Effect of hyperbaric oxygen therapy on complete blood count

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ABSTRACT

Complete blood count (CBC) is a routine diagnostic procedure for patients and a part of routine health inspection for healthy individuals. The effect of hyperbaric oxygen (HBO_2) therapy on CBC is not known. The objective of this study was to determine the effects of HBO_2 on blood parameters in CBC with long-term HBO_2 therapy.

In this study, patients received HBO_2 at the department of Underwater and Hyperbaric Clinical Medicine. CBC results were obtained at specific time points during HBO_2 therapy. The study recruited a total of 140 patients who met the research inclusion criteria. Patients were treated for 55.5±41 days. During the treatment period, they underwent HBO_2 sessions for an average of 35.9±24.9 times. Five groups were created as follows: before the treatment; between 1-20 sessions; between 21-40 sessions; between 41-60 sessions; and more than 60 sessions.

The results of the present study showed that a number of alterations occurred in CBC values in patients who received HBO_2. HBO_2 reduces the number of platelets, but this was not clinically significant. According to the results, HBO_2 does not have any effect on hemoglobin, hematocrit, red blood cells, mean corpuscular volume, mean corpuscular hemoglobin, red blood cell distribution width, mean corpuscular hemoglobin concentration, platelet count, platelet distribution width and mean platelet volume. Except for a temporary reduction in platelet count, HBO_2 has no effect on CBC parameters. Medical professionals may use the outcome of this study in their routine examinations, as it suggests that the changes in CBC driven by HBO_2 are not statistically significant, and could be disregarded. More research is needed to examine the effects of HBO_2 on other blood parameters.

INTRODUCTION

Complete blood count (CBC) is a routine diagnostic procedure for patients, and is a part of routine health inspection for healthy individuals [1]. The purpose of this fast and valuable test is to screen circulating cellular elements of blood [2]. CBC includes hemoglobin (HGB), hematocrit (HCT) and red blood cell indices (RBC), white blood cell index (WBC), mean corpuscular volume (MCV), red blood cell distribution width (RDW), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular hemoglobin concentration per volume of erythrocytes (MCH), platelet count (PLT), platelet distribution width (PDW) and mean platelet volume (MPV). Physiological factors such as age, sex, genetic background, race, region, pregnancy, smoking, altitude and comorbid factors may affect normal CBC values [3].

Hyperbaric oxygen (HBO_2) therapy is a medical treatment modality for using intermittent inhalation of 100% oxygen in a closed system where the entire body of a patient is under barometric pressure of more than 1.4 atmospheres absolute (ATA) [4]. HBO_2 and diving increase the release of erythrocytes via splanchnic contractions, which can alter the volume and shape of erythrocytes [5]. HBO_2 leads to a decrease in hematocrit, as well as a reduction in the platelet aggregation. Treatment prevents deformation of the form of red blood cells by increasing their flexibility. Thus, erythrocytes can cross the narrowed capillary membrane more easily [6].

KEYWORDS: blood cell count; hyperbaric oxygenation; blood cells; erythrocytes; blood platelets

Interestingly, hyperoxia has been shown to suppress erythropoiesis [7,8]. Thorsen, et al. tried to explain this effect with decreased erythropoietin production in response to hyperoxia, or a decrease in red blood cell production in bone marrow due to toxic effects of hyperoxia [13].

The goal of this study was to determine the effects of HBO_2 on blood parameters in CBC in long-term therapy sessions. Studies examining the effects of hyperbaric environment on CBC have commonly involved human participants [8,13,14,15]. The main reasons for contradictory results in these studies are low numbers of study participants, insufficient study range and a limited number of parameters. The present study aimed to recruit one of the largest series in this context, and comprised 10 different parameters of CBC values to evaluate their relation to HBO_2 in a long-term based patient follow-up.

