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The Effect of Hyperbaric Oxygen in Reducing Blood Cortisol Levels in Patients with Sleep Disorders

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KEYWORDS
Sleep disorders; Cortisol; HBO

ABSTRACT
Sleep disorders disrupt normal sleep patterns, including timing, duration, and quality, often linked to elevated cortisol levels and high nerve metabolism requiring oxygen. Hyperbaric oxygen therapy (HBO), delivering pure oxygen in high-pressure settings (≥1.4 ATA), may alleviate hypoxia and reduce cortisol, offering potential treatment for sleep disorders. This research uses a quasi-experimental design with a randomized pre-post control group design. The population studied was male sleep disorder sufferers, aged 25-40 years at the psychiatric poly of Dr. Ramelan Surabaya Hospital, with a sample of 9 members of the Indonesian Navy who met the inclusion and exclusion criteria. This research is related to development research in the field of health and maritime, with a focus on diving and hyperbaric oxygen therapy, which is expected to be published in the International Journal indexed Shinta 2. This research has the potential to enrich the understanding of the effects of Oxygen Hyperbaric (OHB) therapy in overcoming sleep disorders, as well as contributing to the health and maritime sectors. The research concluded that OHB therapy in sleep disorder patients resulted in a slight reduction in mean cortisol levels (from 79.09 ng/ml to 76.38 ng/ml). Although the majority of patients (56%) experienced a decrease in cortisol levels after therapy, there was no statistically significant effect of OHB therapy on cortisol levels in sleep disorder patients.

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Introduction

Sleep disorders are one of the most common clinical problems (Hauri, 2021). Quality sleep is one of the basic human needs to maintain a healthy body and mind. During sleep, the body regenerates cells, strengthens the immune system, and processes information received by the brain throughout the day. If a person does not get enough sleep or the quality of sleep is poor, the body functions physically, mentally, socially, and emotionally. In the long run, lack of sleep can also increase the risk of various diseases and reduce one's quality of life (Eshak, 2022; Karna et al., 2023). Sleep disorders are estimated to affect about 10 to 30% of the general population. Nevertheless, the incidence rate exhibits variability within the population, influenced by a diverse range of factors. For example, certain ethnic groups, sociodemographic conditions, one's medical health, lifestyle habits

such as diet or physical activity, support from the family structure, and work environment stresses are also influential (Eshak, 2022).

Sleep disturbances are often associated with depression and stress-induced disorders, which are also associated with elevated cortisol levels, changes in norepinephrine (NE), as well as disturbances in hypothalamic-pituitary-adrenal (HPA) axis function (Bao & Swaab, 2019; Knezevic et al., 2023). When the HPA (hypothalamic-pituitary-adrenal) axis is overactive, it can interfere with sleep quality. Overactivity of this axis can cause sleep to become fragmented, reducing deep sleep time and reducing total sleep duration. Stress is one of the triggering factors for this HPA axis activation. Stress activates the hypothalamus, which stimulates the release of corticotropin hormone (CRH), which in turn triggers the release of other stress hormones, such as cortisol (Kageyama et al., 2021).

When the HPA axis is activated, one of the outcomes is the enhanced production of adrenocorticotropic hormone (ACTH), which subsequently prompts the adrenal glands to release the hormone cortisol. In inflammatory conditions, where the body is experiencing inflammation, there are increased levels of pro-inflammatory cytokines such as "interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) in the blood". These cytokines play an important role in stimulating the formation of ACTH, which in turn increases the production of cortisol, a hormone that plays a role in the body's response to stress and inflammation (Jesica & Friadi, 2019; Pereira et al., 2018). This increase in cortisol may be the main cause of sleep disturbances. Sleep disorders can also involve high nerve metabolism to maintain the electrical potential of nerves that require large amounts of oxygen, resulting in significant oxidant production (Knezevic et al., 2023; Palagini & Bianchini, 2022).

Hyperbaric oxygen therapy (HBO) involves a medical process where the patient is placed in a chamber designed to withstand higher than normal pressure. Inside the chamber, the patient breathes pure (100%) oxygen, which allows the oxygen to dissolve better in the blood and reach the body tissues that need recovery or treatment (Kirby et al., 2019).

