

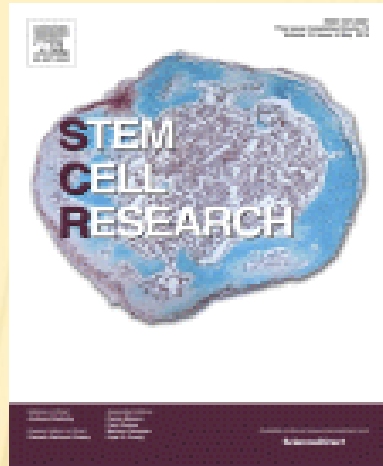
“New Pearls Of Wisdom In The Hyperbaric Medicine Literature”



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Stem Cell Research

Volume 12, Issue 3, Pages 599-832 (May 2014)



CD34 +/-CD45-dim stem cell mobilization by hyperbaric oxygen — Changes with oxygen dosage

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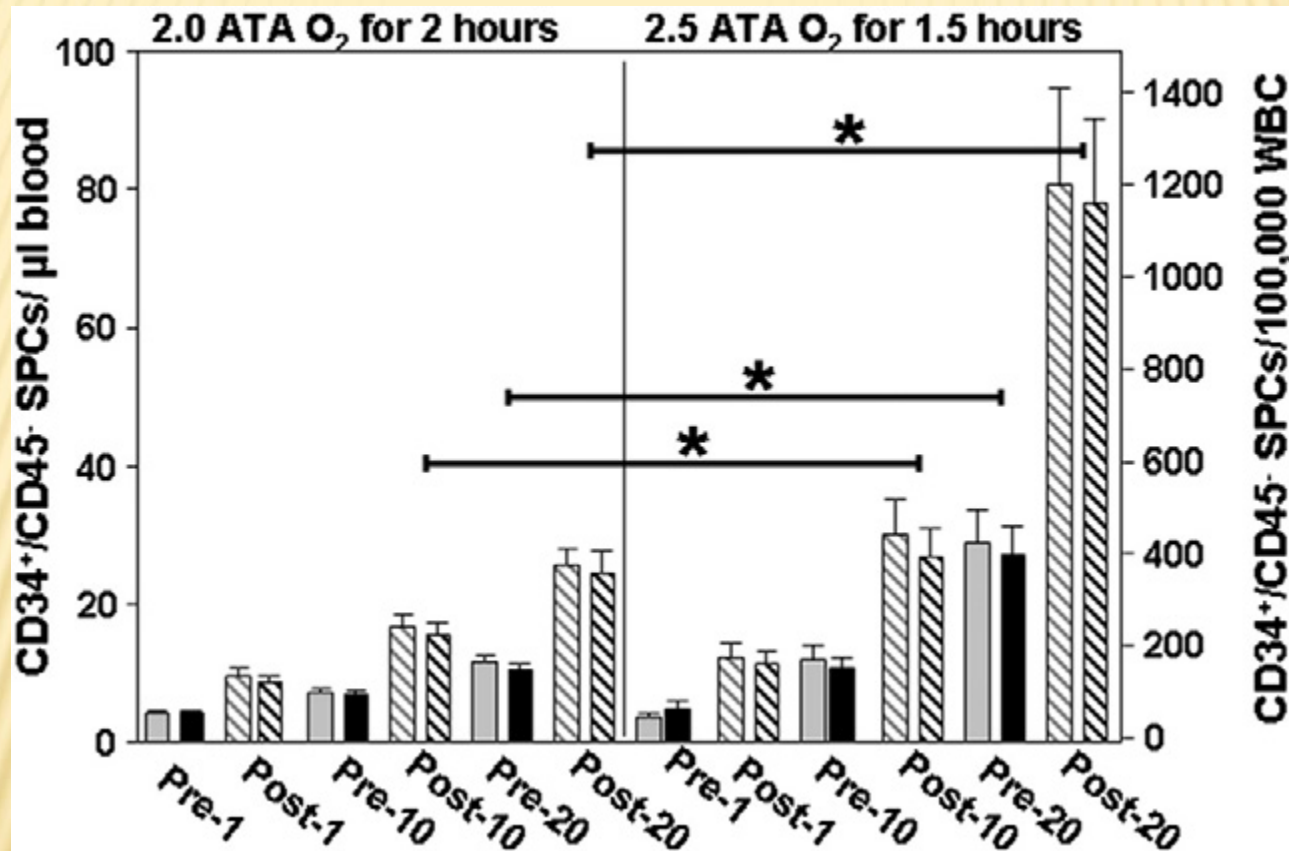
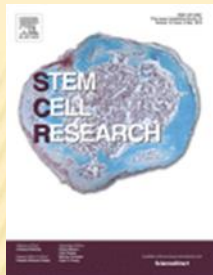


Figure 1 Leukocyte mobilization by HBO2. The number of circulating CD34⁺, CD45⁻ cells in blood before and after the 1st, 10th and 20th treatment of 20 patients exposed to at either 2.0 or 2.5 ATA. Data were normalized to blood volume (gray boxes quantified on the left ordinate axis) or to total circulating leukocyte count (black boxes quantified on the right ordinate axis) and are mean \pm SE, * indicates significant difference between 2.0 and 2.5 ATA groups (ANOVA). All post-HBO2 values are significantly different from pre-HBO2 values at each treatment time in both groups (t-test).



