Correlation Analysis Between Hyperbaric Oxygen Therapy and Quality of Sleep

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ABSTRACT. A good sleep quality and quantity is essential to achieve a healthy body and mind. Hyperbaric oxygen therapy (HBOT) is a treatment involving a specialized chamber where pressure and pure oxygen will be supplied, which can influence inflammation, oxidative stress, cortisol, and melatonin, which may influence sleep quality. Therefore, the purpose of this study is to identify if there is a significant and positive correlation between hyperbaric oxygen therapy and sleep quality. In this study, participants' sleep quality is assessed by Pittsburgh Sleep Quality Index before and after undergoing HBOT treatment. The participants are also divided into 5 groups based on the number of HBOT treatment that they have undergone. The result of this study is that there is a significant positive correlation between hyperbaric oxygen therapy and sleep quality (p-value<0.001), along with sleep quantity (p-value<0.001). And subjects can acquire the best sleep quality after more than 41 hyperbaric oxygen therapy at 3 ATA (p-value <0.07).

Keywords: Hyperbaric Oxygen Therapy; Sleep Quality; Sleep Quantity; PSQI

1. INTRODUCTION

One of the basic needs for every person is sleep. An adequate amount of sleep is crucial for the body, in terms of brain function and body systems, to repair and recharge (Medic et al., 2017). Sleep is important for it is also influential in promoting growth and development, for the level of growth hormones rises during sleep (Devesa et al., 2016).

Research shows that people with insufficient sleep in the long term have a higher risk of medical problems including hypertension, lower immunological response, stroke, diabetes, obesity, and depression (Committee on Sleep Medicine and Research, 2006; Medic et al., 2017). The two essential parts of sleep are quantity and quality (Kohyama, 2021). Sleeping problems, such as insomnia and obstructive sleep apnea, causes poor quality of sleep.

Research estimates that approximately one billion adults worldwide suffer from obstructive sleep apnea (Benjafield et al., 2019). Insomnia is also another sleeping disorder where around 10 to 30% people worldwide suffer from (Bhaskar et al., 2016). Latest studies have also shown that COVID-19 has increased the number of people who experience sleeping difficulties, namely falling asleep, staying asleep, waking up early, and other types, by 14.5% (Robillard et al., 2020). These studies have shown that many people do not have a good quality and quantity of sleep, which can affect their mental and body health (Clement-Carbonell et al., 2021).

Researchers have found that low oxygen saturation can lead to sleep disorders which include insomnia, poor quality of sleep and daytime sleepiness (Johansson et al., 2015). Besides oxygen saturation, high inflammation is found to be able to negatively affect the quality of sleep (Dzierzewski et al., 2020). A high oxidative stress has also been found to be able to lead to poor sleep quality. Oxidative stress transpires when there is a disproportion between the production scale of oxygen free radicals, or reactive oxygen species (ROS), and the capability of the body to detoxify those byproducts. An experimental study in mice found that a high level of ROS causes short sleep and disrupted normal sleep cycle (Hill et al., 2018).

Moreover, Cortisol is a hormone that assist in waking people up and staying up. Naturally, the level of cortisol fluctuates through the day, peaking in the morning and in the lowest level at night, or in the beginning of sleep. An individual will wake up when the cortisol level has reached the highest level at the moment (Azmi et al., 2021). Despite that, various factors can disrupt the natural pathway of cortisol levels such as stress and anxiety which increase the cortisol level for cortisol is released in reaction to stress by the adrenal gland. Therefore, cortisol is also known as the stress hormone which leads to the inability to sleep or staying asleep and thus disrupting the normal circadian rhythm (Cay et al., 2018).

In addition, melatonin is a hormone, with a powerful antioxidant effect, that promotes sleepiness, therefore the level of melatonin is high at night (National Institute of General Medical Sciences, 2022). The production of melatonin can also be disrupted by various factors, including exposure to artificial light (such as blue light emitted by electronic devices), a disrupted sleep-wake cycle (can be caused by jet lag, work, or sleep disorders), aging (secretion tends to decrease with age), stress (high cortisol level), and certain medications (namely ibuprofen, birth control pills, and antidepressants medications).