MATERIALS AND METHODS

The study was conducted at the Department of Underwater and Hyperbaric Clinical Medicine at Istanbul University, between January 1 and December 31, 2011. In the enrollment period of study patients, there were no restrictions in the type of indication for HBO_2: Patients given HBO_2 at any frequency and duration were included. A total of 217 patients were enrolled, and 77 patients were then excluded according to the following exclusion criteria: oral or intravenous iron therapy during hospitalization; taking erythrocytes suspension and/or erythropoietin treatment for chronic kidney disease; no CBC records in the medical archive despite being treated as outpatient; and available CBC records at another health center. A total of 140 patients who received HBO_2 were qualified for the study. Subsequently, study groups were created.

Five groups were created: before treatment; between 1-20 sessions; between 21-40 sessions; between 41-60 sessions; and more than 60 sessions. Patients with multiple CBC records for an interval, CBC records corresponding to the 10th, 30th and 50th HBO_2 sessions, where available, were studied. The examination list of patients according to "study groups /received session" is as follows;

- Group 1: Pre-treatment measurements: 12.5 ± 5.6 days prior to start of HBO_2 treatment.
- Group 2: 1-20 session measurement: 9.3 ± 3.4 HBO_2 sessions.
- Group 3: 21- to 40-session measurement: 28.5±3 HBO_2 sessions.
- Group 4: 41- to 60-session measurement: 48.8±3.7 HBO_2 sessions.
- Group 5: 61 and >61 session measurement: 78.7±17.8 HBO_2 sessions.

Treatment was applied in a large pressure chamber (Zyron 12, Hypertech Corp., Turkey). HBO_2 was performed daily with intermittent 100% oxygen at 2.5 ATA for 120 minutes (Figure 1).

CBC measurements were acquired at the Laboratory of Biochemistry, Istanbul Faculty of Medicine, Istanbul University. Briefly, patients rested for 10 minutes before venipuncture and blood was taken from the antecubital vein. Then 5 mL of blood was collected in purple-capped tubes containing ethylenediaminetetraacetic acid, and the results were obtained with a multiparameter automated hematology analyzer (Cell-Dyn Sapphire, Abbott Diagnostics, U.S.).

CBC results were obtained within the treatment time. Patients were accepted with different HBO_2 indications, and consulted with various clinics. HGB, RBC, HCT, MCV, MCH, MCHC, PLT, RDW, PDW and MPV values were examined within CBC. White blood cells (WBC) were excluded from the evaluation due to variability issues in WBC numbers during infection and healing.

The results were transferred to the Microsoft Excel 2010 program. Values of the five groups were examined as minimum-maximum values, standard deviation, medians and within their change charts. Statistical assessments of the results were performed by SPSS 17.0 (SPSS Inc., Chicago, Illinois, U.S). A paired sample t-test was used to compare the study groups; a P-value of ≤0.05 was considered statistically significant.

RESULTS

The patient list consisted of 99 males (70.7%) and 41 females (29.3%). The average age was 48.9±16.9. Of the patients 72, (51.4%) were hospitalized, while 68 (48.6%) were treated as outpatients. While the majority of patients (95.7%) received a routine treatment, six patients (4.3%) required an urgent treatment. The average duration of a treatment session per patient was 55.5±41 days, and during this period, they underwent HBO_2 sessions for an average of 35.9±24.9 times (Table 1). For all participants, the distribution of HBO_2 indications and the distribution of the total number of sessions are presented (Tables 2 and 3,