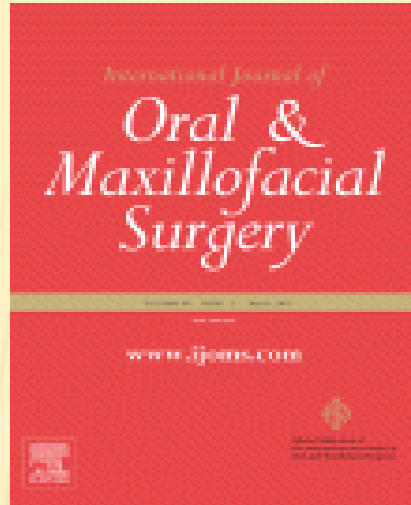
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Table 2: Intracellular protein content (fold-elevation post- versus prior to HB02)

	Protein	Treatment #	2.0 ATA Protocol	2.5 ATA Protocol
×	HIF-1	1	2.35 ± 0.24	3.29 ± 0.55
×		10	2.65 ± 0.21	2.67 ± 0.22
×		20	2.54 ± 0.38	2.77 ± 0.26
×	HIF-2	1	2.33 ± 0.24	2.68 ± 0.30
×		10	2.48 ± 0.15	2.54 ± 0.20
×		20	2.54 ± 0.23	2.60 ± 0.21
×	HIF-3	1	2.27 ± 0.22	2.67 ± 0.31
×		10	2.38 ± 0.24	2.29 ± 0.15
×		20	2.43 ± 0.26	2.27 ± 0.15
×	Trx	1	2.34 ± 0.24	2.51 ± 0.26
×		10	2.36 ± 0.22	2.28 ± 0.13
×		20	2.44 ± 0.24	2.50 ± 0.29
×	PARP	1	2.36 ± 0.22	2.64 ± 0.26
×		10	2.39 ± 0.22	2.42 ± 0.19
×		20	2.57 ± 0.27	2.47 ± 0.22

International Journal of Oral and Maxillofacial Surgery
Volume 44, Issue, March 2015, Pages 301-307



**Effect of hyperbaric oxygen treatment on irradiated oral mucosa:
microvessel density**

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Accepted 19 December 2014, Available online 17 January 2015

Effect of hyperbaric oxygen treatment on irradiated oral mucosa: microvessel density

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Patient Characteristics

	Subject	Sex	Age, years	Site of cancer	Radiation dose, Gy	Time since radiation, years
•	HBOT group					
•	1	M	78	Tonsil	64	3
•	2	M	55	Retromolar	60	6
•	3	M	66	Tonsil	64	3
•	4	M	62	Floor of mouth	70	3
•	5	F	69	Tonsil	70	3
•	6	F	51	Tonsil	70	6
•	7	F	56	Parotid gland	70	6
•	8	M	67	Tongue	70	2
•	9	M	63	Origo incertaa	50	6
•	10	M	70	Buccal	70	5
•	11	M	56	Floor of mouth	64	5
•	12	M	51	Tonsil	64	5
•	Mean (range)			62 (51–78)	66 (50–70)	4 (2–6)
•	Controls					
•	1	M	65	Gingiva	70	6
•	2	M	55	Retromolar	64	2
•	3	M	56	Tonsil	70	3
•	4	M	63	Retromolar	64	4
•	5	F	55	Tongue	64	5
•	6	F	73	Floor of mouth	64	4
•	7	M	53	Origo incertaa	50	2
•	8	M	62	Floor of mouth	70	4
•	Mean (range)			60 (53–73)	65 (50–70)	4 (2–6)

Effect of hyperbaric oxygen treatment on irradiated oral mucosa: microvessel density

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Measurements of vascularization and cell proliferation (mean \pm SD)