Hyperbaric oxygen therapy (HBOT) is a safe treatment that involves giving the patient pure oxygen in a chamber with a pressure range from more than 1 to 3 atmosphere absolute (ATA). Studies have shown that HBOT are able to reduce the oxidative stress (Wolde et al., 2022), reduce inflammation (Rossignol, 2012), reduce cortisol level (Lund et al., 1999), increase melatonin level (Simsek et al., 2015), and increase oxygen saturation level, therefore HBOT should be able to improve sleep quality and quantity.

In this study, the sleep quality will be observed with HBOT with a pressure of 3 atmosphere absolute (ATA) for seventy-five minutes. Pressure is crucial because a rise in pressure will result in an escalation of the amount of oxygen dissolved in the blood. A rise in the amount of oxygen in the blood has positive effects in reducing inflammation, tissue death, and lack of oxygen (Levitan et al., 2021). In addition, compared to normal conditions, the oxygen at 3 ATA is estimated to be able to spread more than four times the distance from capillaries to boost oxygenation and repair cells (Levitan et al., 2021).

The purpose of this study is to analyze the relationship between 3 ATA hyperbaric oxygen therapy and the quality of sleep. This research would also like to analyze the relationship between 3 ATA hyperbaric oxygen therapy and the quantity of sleep. Results of this study can provide information whether 3 ATA hyperbaric oxygen therapy can be a beneficial treatment to improve sleep quality and quantity, along with the minimum number of treatments to improve the quality of sleep.

Therefore, the research questions in this study are as listed below:

1. Is there a significant and positive correlation between 3 ATA hyperbaric oxygen therapy and sleep quality?
2. Is there a significant and positive correlation between 3 ATA hyperbaric oxygen therapy and sleep quantity?
3. How many 3 ATA hyperbaric oxygen treatments does it take for sleep quality to significantly improve?

2. METHODOLOGY

2.1 Procedure of HBOT

The therapy begins with compression phase where the pressure increases from 1 ATA to 3 ATA, which is approximately equal to 0 m or sea level to a depth of 20 m. One pressure is increase for every 10m below sea level. The oxygen supply is given at a depth of 10 m, or 1 ATA, with a flow rate of 10 L/min. Therapy phase is done twice for each session of HBOT. The first therapy phase begins at a depth of 20 m for 10 minutes, continued by air-break phase, where the oxygen supply is stopped, for 2 minutes. After that, the second therapy phase begins for 20 minutes, with the oxygen supply back on. Another air-break phase follows for 2 minutes. The last phase is decompression phase, where the pressure decreases from 3 ATA to 1 ATA.

2.2 Data Collection

The data in this study is collected by using questionnaires and interviews that are done both offline, in the Asyifa Rempoa Hyperbaric Center, and online, contacting Asyifa’s patients via WhatsApp. The instrument used is the Pittsburgh Sleep Quality Index (PSQI) to measure the sleep quality and to distinguish the sleep quantity. With that, the first part of the study is to determine the participants' sleep quality and quantity, with the PSQI, before undergoing any HBOT. The second part of the study is to determine participants' sleep quality and quantity, with the PSQI, after undergoing HBOT.

Further questions are asked to participants in the last part of the study, to make sure the result of the sleep quality is due to HBOT and no other factors, such as medications, supplements, or other treatments. The participants are also asked regarding the number of HBOT that they have undergone.

2.3 Data Analysis Technique

All data that has been collected will be processed and the sleep quality will be calculated by Microsoft Excel. And will further be analyzed using Statistical Package for the Social Sciences (SPSS) version 25. Wilcoxon test, a nonparametric test, is used to determine whether the HBOT has a significant positive effect on sleep quality and quantity. To compare the groups of number of treatments, Kruskal Wallis test is used followed by post hoc testing using Duncan test.

3. RESULT

3.1 Participants Profile

There are a total of 102 participants in this study. All participants in this study are those who have satisfied the requirements of this study, to minimize other eligible factors, namely medication, supplements, or other therapies, contributing to the result of the study.

All 102 participants are qualified for this study because they are not undergoing other therapies that might affect the result of this study. The participants qualify should also not start taking any new medications or supplements after starting hyperbaric oxygen (HBO) therapy.