The therapy was initially used in maritime cases, namely in the field of diving and hyperbaric, but in its development it can be widely used as an additional therapy for various clinical pathological cases, especially those related to hypoxia or ischemic conditions, one of which is sleep disorders (De Wolde et al., 2021; Shinomiya & Asai, 2020). HBO interventions to address hypoxia, lower inflammation, normalize HPA axial abnormalities, lower nocturnal CRH hyperactivity, and lower cortisol may be beneficial in treating sleep disorders (Oyaizu et al., 2018). Therefore, it is necessary to further study the effect of HBO on sleep disorders through a decrease in the hormone cortisol. This study used the population of Dr. Ramelan RSPAL psychiatric polyclinic patients and did not involve students.

Based on the explanation in the background, the researcher formulated the problem as follows: "How does hyperbaric oxygen therapy (HBO) affect the reduction of blood cortisol levels in individuals with sleep disorders?"

As the basis for the Hyperbaric Medicine consensus on the use of HBO in people with sleep disorders in carrying out daily tasks, preventing disease, improving health and quality of life and preventing premature death so that HBO can be used as an adjuvant therapy along with standard therapies and drugs that have been established.

The results of this study can be used for scientific information in the development of science about the effects and mechanisms of HBO on the reduction of blood cortisol levels in patients with sleep disorders so that it can be useful as a basis for further research.

This research is a form of reflection and realization of the Regulation of the Minister of Health Number 61 of 2013 concerning Matra Health. Matra Health is a special form of health effort that is organized to improve physical and mental abilities to adjust to a meaningfully changing environment, both in the land, sea, and air environments where there is hyperbaric health. Therefore, it is important to take a concrete action, namely research on the effect of hyperbaric oxygen in reducing blood cortisol levels in patients with sleep disorders.

Materials and Methods

Research Design

This study used a quasi-experimental design with a randomized pre-post control group design approach. This means that participants were randomly divided into treatment and control groups. Measurements were taken before (pre) and after (post) the intervention to see the difference in effect. The research subjects consisted of 9 men aged 25-40 years who experienced sleep disorders, and underwent treatment at the psychiatric polyclinic of Dr. Ramelan Naval Hospital Surabaya. The study subjects were divided into three groups: a control group that did not receive HBO therapy (K1), and two treatment groups that received hyperbaric oxygen therapy (HBOT) with 100% pure oxygen at a pressure of 2.4 ATA. This therapy was carried out for 3 sessions of 30 minutes each, with a 5-minute break to breathe using normal air, for 5 consecutive days (K2). Cortisol levels were measured using the enzyme-linked immunosorbent assay (ELISA) method, one day before the first session of HBO and one day after the fifth session of HBOT.

Place and Time of Research

The location and time of the research was carried out at the Laboratory of Faal and Hyperbaric Lakesla Drs. Med. R. Rijadi S., Phys Surabaya in February-August 2023

Data Collection or Collection Procedure

Study participants were asked to complete a questionnaire to gather information that helped ensure sample homogeneity. They were also asked to sign a statement of willingness to participate in the study, including complying with the rules and undergoing research procedures until completion. In addition, participants were given an explanation of their rights and obligations during the study. Prior to the implementation of the study, an ethical feasibility test was conducted at Lakesla Surabaya.

Preparation of Research Subjects

Patients with sleep disorders admitted to the psychiatric clinic of Dr. Ramelan Surabaya Naval Hospital were selected based on inclusion and exclusion criteria. Participants should be in optimal physical condition, which means they should not engage in strenuous activities that could affect the test results, as well as ensuring they get enough sleep. In addition, participants should avoid habits such as heavy meals, drinking coffee or smoking before the test as these may affect the results. After fulfilling these conditions, participants underwent hyperbaric oxygen therapy at a predetermined location at Lakesla Drs. R. Rijadi Sastroepanoelar, Phys, Surabaya to see its effect on their sleep disorders.

Implementation of HBO Treatment

HBO therapy was performed using the US Navy's 9-dose protocol, which involves administering pure oxygen (100%) at a higher pressure than normal air inside a steel high-pressure hyperbaric chamber (RBT). The chamber was maintained at 28°C with 50% air humidity. The therapeutic procedure involves inhaling oxygen at a pressure of 2.4 ATA for three sessions of 30 minutes each, with two 5-minute breaks to breathe normal air, performed for five consecutive days.