	<u>HBOT Group</u>			<u>Controls</u>		
	Baseline	6 months	P-value	Baseline	6 months	P-value
<u>Blood vessels</u>						
<i>Sub-epithelial area</i>						
MVD	45.4 \pm 13.9	98.0 \pm 15.9a	0.002	45.6 \pm 15.7	49.3 \pm 10.5	NS
MVA	1.5 \pm 0.6	4.4 \pm 1.9a	0.003	1.5 \pm 0.6	1.6 \pm 0.5	NS
<i>Deeper connective tissue</i>						
MVD	30.4 \pm 10.1	45.1 \pm 16.4a	0.01	28.1 \pm 9.6	34.4 \pm 7.8	NS
MVA	2.5 \pm 1.3	3.7 \pm 1.3a	0.041	2.2 \pm 0.9	2.7 \pm 1.4	NS
<u>Lymph vessels</u>						
<i>Sub-epithelial area</i>						
MVD	18.3 \pm 8.1	36.1 \pm 12.6a	0.002	19.4 \pm 6.2	16.9 \pm 8.8	NS
MVA	1.3 \pm 0.7	2.7 \pm 1.8a	0.019	1.2 \pm 0.6	1.5 \pm 0.7	NS
<i>Deeper connective tissue</i>						
MVD	14.6 \pm 7.2	16.8 \pm 7.0	NS	13.1 \pm 7.0	15.0 \pm 5.3	NS
MVA	1.7 \pm 1.1	1.5 \pm 0.9	NS	2.0 \pm 0.9	1.8 \pm 1.1	NS
<u>Proliferation index: Ki-67 (%)</u>						
	23.2 \pm 4.5	21.8 \pm 1.6	NS	19.4 \pm 4.0	20.0 \pm 4.3	NS

Fig. 1 Irradiated buccal mucosa before (a) and 6 months after (b) hyperbaric oxygen treatment (HBOT). The sections are stained with haematoxylin and eosin. Scale bar: 200µm

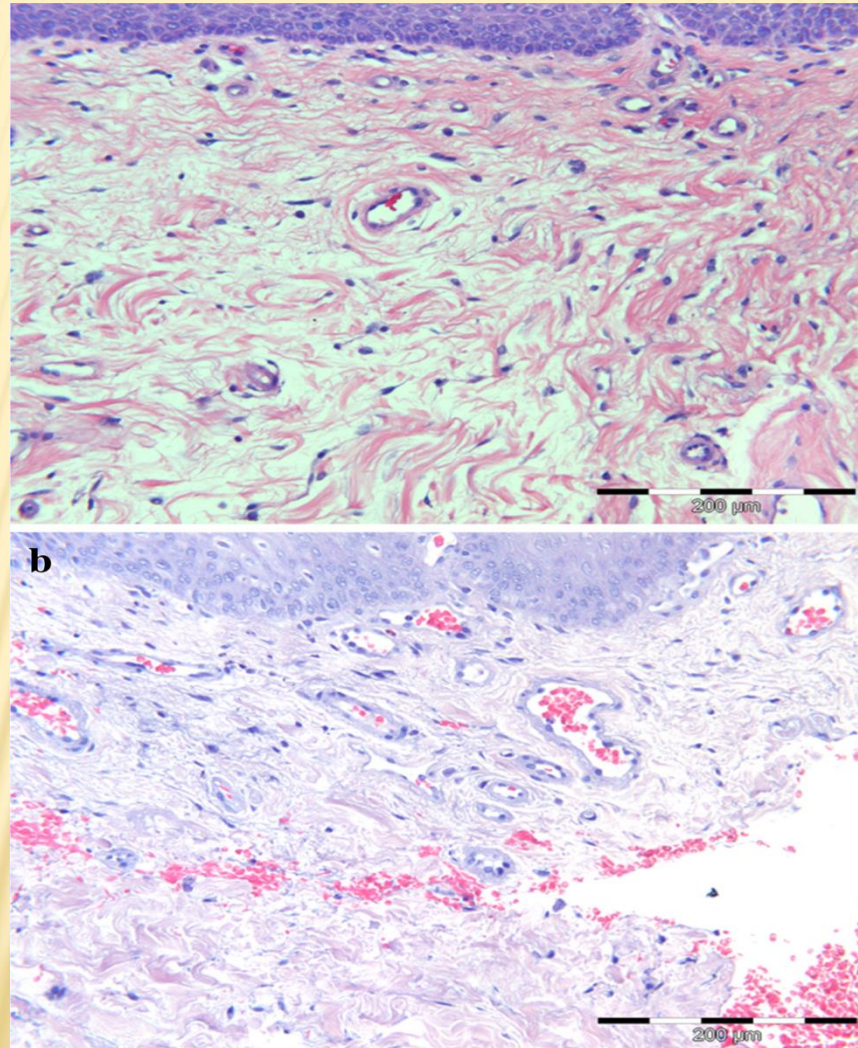


Fig. 3. Irradiated oral mucosa before (a) and 6 months after (b) hyperbaric oxygen treatment (HBOT). The sections are stained with CD31 and D2-40. Blood vessels appear as brown and lymphatic vessels as red. Scale bar: 200 μ m.