The majority participants in this study are identified as female with a percentage of 59%. The remaining 41% of the participant are identified as male. Furthermore, the participant's age ranges from 21- to 78-year-old, which is a combination of young adults, middle-aged adults, and older adults. Participants that are categorized as young adults (age ranges from 18 to 35) in this study has a percentage of 20%. Most of the participants are categorized as middle-aged adults (age ranges from 36 to 55) with a percentage of 70%. The remaining 10% of participants are categorized as older adults (56-year-old or older).

Table 1. Groups of participants according to HBOT sessions.

Groups	Treatment Ranges	Frequency
1	1-10	28
2	11-20	27
3	21-30	24
4	31-40	15
5	41-50	8

The number of HBOT sessions that the participants have received are varied, ranging from 1 to 50 sessions; therefore, they are divided into 5 groups according to the number of treatments that they have received (Table 1). 28 of the participants are classified into Group 1 who has undergone 1 to 10 HBOT sessions. Participants that are classified into Group 2 are those who have received 11 to 20 HBOT sessions. Those who have undergone 21 to 30 HBOT sessions are classified into Group 3, while Group 4 are those who have undergone 31 to 40 HBOT sessions. And the last group is for participants who have undergone 41 to 50 treatments. Group 5 only consists of 8 participants, and group 4 consists of 15 participants because there are limited patients in Clinic Asyifa who have undergone 31 or more HBOT sessions.

3.2 Hyperbaric Oxygen Therapy and Sleep Quality

Wilcoxon test is used to analyze whether there are differences in sleep quality after undergoing HBOT at 3 ATA. The test is done by comparing two groups of the PSQI score, which is before and after the participants received the treatment.

Table 2. Comparison of sleep quality by PSQI score between before and after.

	Before	After
Sleep Quality	8.73 ± 4.16	5.70 ± 2.62
Number of Participants	102	
Level of Confidence	93%	
P-value	0.000	

The data in table 2, expressed the value of sleep quality in mean ± standard deviations. The data shows that there is a difference in sleep quality after HBOT, where the mean value of participants decreases after undergoing HBOT. Moreover, the P-value, determined by using Wilcoxon test, is below 0.07 (p value is <0.001) which can lead to a conclusion that there is a significant positive correlation between hyperbaric oxygen therapy at 3 ATA and sleep quality.

3.3 Hyperbaric Oxygen Therapy and Sleep Quantity

To determine whether there are differences in sleep quantity after undergoing HBOT at 3 ATA or not, a nonparametric test, the Wilcoxon test is used. The result is as the table below, with the value of sleep quantity expressed in mean ±standard deviations

Table 3. Comparison of sleep quantity by PSQI score between before and after.

	Before	After
Sleep Quantity	1.64 ± 1.08	1.30 ± 0.97
Number of Participants	102	
Level of Confidence	93%	
P-value	0.000	

In table 3, it can be seen that the mean value after undergoing HBOT is lower than before undergoing HBOT, which indicates that there is a correlation that tends to be positive between sleep quantity and HBOT. In addition, the P-value determined by Wilcoxon test is <0.001 which indicates that there is a significant positive correlation between hyperbaric oxygen therapy at 3 ATA and sleep quantity.

3.4 Hyperbaric Oxygen Therapy and Sleep Quantity

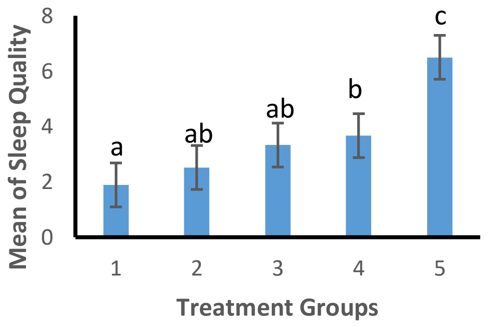

Figure 1. Bar chart to compare the treatment groups on sleep quality. The same letter in the means of sleep quality represents that they are not significantly different from each other (P-value > 0.07 by Kruskal-Wallis's test followed by Duncan test).

The bar chart, in figure 13, describes the mean of sleep quality for each group treatment. The ± standard deviation of the sleep quality mean is represented by the error bars in the bar chart. From the chart, the mean of sleep quality continues to increase from each treatment groups, which indicates that the sleep quality improves after a significant number of treatments. It can also be seen in Figure 13 that means of Group 4 is not very different from Group 3 perhaps because of fewer number of participants in Group 4.