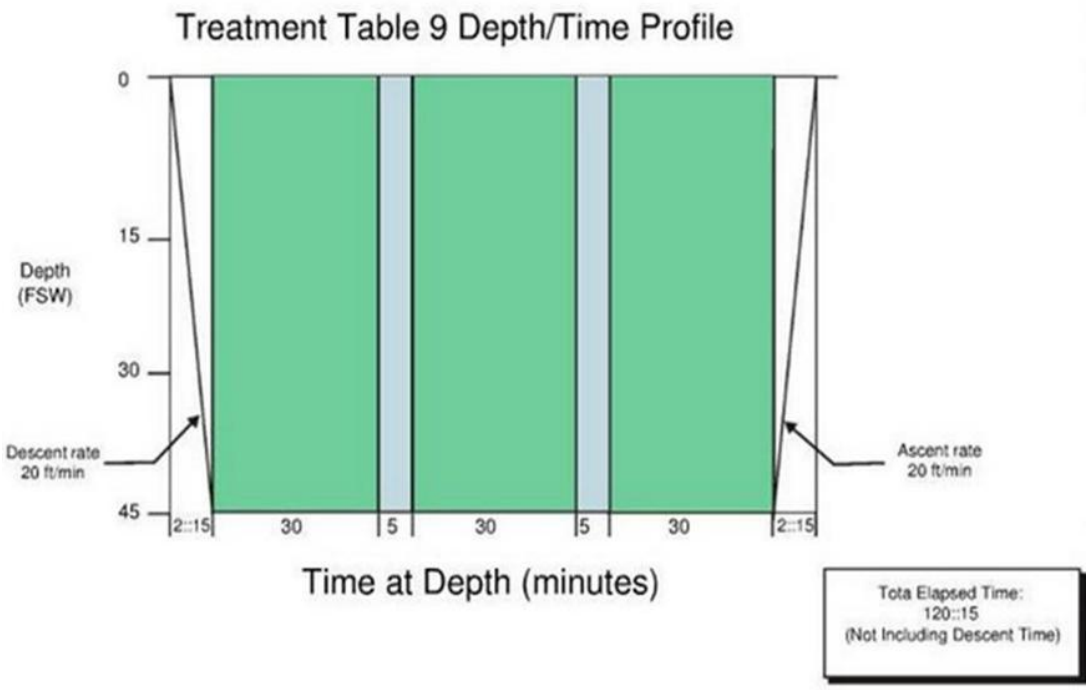

Figure 1. HBO Dosage Table 9 US Navy

Cortisol Level Data Collection

Cortisol levels in blood serum taken through venous blood using a 3cc syringe at 06.00 – 08.00 WIB one day before HBO treatment and 1 day after HBO treatment in both K1 and K2 groups. The method used is ELISA with micrograms per deciliter (mcg/dL).

Data Analysis

Before choosing the right statistical analysis method, the research data will first be tested using SPSS version 22. Because the variables measured in this study use a numerical scale, the Shapiro-Wilk normality test will be applied to determine whether the data distribution follows a normal distribution or not. The results of this normality test will be the basis for determining whether to use parametric or non-parametric statistical tests in further analysis. If the data is normally distributed, Levene's homogeneity test is conducted to test the similarity of variation (variance) between groups or samples. This test is important to ensure that the groups being compared have similar levels of data distribution. If the variation between groups is found to be homogeneous (the same), then the Paired T-Test is used, which is suitable for comparing two groups of paired and normally distributed data. However, if the variation between groups was not homogeneous, the data did not meet the

assumptions required for a parametric test, so the Wilcoxon test, which is a non-parametric test, was used as an alternative to test for differences between groups.