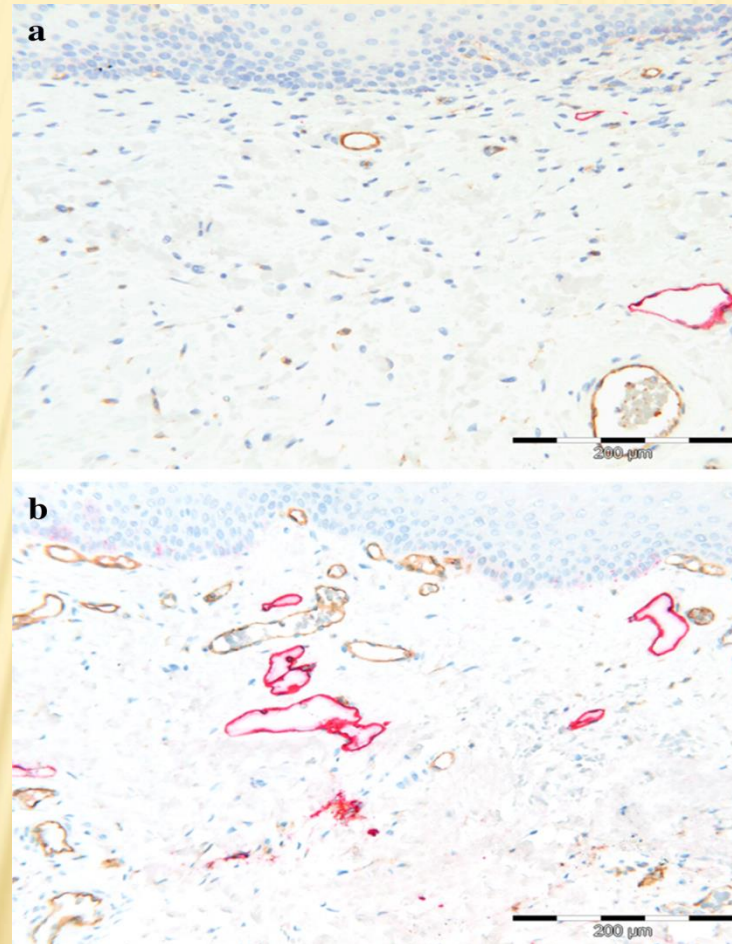
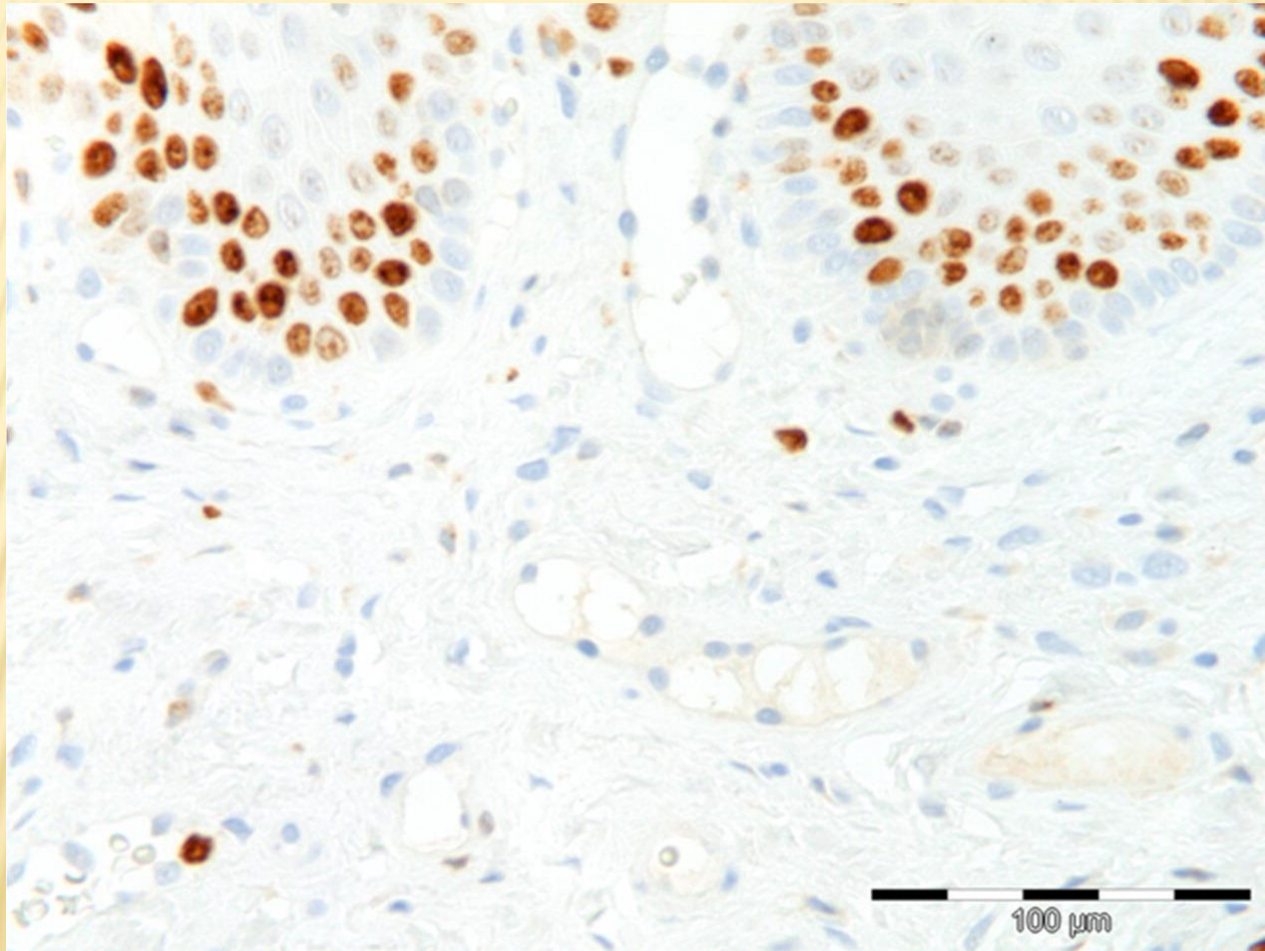