It can be seen from the bar chart that there is no significant difference between Group 2 and Group 3 as indicated by the same letter (ab) above the standard deviation bar. Furthermore, Group 2 and Group 3 is not significantly different with Group 1 (a) and Group 4 (b). However, Group 5 (c) is significantly different from the other four groups and shows the best result of sleep quality improvement for it has the highest mean of sleep quality. Therefore, it can be concluded from the result of this study that subjects need more than 41 HBOT treatments at 3 ATA to obtain better sleep quality.

4. DISCUSSION

4.1 Hyperbaric Oxygen Therapy and Sleep Quality

Data collected from this study suggests that HBOT affect sleep quality parameters, such as sleep disturbances, time needed to sleep after laying down, sleep efficiency, the use of medication, and daytime dysfunction. 89 out of the 102 participants experience improvement on their sleep quality based on their PSQI score after HBOT.

It can be seen from the data collected that before undergoing HBOT, most of the participants experience sleep disturbances, such as waking up in the middle of the night, not able to breathe comfortably, or having pain. However, after HBOT, the participants experience improvement, where they stop or rarely wakes up in the middle of sleep, can breathe more easily, and experience less pain. In this study, 42 of the participants experience pain that disrupt sleep, and 30 of the participants experience improvement after undergoing several HBOT sessions. HBOT can help treating patients with pain, for oxygen at a higher level of pressure in HBOT helps repair the damaged tissue and relieving the pain (Bhutani & Vishwanath, 2012). Due to the pressure of HBOT, the oxygen supplied will dissolves into all the body's fluids, including plasma. This allows the oxygen to reach the damaged area where blood flow might be blocked due to injury, inflammation, or condition such as plaque buildup. The diffuse oxygen then facilitates angiogenesis, a process of forming new blood vessels, which is essential to supply the regenerating tissues with oxygen and nutrients, such as protein and vitamins, necessary for their growth and repair (Yümün et al., 2016). Furthermore, the healing process required energy to perform various functions, such as the synthesis of new proteins, or migration of fibroblast, a specialized cell that produce collagen and other extracellular matrix that has a function of structural support to tissues. Fibroblasts will move into the injured area to help rebuild and repair the damaged tissue (Hall & Hall, 2020). Oxygen is essential to convert glucose into energy in the form of ATP in the oxidative phosphorylation of cellular respiration, which happened in mitochondria. In the oxidative phosphorylation process, oxygen is the last electron acceptor in the electron transport chain which allows the chemiosmosis process, the synthesize of ATP, to begin. Therefore, by supplying oxygen, HBOT can boost the production of energy needed for the healing process. And by promoting the healing of damaged tissue and reducing the inflammation, HBOT are able to reduce the pain.

There are 21 out of the 102 participants in this study that were not able to breathe comfortably at night, however all of them experience improvement after undergoing HBOT. Although there are various possible reasons on why an individual may have a hard time to breathe comfortably, such as obstruction of the airways, anxiety or panic disorders, or nasal polyps. An increase of oxygen from HBOT can encourage the healing system of the body, including reducing stress level and anxiety (Feng & Li, 2017; Lin et al., 2019). HBOT improves oxygenation in the brain by building and repairing blood vessels that are damaged to allow oxygen to fill the brain, even those areas that the blood vessel was not able to access before due to the damaged of tissue, improving the nerve function and stimulating a relaxed state in the brain, thereby lessen stress and anxiety level (Feng & Li, 2017).

