HYPEROXIC MYOPIA*

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FOR MORE THAN A CENTURY MEN HAVE EXPOSED THEMSELVES to elevated atmospheric pressures. While work in these environments has been associated with many symptoms, chronic blurring of vision has not been one of them.[1] Divers, caisson and tunnel workers have developed acute hemianopsias and visual loss as a result of central nervous system "bends" but neither refractive changes nor progressive chronic blurring of vision have been described. Similarly, oxygen breathing at normal and elevated atmospheric pressures has been employed therapeutically for many years but with the exception of retrolental fibroplasia, neither chronic blurring of vision nor refractive change have been described in association with this form of treatment. It was therefore of interest to us when patients being treated in the Duke hyperbaric facility reported blurring of vision toward the end of a repetitive series of hyperoxic exposures. Attendants of these patients undergoing similar compression and decompression schedules, but breathing air instead of oxygen had noted no visual disturbance.

To investigate this blurring of vision, a group of patients scheduled to undergo hyperoxic treatment for osteoradionecrosis[2,3] were refracted and their keratometer and tonometer measurements obtained before, during and after hyperoxic exposures. The blurring of vision was found to be the result of myopia which increased during the period of exposure and which then, following termination of treatment, gradually returned toward pretreatment levels.

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MATERIALS AND METHODS

The study population consisted of patients undergoing repeated hyperoxic exposure for the treatment of osteoradionecrosis. The mean age of the patients studied was 59 years with a range of 51 to 69 years. These patients were exposed on a daily basis to two atmospheres absolute pressure and breathed 98% oxygen for 120 minutes at this pressure. They were decompressed in accordance with a conservative modification of the US Navy diving tables. The treatment schedule called for 40 such daily exposures given consecutively excluding Sundays. Oxygen was delivered by means of a head tent and the external portion of the eye was directly exposed to 98% oxygen.[4]

The Snellen visual acuity, refractive error, applanation intraocular tension, and corneal curvature of the patients were measured within three days of the first exposure, and again at the end of the treatment regimen. Measurements were also obtained at follow-up visits and during the treatment period in some patients. In three patients a second series of 40 hyperoxic exposures was undertaken at 60, 113, and 106 days respectively following the end of the first series. In these patients the "pretreatment" value recorded is that obtained just before the beginning of the second

TABLE I
CHANGE IN REFRACTION WITH HYPEROXIA
(SPHERICAL EQUIVALENTS)

Patient	Initial	Post Rx
H	+0.00 D	−1.50 D
	+0.62	−1.12
H	−0.87	−0.87
	−0.37	−0.87
Pr	+0.13	−2.13
	+0.13	−2.00
Pr	+0.13	−2.00
	+0.18	−1.37
J	−0.50	−2.50
	−0.50	−3.00
J	−0.75	−2.00
	−1.00	−2.50
L	+1.00	−0.50
	+0.75	−1.00
Po	0.00	−1.62
	0.00	−2.12
DeH	+0.25	−1.75
	−0.25	−2.00
Den	0.00	−1.62
	0.00	−0.75
Mean	−0.05 D	−1.66 D

TABLE II
PRE AND POST HYPEROXIA TENSIONS
AND KERATOMETER MEASUREMENTS*

Patient	Initial		Post Rx	
	Diopters	mm Hg	Diopers	mm Hg
H	44.25	14	44.18	15
	43.94	14	43.87	15
H	44.12	13	44.31	13
	43.87	15	44.00	13
Pr	44.31	12	43.75	15
	43.06	12	43.00	14
Pr	43.62	9	43.56	11
	42.75	11	42.87	10
J	43.12	17	42.87	14
	43.06	15	43.13	14
J	42.68	15	42.82	18
	42.75	15	42.81	18
L	43.93	14	43.82	10
	44.06	14	43.82	11
Po		16		12
		16		12
DeH		22		19
		23		21
Den		16		14
		16		14
Mean	43.54	14.95	43.49	14.15

*Spherical equivalents

series. Although the patients received antibiotics, sedatives, and pain medications, these did not systematically differ from those employed prior to hyperoxic treatment.