FIGURE 1. HBO_2 treatment scheme

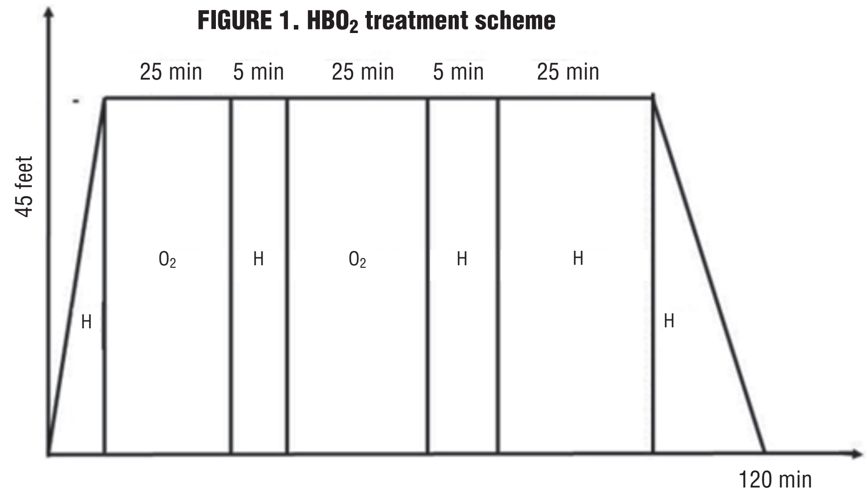


TABLE 1: Descriptive values of the study N=140

variants	mean ± SD
age – year	48.9 ± 16.9
male gender %	70.7
female gender %	29.3
hospitalized %	51.4
outpatient %	48.6
routine treatment	95.7
emergency treatment	4.3
average treatment time per patient	55.5 ± 41
average treatment session per patient	35.9 ± 24.9

respectively). CBC parameters for each HBO_2 group are represented in detail (Table 4). Average HGB values decreased in patients at earlier sessions during HBO_2. As the treatment continued, the values seemed to improve, but those changes were not statistically significant (Figure 2, Table 4).

RBC counts seemed to decrease at the beginning of the treatment, but increased toward the end of the sessions. In the statistical analysis, only the 41-60 session measurement was observed as significantly increased compared to the 1-20 session measurement (P=0.0). There were no other significant changes among other values (Figure 2, Table 4).

In HCT measurements, a rapid decrease was apparent in the first two measurement steps. In the statistical analysis, only the second measurement value was

TABLE 2: Distribution of patients according to number of sessions

number of sessions	N	%
1-20	49	35.0
21-40	39	27.9
41-60	34	24.2
> 61	18	12.9
TOTAL	140	100

TABLE 3: Distribution of patients according to indications

indications	N	%
diabetic foot ulcers	51	36.4
chronic refractory osteomyelitis	14	10
other chronic wounds	20	14.3
avascular necrosis	11	7.9
sudden hearing loss	17	12.1
carbon monoxide poisoning	1	0.7
central retinal artery occlusion	3	2.1
decompression sickness	2	1.4
crush injury	6	4.3
radionecrosis	10	7.1
risky flap application	2	1.4
necrotizing of tissue infections	3	2.1
TOTAL	140	100