Fig. 4. Immunostaining with Ki-67. There was prominent cell proliferation in the parabasal layer.
Scale bar: 100 μ m



JAMA Internal Medicine

JAMA Intern Med. 2015;175(1):43-52. doi:10.1001/jamainternmed.2014.5479

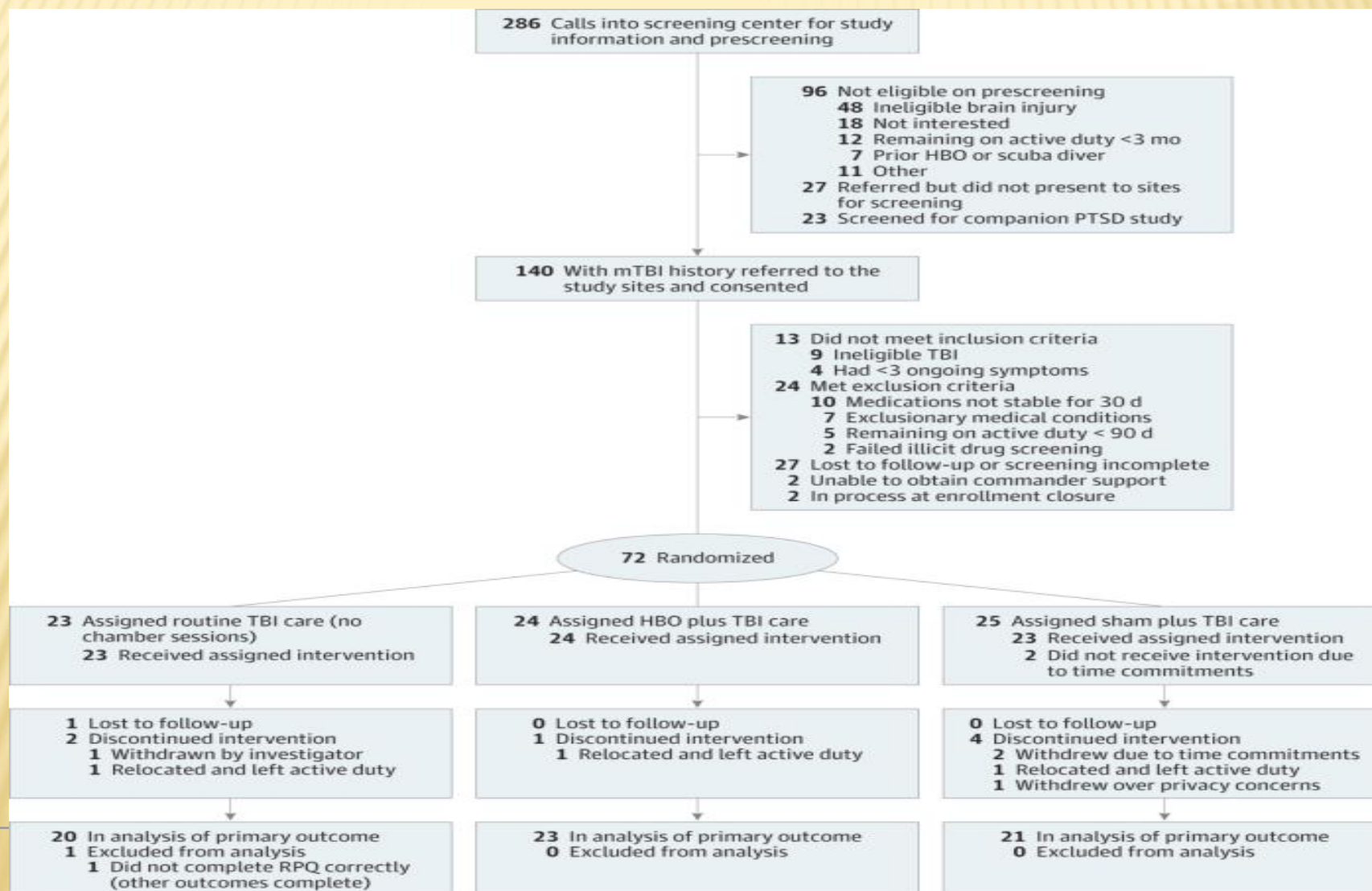


Effects of Hyperbaric Oxygen on Symptoms and Quality of Life Among Service Members With Persistent Postconcussion Symptoms

A Randomized Clinical Trial

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From: **Effects of Hyperbaric Oxygen on Symptoms and Quality of Life Among Service Members With Persistent Postconcussion Symptoms: A Randomized Clinical Trial**



From: **Effects of Hyperbaric Oxygen on Symptoms and Quality of Life Among Service Members With Persistent Postconcussion Symptoms: A Randomized Clinical Trial**

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Table 2. Changes From Baseline in Postconcussion Symptom Scores Using the Rivermead Post-Concussion Symptoms Questionnaire and Subscales Among the Intent-to-Treat and Per-Protocol Populations^a

Intervention	Intent-to-Treat Population				Per-Protocol Population		
	Baseline, Mean (SD)	After Intervention, Mean (SD)	Change Score (95% CI)	<i>P</i> Value ^b	Baseline, Mean (SD)	After Intervention, Mean (SD)	Change Score (95% CI)