90 out of 102 of the participants often needs more than 20 minutes to be able to fall asleep after laying down (sleep latency). Most of the 90 participants were not able to fall asleep due to anxiety or stress (by personal communication during interview). However, after undergoing HBOT, 60 out of those 90 participants were able to lower their sleep latency. In this study, the average of all participants sleep latency was able to be reduced by about 30 minutes after HBOT treatment. The inability to quickly sleep after laying down and waking up during the night can be caused by an abnormal rhythm of melatonin and cortisol level. In a normal condition, the cortisol level, the stress hormone, is high during the day to wake a person up and stay up, while the melatonin, the sleep hormone, level is low. However, during the night, the melatonin level is high to help a person to fall asleep and remain asleep, while the cortisol level is low. High cortisol during the night can be caused by various factors, namely, stress, anxiety, sleep deprivations, and irregular sleep patterns (Cay et al., 2018). And as discussed before, HBOT can reduce stress and anxiety, and as a result, HBOT can lowers the cortisol level (Lund et al., 1999; Feng & Li, 2017; Lin et al., 2019). HBOT can also increases the production of melatonin for it is an antioxidant that was found to elevated to scavenge excessive production of ROS caused by HBOT (Simsek et al., 2015). In addition, melatonin inhibits a hormone called adrenocorticotropic hormone (ACTH) that directly acts on adrenal gland in producing cortisol (Campino et al., 2011). Hence, an increase in melatonin could reduce the release of cortisol. Thus, HBOT can help reduce waking up at night during sleep and sleep latency, thereby promotes sleep quality.

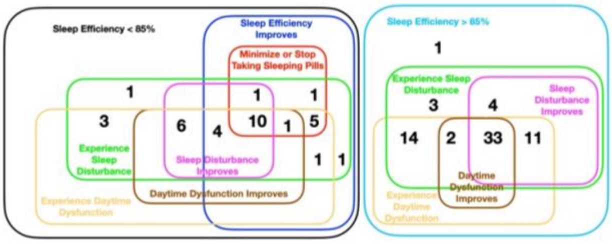

Figure 1. Venn Diagram of 102 participants after HBOT on sleep efficiency, sleeping pills usage, sleep disturbance, and daytime dysfunction.

The Venn diagram in figure 14 showed that 24 out of the 34 of the participants that has sleep efficiency lower than 85% were able to increase their sleep efficiency after undergoing HBOT. The participants were able to improve their sleep efficiency since the participants were able to reduce their sleep latency, along with the sleep disturbance, hence the participants were able to increase their sleep efficiency, which is the hour of sleep (sleep duration) compared to the overall hour spent sleeping, which includes both sleep duration and sleep latency. Sleep efficiency of ten out of the 34 participants did not increase, and this could be due to the fact that their sleep latency did not improve after undergoing HBOT treatment. Furthermore, when an individual was able to sleep with a longer duration and without or with less disturbance, it could limit the individual's daytime dysfunction.

In sleep efficiency lower than 85% group, 30 out of 34 participants experience daytime dysfunction. Furthermore, 21 out of those 30 participants were able to minimize their daytime dysfunction. On the other hand, in sleep efficiency higher than 85% group, 60 experience daytime dysfunction and the rest of the participants (8 participants) do not. After HBOT, 35 out of those 60 participants were able to feel improvement on their daytime dysfunction.

In this study, there are 18 participants that used to consumed sleep pills before HBOT due to the inability to fall asleep as well as sleep efficiency lower than 85%. However, after HBOT, their sleep latency, along with their sleep efficiency was able to improve, therefore they all are able to minimize or stop the consumption of sleep pills.

In addition, in this study, 82 out of the 88 participants that experience poor sleep quality before HBOT were able to improve their sleep quality after undergoing HBOT. All the participants that do not experience improvement after HBOT are those that have just undergone less than 5 HBOT sessions, which suggests that it needs more than 5 HBOT sessions to improve sleep quality.

4.2 Hyperbaric Oxygen Therapy and Sleep Quantity

In this study, out of the 102 participants (total participants), there are 62 participants that has an average sleep less than 7 hour before HBOT. However, 33 out of those 62 participants with poor sleep quantity (less than 7 hour of sleep), were able to show an improvement on their sleep quantity after HBOT.

Due to work, some of the participants sleep quantity is limited. Nevertheless, the result of the analysis based on the Wilcoxon test shows that there is a positive correlation between HBOT and sleep quantity. HBOT can help improve sleep quantity by several possible factors, namely by reducing sleep latency and sleep disruptions, such as waking up during the night. As discussed before, some people have a hard time to fall asleep and since HBOT can decrease sleep latency by increases melatonin for its antioxidant properties and lowering the cortisol level. Thereby, the sleep quantity can increase.