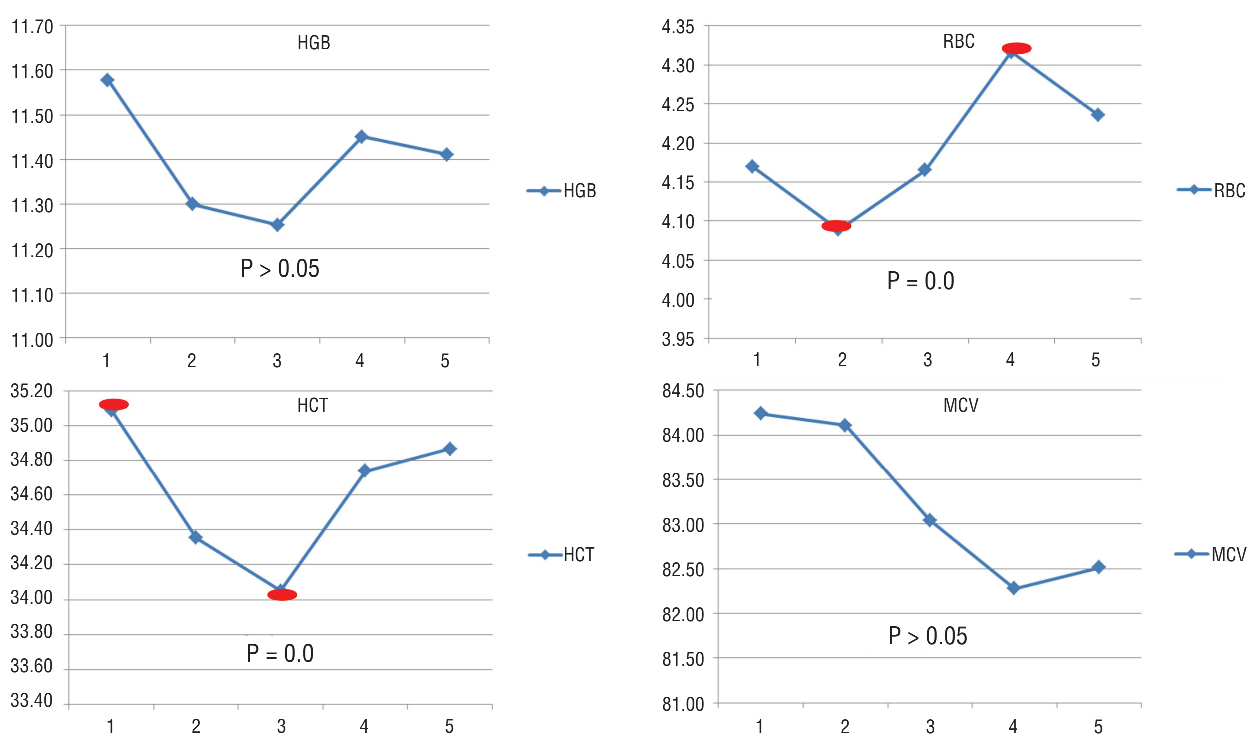
TABLE 4: Mean and standard deviation values of the CBC parameters

parameters	Group 1	Group 2	Group 3	Group 4	Group 5
HGB	11.6 ±1.9	11.3±2	11.3±1.6	11.5±1.6	11.4±1.7
RBC	4.2±0.7	4.1±0.7	4.2±0.6	4.3±0.8*	4.2±0.6
HCT	35.1±5.6	34.4±5.9¥	34.1±5	34.7±4.4	34.9±5.5
MCV	84.2±6.9	84.1±6.4	83±6.5	82.3±5.1	82.5±5.6
MCH	27.8±2.7	27.7±2.5	27.5±2.5	27.1±2	27.1±2.2
MCHC	33.1±1.1	32.9±1.1	33±1	32.9±0.9	32.7±0.9
PLT	313.5±123.8	286.8±98.4Ψ	274.4±82.6Ψ, ʅ	250.1±73.5Ψ, ʅ,α	231.8±66.8Ψ, ʅ
RDW	14.2±2.3	14.7±2.4β	14.8±2.8	15.1±2.2	15.4±2
PDW	16.2±2.6	16.6±1.8	16.5±1.6γ	16.9±1.5	17.4±1.2ϕ
MPV	8.3±1.2	8.4±1.3	8.6±1.5	8.7±1.2	8.9±1.8

*: p≤0.05, Group 4 RBC compared with Group 2, ¥: p≤0.05, Group 2 HCT compared with Group 1, Ψ: p≤0.05, Group 2-3-4-5 PLT compared with Group 1, ʅ: p≤0.05, Group 3-4-5 PLT compared with Group 2, α: p≤0.05, Group 4 PLT compared with Group 3, β: p≤0.05, Group 2 RDW compared with Group 1, γ: p≤0.05, Group 3 PDW compared with Group 1, ϕ: p≤0.05, Group 5 PDW compared with Group 2.
*: Mean and standard deviation values of the CBC parameters.

hemoglobin (HGB), hematocrit (HCT), red blood cell indices (RBC), white blood cell index (WBC), mean corpuscular volume (MCV), red blood cell distribution width (RDW), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular hemoglobin concentration per volume of erythrocytes (MCH), platelet count (PLT), platelet distribution width(PDW), mean platelet volume(MPV). *: p≤0.05 is statistically significant

