

## Peer Review File

Article information: <https://dx.doi.org/10.21037/ajo-23-5>

### Reviewer A

Thank you for your submission to AJO. This is a systematic review of the available literature for the utility of using hyperbaric oxygen therapy in cervical necrotising fasciitis. While there is limited data available due to the rarity of this illness, this paper adds to the existing literature and warrants publication.

### Reviewer B

This is a useful retrospective review of CNF and a summary of the literature that improves our understanding of current practices and management

### Editorial Comments

Abstract

1. Please also briefly specify the timeframe, and eligibility criteria of the studies (e.g., language considerations, study design), and indicate the methods of assessing risk of bias.

**Reply 1: This has been completed**

2. In the "Abstract-Conclusion", please provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency, and imprecision).

**Reply 2: This has been completed**

Introduction

3. Lines 68-71: "There is currently discordance in the literature regarding the value of HBOT in the head and neck region.(9) There are a limited number of case series in the literature with significant demographic and therapeutic heterogeneity, with a lack of randomised control trials". Please also consider citing the following similar articles:

- Faunø Thrane J, Ovesen T. Scarce evidence of efficacy of hyperbaric oxygen therapy in necrotizing soft tissue infection: a systematic review. *Infect Dis (Lond)*. 2019 Jul;51(7):485-492.
- Schröder A, Gerin A, Firth GB, Hoffmann KS, Grieve A, Oetzmann von Sochaczewski C. Correction to: A systematic review of necrotising fasciitis in children from its first description in 1930 to 2018. *BMC Infect Dis*. 2019 May 27;19(1):469.
- Devaney B, Frawley G, Frawley L, Pilcher DV. Necrotising soft tissue infections: the effect of hyperbaric oxygen on mortality. *Anaesth Intensive Care*. 2015 Nov;43(6):685-92.

**Reply 3: Thankyou for this addition. I was unable to add Schroder et. al as a reference here, as they did not discuss the use of HBOT at all. Devaney et. al did discuss the value of HBOT, but they did not clarify its effect in the Head and Neck region. I have changed the sentence to "There is currently discordance in the literature regarding the value of HBOT in necrotizing fasciitis, particularly**

in the head and neck region.(9,12)” to allow the addition of this reference.

4. In addition, please specify the innovation and significance of this systematic review compared to other similar ones (In particular, the authors published a similar review, i.e. ref. 5): what does this review add to existing knowledge? How does this review differ from previous reviews? Please clearly state this.

Reply 4: Ref 5 (Gunaratne et. al) was not specific to Hyperbaric Oxygen, and was unable to clarify the effect HBOT independently. It did, however use the same articles up to 2017, but incorporated all cases of CNF, and not just those treated with HBOT. It acts as a good comparison for the baseline mortality rate, against our database of only HBOT cases. I have added the following sentence:

“To our knowledge, this is the largest database of cases of CNF treated with HBOT in the literature.”

#### Methods

5. Please specify the date of search (specified to date, month, and year), and timeframe (specified to month and year).

Reply 5: Completed on line 86-87

6. Please present the entire search strategies for all databases, including any filters and limits used (rather than simply stating “(cervical OR neck) AND (necrotizing fasciitis OR necrotizing fasciitis”).

Reply 6: Thankyou, this has now been completed on lines 83-91

7. Did the authors conduct a manual or gray database or reference search to broaden the search?

Reply 7: a reference serve was conducted. This has been added to lines 88-89

8. Please explain the reasons for excluding pediatric cases in the text. Also, please unify the age range for pediatrics (“<17” in line 96 and “<18” in Figure 1).

Reply 8: This was an error. This has been fixed to be <18

9. Lines 95-96: "Only cases that used of HBOT as a treatment were included in the study". Lines 241-242: "data is limited to case studies, case series and retrospective analyses". We recommend the authors refine the eligibility criteria, especially the type of study, to avoid confusing readers.

Reply 9: Completed and calrified – line 101-104. Line 241 (now ~255) has also been edited to remove “retrospective analyses” which was unclear and unnecessary. The goal was to states that there are no randomised control trials on the topic.

10. Lines 103-104: "Cases of disparity were discussed, and a consensus decision was made if required. (See Figure 2)". We suggest the authors could specify the resolution of those inconsistent decisions in the Methods.