RESULTS

The refraction and intraocular tension of 20 eyes were determined before and after a series of 40 hyperoxic exposures totaling 80 hours (Tables I and II). Keratometer measurements of corneal curvature were obtained on 14 of these eyes before and after treatment. These data are summarized in Table II. The mean change in spherical equivalent refraction was − 1.61 diopters. The mean change in corneal dioptric power was 0.05 diopters flatter (not significant) and the intraocular pressures decreased by a mean of 0.8 mm Hg (not significant). The observed change in the corneal dioptric power was both too small and in the wrong direction to account for the observed changes in refractive state.

During the period of hyperoxic treatment there was an average change in myopia of about 0.25 diopter per week with only two

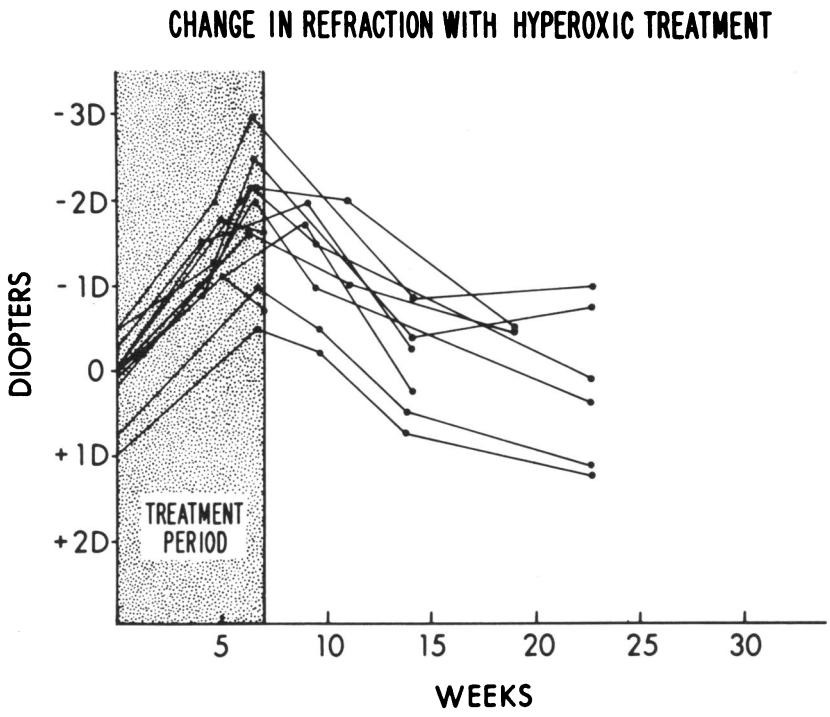

FIGURE 1

instances where the last treatment value was lower than the mid-treatment value. As can be seen in Figure 1, there is evidence that if the treatment had continued, the myopic change might have continued as there is little evidence for a plateau or steady state having been attained. The myopic change did not persist following treatment but gradually tended to return to the pretreatment state (Figure 1). At the last follow-up examination, the refractive error differed from the pretreatment value by − 0.23 D. The average interval between the last exposure to oxygen and this last follow-up examination averaged 12.5 weeks. It is possible that with longer follow-up this residual difference might vanish as the data do not indicate that a steady state had been reached.

When the follow-up keratometer readings are compared with both the initial and end of treatment values, again there is no myopic trend, the corneas being 0.23 D and 0.08 D flatter respectively. These small changes are again in the direction opposite that expected if the corneas were involved in the myopic process. Al-

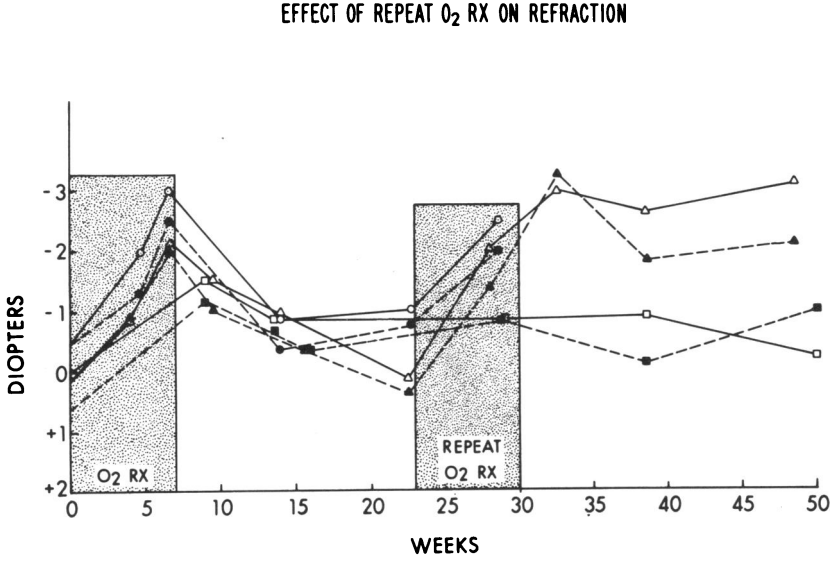

FIGURE 2

though the mean intraocular pressure decreased slightly, the difference was not statistically significant.