FIGURE 2. CBC parameters graphs



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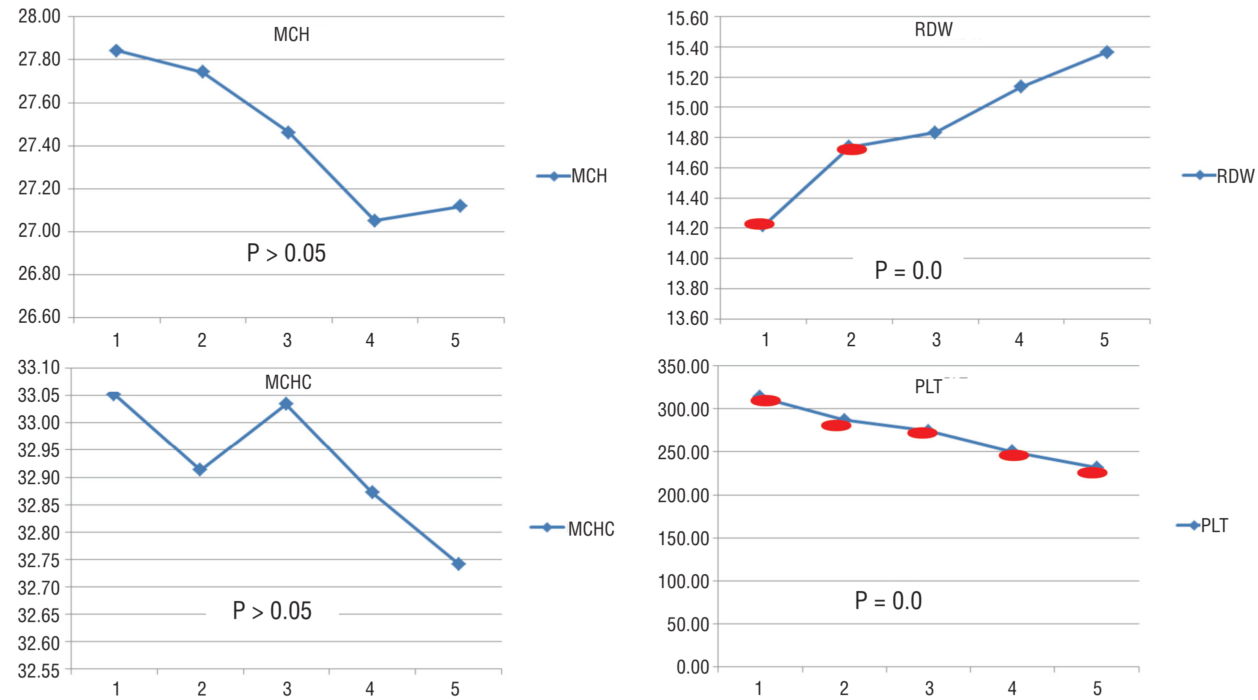