Rivermead Post-Concussion Symptoms Questionnaire 3 Subscale							
Standard care	5.4 (2.7)	5.1 (2.8)	0.0 (−1.0 to 1.0) (n = 20)	.97	5.4 (2.7)	5.1 (2.8)	0.0 (−1.0 to 1.0) (n = 20)
HBO	5.5 (3.3)	4.2 (3.0)	1.2 (0.0-2.4) (n = 23)	.04	4.7 (3.2)	3.1 (2.2)	1.6 (−0.1 to 3.3) (n = 11)
Sham	4.7 (3.1)	3.5 (3.3)	1.5 (0.1 to 2.9) (n = 21)	.03	4.8 (3.7)	2.7 (2.8)	2.2 (0.7 to 3.6) (n = 13)
Rivermead Post-Concussion Symptoms Questionnaire 13 Subscale							
Standard care	27.1 (12.2)	25.5 (13.9)	0.5 (−4.0 to 5.0)	.87	27.1 (12.2)	25.5 (13.9)	0.5 (−4.0 to 5.0)
HBO	27.5 (13.1)	22.5 (12.4)	4.2 (−0.8 to 9.1)	.02	25.0 (13.4)	15.6 (10.9)	9.4 (2.9 to 15.9)
Sham	25.5 (11.6)	20.7 (12.8)	5.5 (0.7 to 10.3)	.04	25.9 (14.0)	17.4 (13.3)	8.5 (2.8 to 14.2)
Total Rivermead Post-Concussion Symptoms Questionnaire							
Standard care	32.5 (14.4)	30.6 (16.1)	0.5 (−4.8 to 5.8)	.91	32.5 (14.4)	30.6 (16.1)	0.5 (−4.8 to 5.8)
HBO	33.0 (15.8)	26.7 (14.8)	5.4 (−0.5 to 11.3)	.008	29.7 (16.3)	18.7 (13.0)	11.0 (3.2 to 18.8)
Sham	30.2 (14.2)	24.2 (15.4)	7.0 (1.0 to 12.9)	.02	30.8 (17.6)	20.1 (15.7)	10.7 (3.9 to 17.5)

Abbreviation: HBO, hyperbaric oxygen.

^a The 95% CIs were calculated using 95% binomial exact CIs.

^b Wilcoxon signed rank test.