Three patients underwent a second series of 40 hyperoxic exposures. The changing refractive state of these patients is plotted in Figure 2. Two of these patients again became more myopic during the second treatment series. The third patient who had cataractous lens opacities did not change significantly. One of the patients who became more myopic had still not returned to her pretreatment refractive state after 20 weeks of follow-up. In this patient the 80 hyperoxic exposures may have induced a permanent myopic refrative change. The corrected vision in all patients remained unchanged.

DISCUSSION

A variety of drugs are known to occasionally produce transient myopia without miosis or cyclotonia. The most familiar of these to ophthalmologists are the carbonic anhydrase inhibitors: acetazolamide, dichlorphenamide, ethoxolamide, and chlorphenamide. The benzothiadiazide diuretics such as chlorothiazide,

hydrochlorothiazide, bendroflumethiazide, and polythiazide have also produced transient myopia. Chlorthalidone and the aldosterone antagonist, spironolactone may also produce myopia as have the antibacterial agents, sulfadiazine and tetracycline, and the arsenicals, arsphenamine and neoarsphenamine.

Most of the drug-induced myopias noted above are probably the result of rapid alterations in hydration and metabolic balance as is the transient myopia observed in the diabetic whose state of control is changing. In our patients the onset of the myopia, as well as its regression, is much slower than that associated with the use of diuretic drugs. We have eliminated a change in corneal curvature as the cause of the myopia and although a change in anterior-posterior ocular diameter is possible, it would seem unlikely. If swelling of the retina were to occur; for example, the eyes would be expected to become more hyperopic rather than more myopic. It would seem therefore that the myopia is lenticular in origin. Although an increase in cyclotonia could be implicated, the chronicity of the refractive change and the lack of miosis do not favor this hypothesis.

If the change in refraction is lenticular, there are two possible mechanisms that might be at work. One might be a direct effect of elevated oxygen levels on lenticular refractive index or shape and the other might be an effect of repeated compression and decompression. Because of its lack of vascular supply, the lens is a very slow tissue in terms of gas saturation and desaturation. It is unlikely that compression and decompression alone are responsible for the myopia since none of the accompanying attendants (who breathed only air) noted blurring of vision. In the long history of tunnel and caisson compressed air work large numbers of "ground hogs" have been compressed and decompressed on a daily basis and myopia has not been a problem. The change in refraction we observed is probably therefore the result of increased oxygen tension rather than a result of gas coming out of solution in the lens during decompression. The use of the head tent delivery system exposes the external eye to 98% oxygen. This oxygen exposure may produce more rapid and perhaps greater elevations of oxygen tension in the cornea, aqueous, and lens than would be obtained by mask breathing.

Increasing myopia is a common prodromal sign of cataract. Susceptibility to this change may be age-related and the mean age of our patients was 59 years with a range of 51 to 69 years. It is

possible that hyperoxic myopia might not occur in a younger population. Similarly, it is conceivable that prolonged oxygen exposures might be cataractogenic in older individuals.

The myopia which we have observed is slow to develop and relatively long-lasting. Unlike the more transient changes produced by the diuretic drugs or by diabetic alterations in blood glucose, this myopia is difficult to explain on an osmotic basis. Elucidation of this effect of hyperoxygenation may therefore be of value in the study of lens metabolism and cataractogenesis. If hyperoxic exposuressof greater magnitude than those reported here are contemplated, this study suggests that, at least in older individuals, there is a risk of irreversible refractive change. Those administering oxygen at elevated atmospheric pressures should be aware of this potential complication.

SUMMARY

We have reported the development of 1.6 diopters of myopia in a group of patients exposed to repetitive oxygen breathing at two atmospheres absolute pressure. No significant change in corneal curvature accompanied this refractive change. During the three months following termination of the hyperoxic exposure, the myopia gradually disappeared. It is speculated that hyperoxygenation alters the metabolism of the adult lens producing an increase in its dioptric power.