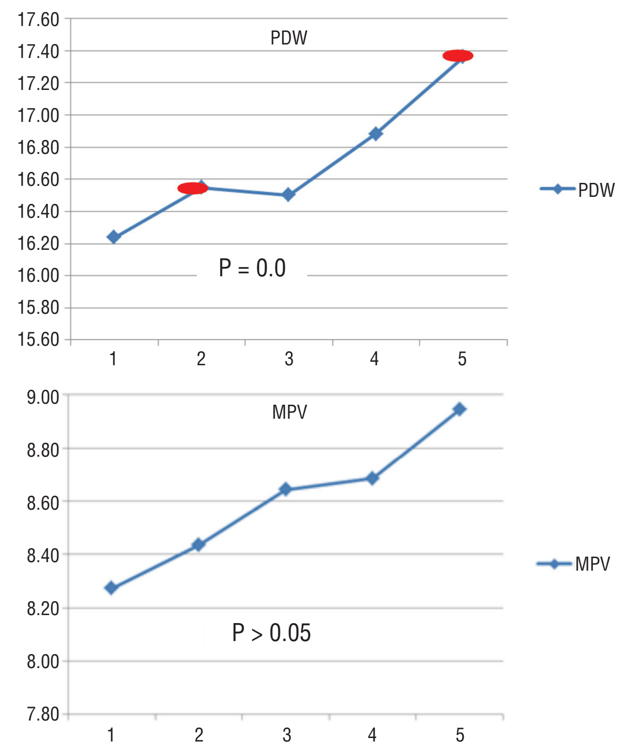

significantly decreased compared to the first measurement value (P=0.0). There were no statistically significant changes in any of the other measurements (Figure 2, Table 4).

After the first measurement, MCV had decreased slightly, but the difference did not reach significance. MCH showed a decline toward the end of the treatment but then showed a slight increase at the end. There was no statistically significant change in the total value. MCHC showed a fluctuated trend initially, but declined at the end of the treatment. There were no significant changes between values (Figure 2, Table 4).

Reduction of the platelet count was seen through the 41-60 session measurement. The first four measurements were found to be significantly reduced. Second, third, fourth and fifth values decreased significantly as compared to the first one (P=0.0, P=0.0, P=0.0, P=0.0, P=0.0, respectively). Third, fourth and fifth measurements showed a statistically significant decrease compared to the second measurement (respectively; P=0.0, P=0.0, P=0.0). Only the fourth measurement was observed to decrease significantly compared to the third measurement (P=0.0). No statistically significant changes were observed in other PLT measurement values (Figure 2, Table 4).

The red cell distribution width tended to increase until the end of the treatment. However, only the second measurement showed significant increase compared to the first (P=0.0). There were no other significant changes in all measurements (Figure 2, Table 4).

In the platelet distribution width, an increase in subsequent values was seen until the end of the treatment. However, the increase in the third measurement was statistically significant compared to the first, and the fifth measurement was significantly increased compared to the second (P=0.0, P=0.0, respectively). There were no significant changes among all other measurements. Despite the graph showing a rapid increase, especially after the first measurement, there was no significant change in mean platelet volume (Figure 2, Table 4).

DISCUSSION

Based on our clinical experience, CBC values may change in patients receiving HBO_2 therapy, but not statistically significantly. It is believed that a decrease, particularly in HGB and HCT levels, occurs in routine CBC and biochemistry profiles during follow-up. In the planning stage, the goal of our study was to evaluate the effects of HBO_2 on CBC parameters. Therefore, no restriction was made in terms of the total number of HBO_2 sessions or the indication type when selecting patients. To have a cross-sectional structure, it was decided to evaluate all patients undergoing treatment in a year's time. Inevitably, blood content and the interpretation of the results had various limitations. The patients included in the scope of our study represented a wide range of indications. CBC parameters in patients undergoing HBO_2 are likely to be affected due to factors such as dressing, minor amputation, negative pressure wound closure system, debridement, nutrition and comorbid conditions. Furthermore, additional medical and supportive treatments administered to the patients may have different effects on CBC.

Chronic inflammation is present in many indications for HBO_2. Inflammation affects hematopoiesis. In particular, the presence of chronic inflammation suppresses the production of blood cells in bone marrow. Inflammation evokes the release of some cytokines, which are known to suppress the growth of erythroid cells. IL-1 suppresses the erythropoietin capacity and prevents the stimulation of erythroid precursors [9]. IL-1 and TNF-α have been shown to inhibit erythropoietin production in cell cultures [10]. HBO_2 acts by reducing the levels of IL-1, IL-6, and TNF-α. In this way, HBO2 prevents the effects of inflammation on blood production, and allows the continuation of this process [11].

The outcome of limb recovery is significantly associated with HGB levels in patients with diabetic foot [12]. Each treatment promotes healing. Before the study, our clinical experience led us to foresee a decrease in HGB values in patients receiving HBO_2. Indeed, we have shown a decrease in HGB values at the beginning of the treatment. This change is consistent with an experimental study conducted by Thorsen, et al. [13]. On the other hand, longer follow-up of these patients revealed that the values increase to the state resembling the pretreatment values. We concluded that HBO_2 has no negative impact on HGB levels.