Some people also have problems such as waking up late at night or toward mornings and not being able to go back to sleep, this can be due to high cortisol, which leads to a lower sleep quantity. Since HBOT creates a calm state of mind from the oxygen-filled brain that lowers stress and cortisol hence an individual won't wake up in the middle of sleep and won't have a hard time to fall back asleep (Lund et al., 1999; Feng & Li, 2017; Lin et al., 2019). And as a result, sleep quantity can be improved.

5. CONCLUSION

In this study, the PSQI instrument is used to measure the sleep quality of an individual before and after undergoing the Hyperbaric Oxygen Therapy at 3 ATA. The result of the analysis using Wilcoxon test indicates that there is a significant positive correlation between hyperbaric oxygen therapy and sleep quality. 87% of the participants sleep quality were able to improve after undergoing HBOT. The collected data suggests that HBOT can increase sleep quality by increasing sleep duration and sleep efficiency. Along with reducing sleep latency, sleep disturbance, and daytime dysfunction which leads individuals to stop or lower the use of sleeping pills.

The result of the analysis on HBOT and sleep quantity based on the Wilcoxon test also showed that there is a significant positive correlation. 53% of the participants were able to increase their sleep quantity by reducing sleep latency and sleep disturbance. Although, some of the participants sleep quantity are restricted by work. Furthermore, subjects are able acquire the best sleep quality after more than 41 hyperbaric oxygen therapy at 3 ATA.

2.4 References

Azmi, N. A. S. M., Juliana, N., Azmani, S., Effendy, N. M., Abu, I. F., Teng, N. I. M. F., & Das, S. (2021). Cortisol on Circadian Rhythm and Its Effect on Cardiovascular System. *Int J Environ Res Public Health*, *18*(2), 676. doi: 10.3390/ijerph18020676

Benjafield, A. V., Ayas, N. T., Eastwood, P. R., Heinzer, R., Morrell, M. J., Nunez, C. M., Peppard, P. E., Sinha, S., Tufik, S., Valentine, K., & Malhotra, A. (2019). Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. *Lancet Respir Med*, *7*(8), 687-698. doi: 10.1016/S2213-2600(19)30198-5

Bhaskar, S., Prasad, S., & Hemavathy, D. (2016). Prevalence of chronic insomnia in adult patients and its correlation with medical comorbidities. *Journal of Family Medicine and Primary Care*, *5*(4), 780-784. DOI:10.4103/2249-4863.201153

Bhutani, S., & Vishwanath, G. (2012). Hyperbaric oxygen and wound healing. *Indian J Plast Surg*, *45*(2), 316-324. doi: 10.4103/0970-0358.101309

Campino et al. (2011). Melatonin exerts direct inhibitory actions on ACTH responses in the human adrenal gland. *Horm Metab Res*, *43*(5), 337-342. doi: 10.1055/s-0031-1271693

Cay, M., Ucar, C., Senol, D., Cevirgen, F., Ozbag, D., Altay, Z., & Yildiz, S. (2018). Effect of increase in cortisol level due to stress in healthy young individuals on dynamic and static balance scores. *North Clin Istanb*, *5*(4), 295-301. doi: 10.14744/nci.2017.42103

Clement-Carbonell, V. C.-C., Portilla-Tamarit, I., Rubio-Aparicio, M., & Madrid-Valero, J. J. (2021). Sleep Quality, Mental and Physical Health: A Differential Relationship. *Int J Environ Res Public Health*, *18*(2), 460. doi: 10.3390/ijerph18020460

Committee on Sleep Medicine and Research. (2006). *Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem* (H. R. Colten & B. M. Altevogt, Eds.). National Academies Press. https://www.ncbi.nlm.nih.gov/books/NBK19961/

Devesa, J., Almengló, C., & Devesa, P. (2016). Multiple Effects of Growth Hormone in the Body: Is it Really the Hormone for Growth? *Clin Med Insights Endocrinol Diabetes*, *9*, 47-71. doi: 10.4137/CMED.S38201

Dzierzewski, J. M., Donovan, E. K., Kay, D. B., Sannes, T. S., & Bradbrook, K. E. (2020). Sleep Inconsistency and Markers of Inflammation. *Front Neurol*, *11*, 1042. doi: 10.3389/fneur.2020.01042

Feng, J.-J., & Li, Y.-H. (2017). Effects of hyperbaric oxygen therapy on depression and anxiety in the patients with incomplete spinal cord injury (a STROBE-compliant article). *Medicine (Baltimore)*, *96*(29), e7334. doi: 10.1097/MD.0000000000007334

Hall, J. E., & Hall, M. E. (2020). *Guyton and Hall Textbook of Medical Physiology*. Elsevier.