Research Flow

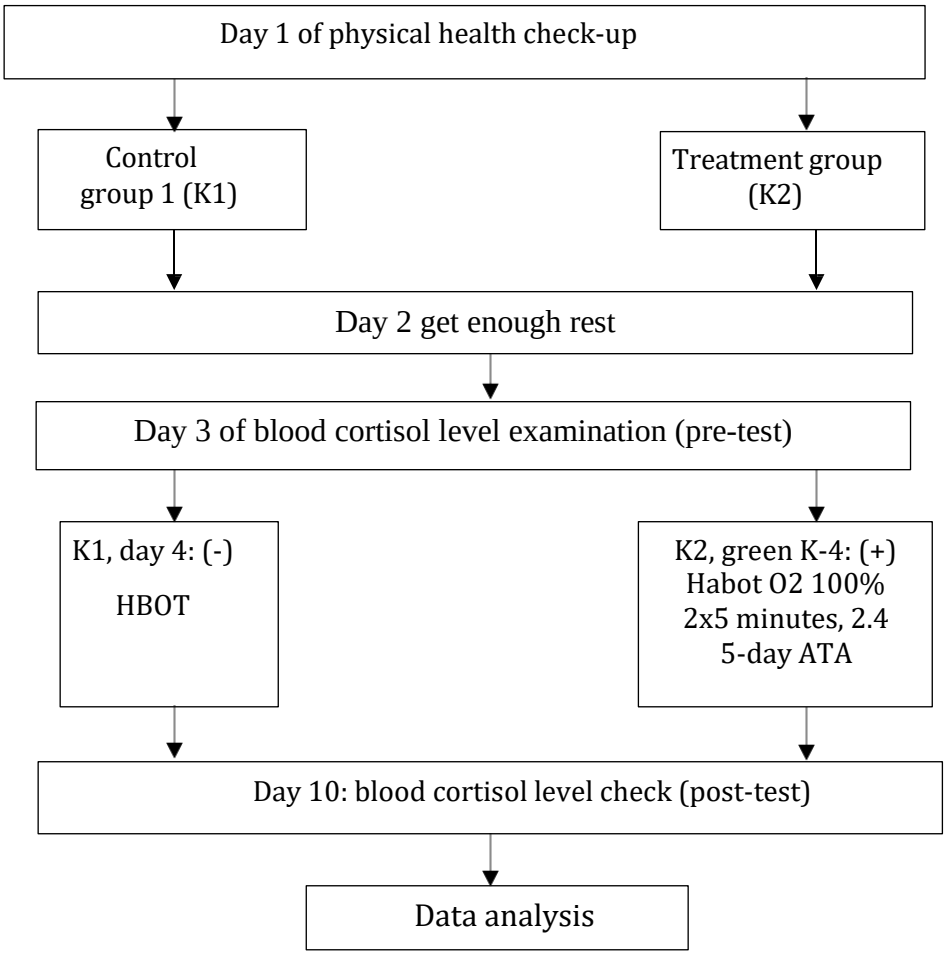

Figure 2. Data Analysis

Results and Discussions

Cortisol Examination Results

This study aims to determine the effect of hyperbaric oxygen therapy (OHB) on cortisol levels in patients with sleep disorders. Cortisol levels were measured using the ELISA (Enzyme-Linked Immunosorbent Assay) technique, which was applied to two groups of patients: those without sleep disorders and those with sleep disorders. Measurements were taken before the start of OHB therapy and after completion of therapy on day 10. The blood samples used were taken through a vein, according to the procedures set up in the study to ensure accurate and consistent results.

Table 3. Cortisol levels in patients with sleep disorder before and after OHB therapy

	Cortisol levels (ng/ml)	
	Before OHB therapy	**After OHB therapy**
mean	79.09	76.38

SD	59.87959	26.50992
Min	9.94	41.73
Max	205	123.1

The results showed that the average cortisol levels in patients with sleep disorders were 79.09 ng/ml before hyperbaric oxygen therapy (OHB) and 76.38 ng/ml after OHB therapy. These results can also be presented in the form of the following graphs:

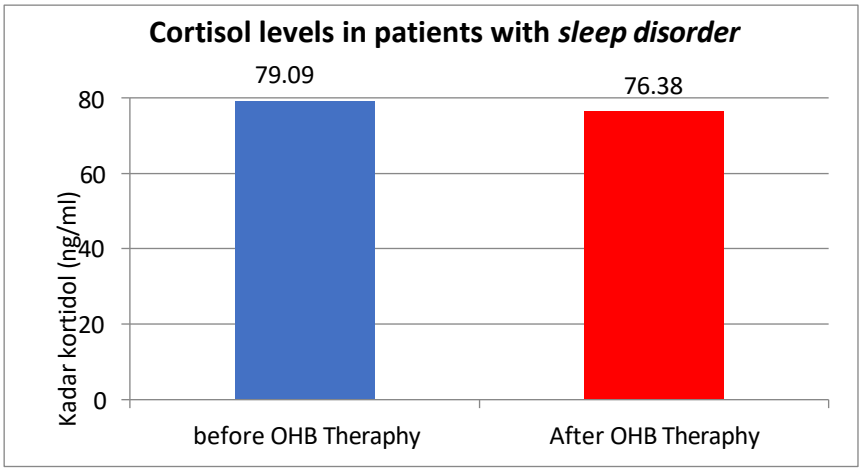

Figure 3. Cortisol levels of sleep disorder patients before and after OHB therapy

Figure 3. shows that the average cortisol levels in sleep disorder patients after OHB therapy are lower than before OHB therap.

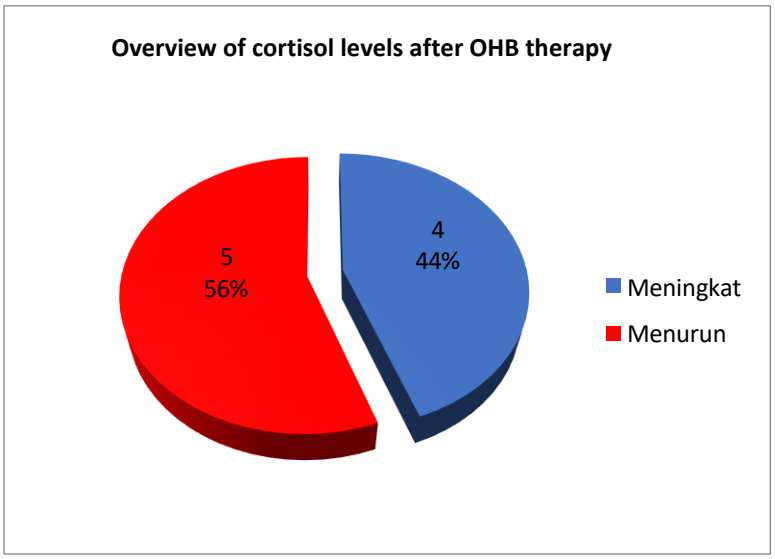

Figure 4. Overview of cortisol levels in sleep disorder patients after OHB therapy

The results shown in Figure 4 illustrate the distribution of changes in cortisol levels in patients with sleep disorders after hyperbaric oxygen therapy (OHB). Most patients, namely

56% or 5 people showed a decrease in cortisol levels after therapy. However, 44% of other patients or 4 people actually experienced an increase in cortisol levels after OHB therapy.

Statistical Analysis of Cortisol Examination Results

All data from the examination of cortisol levels by ELISA were tested for normality using the Saphiro-Wilk test,

Table 4. Normality test

Tests of Normality

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Kadar_kortisol	Before OHB therapy	.178	9	.200*	.923	9	.418
	After OHB theraphy	.207	9	.200*	.945	9	.634

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

The normality test results show that the data on cortisol levels before and after hyperbaric oxygen therapy (OHB) do not deviate from normal distribution, this is because the significant value is 0.418 (p>0.05), and after OHB therapy is 0.634 (p>0.05). A p value greater than 0.05 for both groups of data indicates that the data can be considered normally distributed, which means that the data follows the expected distribution pattern in statistical analysis that requires the assumption of normality, such as parametric tests that will be carried out next.

Further data testing using the Lavene homogeneity test.

Table 5. Homogeneity test

Test of Homogeneity of Variance

		Levene Statistic	df1	df2	Sig.
Kadar_kortisol	Based on Mean	2.928	1	16	.106
	Based on Median	2.341	1	16	.146
	Based on Median and with adjusted df	2.341	1	10.893	.155
	Based on trimmed mean	2.657	1	16	.123

Levene's homogeneity test showed a p value of 0.106, which is greater than 0.05, it can be concluded that the variance between data groups is not significantly different, so the data is considered homogeneous. Since the data is also normally distributed, the next step is to conduct a Paired T Test to compare the difference between the two conditions measured, in this case before and after therapy.

