 35797257.
10. Jones MW, Cooper JS. Hyperbaric Therapy for Wound Healing. StatPearls [Internet]. http://www.ncbi.nlm.nih.gov/books/NBK459172/ (20.06.2024).
11. Mathieu D, Marroni A, Kot J. Tenth European Consensus Conference on Hyperbaric Medicine: recommendations for accepted and non-accepted clinical indications and practice of hyperbaric oxygen treatmen. Diving Hyperb Med. 2017; 47(1): 24–32, doi: 10.28920/dhm47.2.131-132, indexed in Pubmed: 28641327.
12. Bai Z, Wang H, Sun H, et al. Effect of hyperbaric oxygen therapy on the patients with venous leg ulcer: A systematic review and meta-analysis. Asian J Surg. 2023; 46(10): 4131–4137, doi: 10.1016/j.asjsur.2023.01.068, indexed in Pubmed: 36740520.
13. Mathur MN, Patrick WG, Unsworth IP, et al. Cellulitis owing to Aeromonas hydrophilia: treatment with hyperbaric oxygen. Aust N Z J Surg. 1995; 65(5): 367–369, doi: 10.1111/j.1445-2197.1995.tb00661.x, indexed in Pubmed: 7741686.
14. Huang C, Zhong Y, Yue C, et al. The effect of hyperbaric oxygen therapy on the clinical outcomes of necrotizing soft tissue infections: a systematic review and meta-analysis. World J Emerg Surg. 2023; 18(1): 23, doi: 10.1186/s13017-023-00490-y, indexed in Pubmed: 36966323.
15. American Academy of Dermatology 2024 (AAD 2024). https://aad2024.org/ (18.01.2024).
16. Decision 2539/QĐ-BYT 2019 Guideline on technical procedures for treatment with hyperbaric Oxygen. Ministry of Health; 2019.
17. Cimşit M, Uzun G, Yildiz S. Hyperbaric oxygen therapy as an anti-infective agent. Expert Rev Anti Infect Ther. 2009; 7(8): 1015–1026, doi: 10.1586/eri.09.76, indexed in Pubmed: 19803709.
18. Flegg JA, McElwain DLS, Byrne HM, et al. A three species model to simulate application of Hyperbaric Oxygen Therapy to chronic wounds. PLoS Comput Biol. 2009; 5(7): e1000451, doi: 10.1371/journal.pcbi.1000451, indexed in Pubmed: 19649306.
19. Wilkinson D, Doolette D. Hyperbaric oxygen treatment and survival from necrotizing soft tissue infection. Arch Surg. 2004; 139(12): 1339–1345, doi: 10.1001/archsurg.139.12.1339, indexed in Pubmed: 15611459.
20. Perren S, Gatt A, Papanas N, et al. Hyperbaric Oxygen Therapy in Ischaemic Foot Ulcers in Type 2 Diabetes: A Clinical Trial. Open Cardiovasc Med J. 2018; 12: 80–85, doi: 10.2174/1874192401812010080, indexed in Pubmed: 30258500.
21. Devaney B, Frawley G, Frawley L, et al. Necrotising soft tissue infections: the effect of hyperbaric oxygen on mortality. Anaesth Intensive Care. 2015; 43(6): 685–692, doi: 10.1177/0310057X1504300604, indexed in Pubmed: 26603791.