Hill et al. (2018). A bidirectional relationship between sleep and oxidative stress in Drosophila. *PLoS Biology*, *16*(7), e2005206. https://doi.org/10.1371/journal. pbio.2005206

Johansson, P., Svensson, E., Alehagen, U., Jaarsma, T., & Broström, A. (2015). The contribution of hypoxia to the association between sleep apnoea, insomnia, and cardiovascular mortality in community-dwelling elderly with and without cardiovascular disease. *Eur J Cardiovasc Nurs*, *14*(3), 222-231. DOI: 10.1177/1474515114524072

Kohyama, J. (2021). Which Is More Important for Health: Sleep Quantity or Sleep Quality? *Children*, *8*(7), 542. https://doi.org/10.3390/children8070542

Levitan, D. M., Hitt, M., Geiser, D. R., & Lyman, R. (2021). Rationale for hyperbaric oxygen therapy in traumatic injury and wound care in small animal veterinary practice. *J Small Anim Pract*, *62*(9), 719-729. DOI: 10.1111/jsap.13356

Lin, C.-C., Huang, K.-L., Tung, C.-S., & Liu, Y.-P. (2019). Hyperbaric oxygen therapy restored traumatic stress-induced dysregulation of fear memory and related neurochemical abnormalities. *Behavioural Brain Research*, *359*, 861-870. https://doi.org/10.1016/j.bbr.2018.07.014

Lund, V., Kentala, E., Scheinin, H., Klossner, J., Koskinen, P., & Jalonen, J. (1999). Effect of hyperbaric conditions on plasma stress hormone levels and endothelin-1. *Undersea Hyperb Med*, *26*(2), 87-92. PMID: 10372427.

Medic, G., Wille, M., & Hemels, M. E.H. (2017, May). Short- and Long-term Health Consequences of Sleep Disruption. *Nature and Science of Sleep*, *9*, 151-161. doi: 10.2147/NSS.S134864

National Institute of General Medical Sciences. (2022, May 4). *Circadian Rhythms*. National Institute of General Medical Sciences. Retrieved February 6, 2023, from https://nigms.nih.gov/education/fact-sheets/Pages/circadian-rhythms.aspx

Robillard, R., Dion, K., Pennestri, M.-H., Solomonova, E., Lee, E., Saad, M., Murkar, A., Godbout, R., Edwards, J. D., Quilty, L., Daros, A. R., Bhatla, R., & Kendzerska, T. (2020). Profiles of sleep changes during the COVID-19 pandemic: Demographic, behavioural and psychological factors. *Journal of Sleep Research*, *30*(1). https://doi.org/10.1111/jsr.13231

Rossignol, D. A. (2012). Hyperbaric oxygen treatment for inflammatory bowel disease: a systematic review and analysis. *Med Gas Res*, *2*(1), 6. doi:10.1186/2045-9912-2-6

Simsek, K., Sadir, S., & Oter, S. (2015). The relation of hyperbaric oxygen with oxidative stress - reactive molecules in action. *Oxidants and Antioxidants in Medical Science*, *4*(1), 17-22. DOI: 10.5455/oams.010415.rv.016

Wolde, S. D. d., Hulskes, R. H., Jonge, S. W. d., Hollmann, M. W., Hulst, R. A. v., Weenink, R. P., & Kox, M. (2022). The Effect of Hyperbaric Oxygen Therapy on Markers of Oxidative Stress and the Immune Response in Healthy Volunteers. *Frontiers in Physiology*, *13*. https://doi.org/10.3389/fphys.2022.826163

Yümün, G., Kahaman, C., Kahaman, N., Yalçınkaya, U., Akçılar, A., Akgül, E., & Vural, A. H. (2016). Effects of hyperbaric oxygen therapy combined with platelet-rich plasma on diabetic wounds: an experimental rat model. *Arch Med Sci*, *12*(6), 1370–1376. doi: 10.5114/aoms.2016.62905