Reply 10: Completed – line 113

#### Results

11. In figure 1, please specify the number for exclusions. E.g. Records excluded (N = 1255): -Age <18 (n=?); -Duplicate articles (n=?); ...

Reply 11: I am unable to calculate this number, as this was not captured prospectively. Each article

was reviewed and a decision was made regarding inclusion/exclusion, however the reason for this was not documented per article due to the sheer number of articles reviewed.

12. We suggest the authors refine the legend of figure 1, e.g., "Figure 1. PRISMA 2020 flow diagram describing the study selection process and identification of eligible cases. From: Page et al [ref. xx]."

**Reply 12: Thankyou, this has been completed**

13. Lines 132-134: "A total of 161 patients who underwent Hyperbaric Oxygen Therapy for Cervical Necrotizing Fasciitis were identified in 28 published articles. This included 91 males and 68 females (57% male) with a mean age of 50 years (See Table 1)". 91 (male) + 68 (female) = 159 patients instead of 161 patients. Please re-check the data and specify the number of male patients in table 1.

**Reply 13: This has been fixed to represent the correct number, 92 males and 69 females. The table has been fixed to be numerical (number of males) and not percentage. The total number of 161 was correct.**

14. Lines 378-405: "JBI Checklists for Bias Assessment". Please cite the reference.

**Reply 14: A description and website reference have been added to the heading for this.**

15. For ease of reading and double-checking, it would be better to cite the included studies in the tables.

**Reply 15: Each article in the table has now been individually cited**

16. We suggest that authors provide the full name of all bacteria (in the tables and in the text). In addition, the name of each bacterium should be italicized.

**Reply 16: I have removed any shorthand and labelled the bacterial groups by full name. The names listed are the Genus, as there were growths of varying subspecies throughout the literature (or more commonly no further classification other than genus). As such, I have changes to title of the table to clarify this, and italicized the names of bacteria in the table and in the paper.**

## Discussion

17. Lines 191-199: "The largest and most recent systematic review of CNF performed by Gunaratne et. al. in 2018 reviewed mortality outcomes in 861 patients through 201 articles. Articles were isolated according to the same search criteria and involved the same database as our study (until 2017). We used the same search criteria as this study, with similar inclusion/exclusion criteria, however our study only included articles with patients who had undergone HBOT. In the Gunaratne study, the overall mortality rate was 13.36% in all patients with CNF, with or without the use of HBOT. In our study of only HBOT patients, the mortality rate of 7.6% is significantly less (difference in proportion = -0.058, Z = -2.13, p = .017)". Please cite the article made by Gunaratne et al. Is it Ref. 5? If so, why 861 patients instead of 1235 patients? Furthermore, if the study by "Gunaratne et al." in Table 1 is also Ref. 5, why was it published in 2017?

**Reply 17: In the Gunaratne study, they only had mortality data for 861 patients from 201 articles (section 3.6 on patient outcomes)**

**Form that article - "Finally, 201 articles encompassing 861 patients reported final outcome; alive (86.64%) or deceased (13.36%). As expected, the development of DNM was significantly associated with death (OR 2.39; 95% CI 1.37-4.16; P 5 .002)."**

**The correct publication date was 2018 (accepted in 2017, however not published). I have fixed this**

in the table and in the article.

18. Based on comment 4, we suggest the authors could compare the similarities and differences between this systematic review and these similar studies.

Reply 18: I have added the line “To our knowledge, this is the largest database of cases of CNF treated with HBOT in the literature.” In fact, I believe this to be the only formal review of all cases of HBOT for CNF, and so I am unable to compare to any studies which have asked the same specific question

#### Conclusion

19. The "Conclusion" is almost 100% the same as the "Abstract-Conclusion" (only replaced with abbreviations). We suggest you paraphrase the sentences and add more information (e.g., discuss the implications of the results for practice, policy, and future research).

Reply 19: This has been completed and the conclusion has been rewritten

#### Other Information

20. We strongly suggest authors report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.

Reply 20: I have completed the data sharing form and will make my extracted data and spreadsheet used for all analyses available. I'm unclear on how to upload this data, so I will make it available on request to myself (the corresponding author). I have clarified the contact details listed and changed the address and phone number as they are no longer available