From: Effects of Hyperbaric Oxygen on Symptoms and Quality of Life Among Service Members With Persistent Postconcussion Symptoms: A Randomized Clinical Trial

Table 3. Changes From Baseline in Postconcussion and PTSD Symptom Scores Using the Neurobehavioral Symptom Inventory and the PTSD Checklist–Civilian Version and Subscales Among the Intent-to-Treat Population^a

Symptom Subscale	Standard Care Group (n = 23)	HBO Group (n = 24)	Sham Group (n = 25)
Neurobehavioral Symptom Inventory			
Total score, range 0–88			
Baseline score	33.6 (17.6)	34.3 (16.9)	32.6 (16.6)
Mean (95% CI) change score	–1.1 (–7.3 to 5.2)	3.7 (–3.7 to 11.2)	6.9 (1.4 to 12.4)
Cognitive subscale			
Baseline score	8.0 (4.6)	7.9 (4.4)	7.6 (3.3)
Mean change score	0.6	1.1	1.9
Affective subscale			
Baseline score	13.3 (6.5)	13.0 (7.4)	13.6 (6.4)
Mean change score	–0.5	1.7	3.5
Somatic subscale			
Baseline score	12.2 (8.0)	13.4 (6.6)	11.4 (8.1)
Mean change score	–1.1	1.0	1.5
PTSD Checklist–Civilian Version			
Total score, range 17–85			
Baseline score	51.8 (17.4)	48.5 (18.1)	53.5 (18.6)
Mean (95% CI) change score	2.1 (–2.9 to 7.0)	5.0 (–1.7 to 11.6)	11.4 (5.9 to 16.9)
Reexperiencing subscale			
Baseline score	15.5 (6.1)	13.6 (6.2)	15.3 (5.6)
Mean change score	0.6	1.3	3.1
Avoidance subscale			
Baseline score	19.7 (7.3)	17.9 (7.4)	21.7 (8.8)
Mean change score	1.5	2.0	5.2
Hyperarousal subscale			
Baseline score	16.6 (5.5)	17.0 (5.9)	16.5 (5.5)
Mean change score	0.0	1.7	3.0

Abbreviations: HBO, hyperbaric oxygen; PTSD, posttraumatic stress disorder.

^a Continuous variables are shown as means (SDs) unless otherwise noted. The 95% CIs are calculated using 95% binomial exact CIs.

From: Effects of Hyperbaric Oxygen on Symptoms and Quality of Life Among Service Members With Persistent Postconcussion Symptoms: A Randomized Clinical Trial

Table 4. Baseline Scores and Postintervention Change Scores for Additional Outcome Measures Among the Intent-to-Treat Population