Thorsen, et al. followed 16 patients treated with HBO_2 for 21 days, and their study showed a decrease in RBC values [13]. In spite of declining at the beginning of our study, RBC values showed a statistically significant increase at follow-up. We can attribute this temporary decrease to the harmful effect of high-pressure oxygen on erythrocyte morphology, causing reduction in the red blood cell density [7]. Significant increases in subsequent measurements can be explained by Butler's hypothesis, which states: "RBC increases with acclimatization in response to hypoxia which occurs during the dive" [14].

Measurement of HCT average values showed a decrease, especially in the second and third measurement steps. The second measurement was reduced significantly compared to the first measurement. Those changes were statistically significant, but the HCT values were within the normal ranges clinically. In a study by Handy, et al., red blood cells are claimed to be unaffected by HBO_2 [15]. Initially, the study had shown that the pressure reduced the HCT values temporarily, and following this short-term effect, the same values appeared again within 24 hours [16]. This study attained the same conclusions, which is in concordance with previous reports.

Adil, et al. emphasized that MCV values decline notably with diving, and these changes are associated with the hematopoietic system [8]. In the present study, the trend of average MCV measurements showed a decrease in the current measurement. Despite the decrease, the values were recorded ranging from 82-84 fL, defined as within normal clinical range.

The normal clinical range of PLT value is quite large, ranging between 150,000 and 400,000/mm^3 [17]. Moon, et al. showed a decrease in platelet levels of 10 divers in the range of 450-600 meters [18]. However, our patients were compressed to 45 feet for HBO_2 in comparison, so it is not possible to claim its application as similar to our treatment. On the other hand, constantly decreasing measurements in a downward trend were statistically significant. The reduction in PLT values was clinically insignificant since the values remained within normal clinical range.

In the evaluation of other parameters, no statistically significant differences were found in this study. MCH values were suggestive for hypochromic microcytic anemia, but it was not statistically significant. Adil, et al. showed that low MCH values are concordant with the decrease in hemoglobin [8]. The MCHC values showed an average irregular trend initially, and demonstrated a tendency to decrease toward the end of the study. This study, which is consistent with the study by Handy, et al., showed that HBO_2 does not significantly change the MCHC [15]. When we examined the graph formed by RDW measurements, we observed that an increase continued until the end of the treatment.

These changes were accepted as clinically insignificant. HBO_2 also affects PDW values, but the existing values were within the physiological limits. Despite the graphic showing a rapid rise in average MPV after the first measurement, no significant change was found.

STRENGTHS AND LIMITATIONS

This study showed the effects of HBO_2 on the CBC parameters in general. This study intended to present a reliable perspective to the clinicians in routine evaluation of the patients undergoing HBO_2 in terms of CBC parameters. Despite its limitations, the study has been strengthened by the inclusion of a variable and extensive list of patients, along with a long-term follow-up of those patients.

This study shed light on other studies investigating the effects of HBO_2 on CBC. In order to improve outcome of the current study, we believe that recruiting younger age groups with a more stable clinical state, avoiding the patients with comorbid conditions and preferring planned HBO_2 over urgent therapies will be suitable via decreasing certain biases. HBO_2 sessions/blood collections should be preplanned, and complete blood counts should be performed at the same center as our study.

CONCLUSION

This study has shown that hyperbaric oxygen treatment has no effect on CBC parameters except for a temporary reduction in platelet count. For medical professionals in hyperbaric medicine, it is essential to interpret the changes in blood parameters driven by the effects of comorbid factors. Approach to the changes in CBC must be multidisciplinary due to comorbid factors. According to these results, physicians should consider HBO_2 as being a less probable factor among other causes for CBC changes.

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Conflict of interest statement
The authors declare that no conflicts of interest exist with this submission.

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