REFERENCES

1. Nichols CW, Lambertsen CJ: Effects of high oxygen pressure on the eye. *N Engl J Med* 281:25-30, 1969.
2. Hart GB, Mainous EG: The treatment of radiation necrosis with hyperbaric oxygen (OHP). *Cancer* 37:2580-2585, 1976.
3. Mainous EG, Hart GB: Osteoradionecrosis of the mandible — treatment with hyperbaric oxygenation. *Arch Otolaryngol* 101:173-177, 1975.
4. Sheffield PJ, Davis JC, Bell GC, et al: Hyperbaric chamber clinical support: multiplace, in Davis JC, Hunt TK (eds): *Hyperbaric Oxygen Therapy*, Bethesda, Undersea Medical Society, 1977, p 25.

DISCUSSION

DR ARNALL PATZ. The authors are to be congratulated on this most interesting study. To my knowledge this is the first documentation of the transient myopia developing in patients undergoing prolonged hyperoxia treatment.

By measuring corneal curvature with the keratometer and evaluating the intraocular pressure, the possibility that corneal curvature changes or intraocular pressure changes could influence the refraction seems adequately ruled out. I agree with the authors that the nature of the myopia can be considered lenticular in origin. The possibility of a ciliary body spasm (cyclotonia) cannot be absolutely ruled out; but as the authors indicate, the chronicity of the refractive change and the absence of miosis suggest that cyclotonia is probably not involved.

I think it is interesting that the authors have speculated that the myopia may be related to developing cataracts, particularly in older individuals. Although undocumented I think their speculation is reasonable that the oxygen exposure over prolonged periods might be theoretically cataractogenic.

I would like to ask the authors if they are planning experimental studies to examine the lens metabolism in animals subjected to hyperoxia. I think that their clinical observations are of sufficient importance to justify a carefully designed animal experiment to elucidate the mechanism of these changes. The possibility that the prolonged hyperoxia has an inhibitory effect on some of the oxidative enzyme systems in the lens may be fundamental to the changes observed.

The concept of a histotoxic "anoxia" is of interest as studies with oxygen under sustained hyperbaric conditions reveal that oxygen poisoning actually destroys or seriously inhibits many of the oxidative enzymes so that the cell suffers "anoxia" although bathed in a sea of oxygen.

Again I want to congratulate the authors on this excellent paper. I will be interested in learning of their follow-up studies.

DR MICHEL MATHIEU. I would like to suggest the possibility that the changes described following intensive and repeated oxygen use may be due to vasoconstriction. Doctor Hollenhorst will certainly agree when I say that intense migraine attacks can be alleviated by breathing pure oxygen just by its vasoconstrictive effect. The same mechanism, we all know, is implied in retrolental fibroplasia. Could such vasoconstriction act on the ciliary muscle and change its tonus? The fact that these refractive changes are reversible would, I believe, be more easily explained by such than by induction of changes in the lens itself.

DR MYRON YANOFF. Doctor Anderson is to be congratulated on his fine work. Some years ago we conducted a series of experiments on guinea pigs and reported (*Arch Ophthalmol* 87:417-521, 1972) on oxygen administration. We showed that there was endothelial cell damage in the cornea and epithelial cell damage in the lens and speculated at that time that there may be some chronic lens abnormalities due to increased oxygenation.

Again, Doctor Anderson is to be congratulated on his very nice study.

DR W. BANKS ANDERSON, JR. I would like to thank the discussors for their comments: Doctors Patz, Mathieu, and Yanoff.

In answer to the question concerning animal studies, we are at the present time not undertaking any animal work. We are only studying patients and are continuing our follow-up studies as well as looking at all the new patients undergoing this treatment.

As far as vasoconstriction is concerned, I think that it is well known that oxygenation will produce vasoconstriction. We cannot absolutely rule out a ciliary body cause for the refractive change that we observed, but we did not see any miosis and the prolonged duration of the myopia would seem to be evidence against the hypothesis that acute vasoconstriction is responsible.

I appreciate Doctor Yanoff's comments about the endothelial change in the lens. The patients in our group were all well along in years. Their median age was in the 50's. This, of course, was not unexpected since most of these patients had had carcinomas. We had no very young patients and I think it is quite likely that the older the patient, the more likely you would see myopia develop and the younger the patient the more resistant they might be to this oxygen effect.

I thank the discussors again for their comments.