Outcome Measure	Domain and Range	Standard Care Group (n = 23)	HBO Group (n = 24)	Sham Group (n = 25)
Center for Epidemiologic Studies Depression Scale^a				
Baseline score	Depression, range 0–60	19.7 (10.5)	16.1 (10.4)	22.6 (13.6)
Mean change score	NA	–0.2 (7.5)	0.0 (12.2)	7.0 (9.7)
Beck Anxiety Inventory^a				
Baseline score	Anxiety, range 0–63	16.1 (10.5)	16.0 (11.4)	18.3 (13.4)
Mean change score	NA	–1.5 (8.0)	1.1 (9.0)	5.3 (9.1)
Short-Form McGill Pain Questionnaire^a				
Baseline score	Pain, range 0–45	13.5 (9.3)	14.9 (9.5)	10.7 (7.2)
Mean change score	NA	–0.9 (8.3)	–0.5 (8.8)	2.6 (7.0)
Pittsburgh Sleep Quality Index–Total^a				
Baseline score	Sleep, range 0–21	11.9 (4.7)	13.0 (4.6)	13.2 (4.2)
Mean change score	NA	–0.6 (3.7)	1.7 (3.6)	2.0 (4.8)
Global Satisfaction With Life Scale^b				
Baseline score	Global, range 5–35	19.3 (7.5)	19.4 (6.8)	17.5 (7.6)
Mean change score	NA	0.0 (6.0)	2.7 (7.0)	2.6 (6.8)
36-Item Short Form Health Survey^c				
Physical functioning				
Baseline score	Range 0–100	74.1 (20.5)	69.0 (20.8)	63.8 (28.9)
Mean change score	NA	–2.5 (15.0)	–0.7 (19.6)	10.4 (23.0)
Role-physical				
Baseline score	Range 0–100	33.7 (39.6)	30.2 (32.1)	36.5 (38.3)
Mean change score	NA	–1.3 (23.6)	4.3 (46.9)	16.3 (40.8)
Bodily pain				
Baseline score	Range 0–100	39.6 (23.8)	42.1 (25.1)	44.9 (23.4)
Mean change score	NA	–0.7 (18.8)	–2.0 (20.0)	9.6 (19.7)
General health				
Baseline score	Range 0–100	59.5 (17.2)	52.6 (25.2)	48.8 (16.6)
Mean change score	NA	–1.6 (18.5)	0.8 (28.0)	11.8 (14.9)
Vitality				
Baseline score	Range 0–100	42.2 (25.3)	36.0 (25.2)	32.9 (22.8)
Mean change score	NA	–0.3 (20.6)	7.2 (28.8)	6.8 (18.9)
Social functioning				
Baseline score	Range 0–100	51.1 (24.4)	55.7 (26.8)	47.4 (26.1)
Mean change score	NA	1.9 (17.3)	1.6 (26.4)	15.6 (36.9)
Role-emotional				
Baseline score	Range 0–100	53.6 (45.8)	48.6 (43.9)	44.4 (40.1)
Mean change score	NA	–10.0 (32.6)	0.0 (36.2)	16.7 (51.3)
Mental health				
Baseline score	Range 0–100	59.5 (19.8)	54.7 (23.1)	51.2 (25.5)
Mean change score	NA	–3.0 (13.7)	5.0 (24.5)	5.6 (18.3)
Automated Neuropsychological Assessment Metrics^d				
Simple reaction time				
Baseline score	Neural processing	77.7 (36.1)	78.3 (34.2)	81.4 (33.5)
Mean change score	NA	–15.0 (25.2)	1.7 (27.8)	1.7 (35.2)
Procedural reaction time				
Baseline score	Processing speed	81.1 (27.4)	88.1 (27.3)	78.6 (30.0)
Mean change score	NA	–4.5 (20.2)	7.2 (24.1)	–8.7 (23.6)
Code substitution–learning				
Baseline score	Associative learning	90.7 (23.7)	88.0 (20.7)	89.8 (18.7)
Mean change score	NA	–5.4 (13.2)	2.9 (20.3)	–1.0 (19.1)
Mathematical processing				
Baseline score	Working memory	94.0 (16.4)	87.3 (15.0)	84.1 (19.6)
Mean change score	NA	–2.6 (7.6)	3.9 (21.4)	8.1 (25.4)
Matching to sample				
Baseline score	Visuospatial memory	86.0 (15.2)	84.6 (16.6)	87.7 (16.9)
Mean change score	NA	–1.3 (8.7)	6.5 (13.6)	0.4 (22.6)

Abbreviations: HBO, hyperbaric oxygen; NA, not applicable.

^a Higher scores reflect more intense or frequent symptoms.

^b Higher scores reflect better satisfaction.

^c Scores are transformed scores using an age and sex-matched general population. Higher scores reflect better health.

^d Scores represent the throughput scores (speed and accuracy) standardized to age-matched control subjects.

From: Effects of Hyperbaric Oxygen on Symptoms and Quality of Life Among Service Members With Persistent Postconcussion Symptoms: A Randomized Clinical Trial

QUESTION 1

1. All of the following statements are supported by findings in the previously discussed studies EXCEPT:

- (A) HBOT increases the density and area of blood vessels in previously irradiated oral mucosa.
- (B) Stem cell mobilization by hyperbaric oxygen is significantly higher using treatment pressures of 2.5 ATA vs 2.0 ATA.
- (C) Epithelial cell proliferation in previously irradiated oral mucosa is significantly higher after HBOT and therefore suggests an increase in the rate of cancer local recurrence.
- (D) Significant elevations of intracellular regulatory proteins occur within stem cells following hyperbaric oxygen treatment at either 2.5 ATA or 2.0 ATA.

ANSWER 1

(C) - Epithelial cell proliferation in previously irradiated oral mucosa was NOT significantly higher after HBOT and therefore suggests no effect on the rate of cancer local recurrence.

QUESTION 2

2. All of the following statements are incorrect regarding the findings of the previously discussed studies EXCEPT:

- (A) HBOT at 2.5 ATA for 90 minutes vs 2 ATA for 120 minutes, as an adjunct to accepted wound management strategies, resulted in a higher rate of wound healing, lower amputation rates and improvement in symptoms of soft tissue radiation injury.
- (B) Low pressure HBOT showed significant benefit over sham compression in the management of post concussion symptoms after mild traumatic brain injury.
- (C) HBOT was observed to increase the number and area of subepithelial lymphatic vessels in previously irradiated oral mucosa.
- (D) Both low pressure HBOT and sham compression showed poor patient tolerance and no benefit as compared to standard, non compressive management of post concussion symptoms in mild traumatic brain injury.

ANSWER 2

(C) - The increase in lymphatic vessel density may be due to lymph angiogenic - associated VEGF-C that has previously been reported to increase after HBOT (Teas et al.). This may potentially help symptoms related to lymphedema. More studies are therefore needed to evaluate for this possible clinical benefit.