Table 6. Paired T Test

Paired Samples Test

	Paired Differences					t	df	Sig. (2-tailed)
Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper				

Pair 1	Kadar_kortisol_sebelum_OHB - Kadar_kortisol_sesudah_OHB	2.71220	65.69660	21.89887	-47.78666	53.21110	.124	8	.904

Statistical analysis by paired t-test showed that the p value obtained was 0.904, which was greater than 0.05. In statistical tests, a p value greater than 0.05 indicates that the difference found between cortisol levels before and after OHB therapy is not significant enough to be considered as a related result. Therefore, it can be concluded that OHB therapy did not have a significant effect on cortisol levels in sleep disorder patients in this study.

Discussion

This study focuses on how HBOT therapy affects cortisol levels in patients with sleep disorders. In this regard, several previous studies have suggested that cortisol levels and sleep disorders are interconnected, where sleep disorders can affect cortisol levels, and conversely, changes in cortisol levels can also impact a person's sleep quality (Hill et al., 2018). Chrousos et al and Adam and Kumari revealed a link between high cortisol levels during the day and sleep disorders. However, in contrast, the study by Castro Diehl et al. found no association between elevated cortisol levels and the occurrence of sleep disorders. The study conducted by Hansen et al. showed different findings, namely that insomnia is associated with lower cortisol levels during the day. However, from our study, we found that patients with Sleep Disorder had higher average cortisol levels. This could be interesting and new evidence that patients with Sleep Disorder have higher average cortisol levels. This finding is in line with a study conducted by R.A Hackett et al, which states that participants with sleep disorders on average have daily cortisol hormone levels that tend to be high.

The findings of this study revealed that after patients with sleep disorders underwent hyperbaric oxygen therapy (OHB), there was a decrease in average cortisol levels from 79.09 ng/ml to 76.38 ng/ml. This suggests that OHB therapy may contribute to the reduction of cortisol levels in patients with sleep disorders. Furthermore, the majority of patients (56%) experienced a decrease in cortisol levels after therapy. This study supports the findings from Woo et al., which state that HBO therapy can reduce inflammation in the body, which in turn reduces the stress caused by that inflammation. This lower stress also reduces the body's need to produce cortisol, a hormone secreted by the adrenal glands in response to stress. Based on the results of this study, the majority of patients experienced a reduction in cortisol levels after undergoing HBO therapy, which suggests that this therapy can help lower cortisol levels associated with stress and inflammation.

The results of data analysis revealed no significant difference in cortisol levels in sleep disorder patients before and after OHB therapy ($p > 0.05$). This indicates that OHB therapy did not significantly impact cortisol levels. These findings are consistent with prior research by Castro Diehl et al., which also found no significant relationship between elevated cortisol levels and sleep disorders. Conversely, studies by Chrousos and Adam & Kumari have reported a positive association between high cortisol levels and sleep disruptions. Additionally, Woo et al. observed that hyperbaric oxygen therapy can reduce inflammation, potentially mitigating stress and subsequently decreasing cortisol levels. This discrepancy could be attributed to variations in the body's response to OHB therapy among patients. The lack of a significant effect in the present study may suggest that the 2.4 ATA pressure used in OHB therapy is insufficient to induce hormonal stress responses capable of altering

cortisol levels in this patient population. Further studies are needed to elucidate these mechanisms and determine whether higher pressures or longer durations could yield more definitive effects.

Conclusion

From this study, it can be concluded that although the average cortisol levels in sleep disorder patients decreased after hyperbaric oxygen therapy (OHB), this decrease was not statistically significant. The results reported that the average stress hormone (cortisol) level in sleep disorder patients before undergoing hyperbaric oxygen therapy (OHB) was 79.09 ng/ml. After therapy, the average cortisol level decreased to 76.38 ng/ml. And most patients experienced this decrease. However, there was no statistically significant difference due to OHB therapy.

Researchers hope that future research can further explore how hyperbaric oxygen therapy (HBO) can reduce cortisol levels, by explaining the processes or mechanisms involved. This is important to better understand the effects of therapy on this stress hormone. We also hope that the results of this study can be used as a reference in future studies that examine the effectiveness of HBO therapy in regulating cortisol levels, and clarify the relationship between this therapy and changes in cortisol levels in patients with sleep disorders.

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