Effect of alcohol and light on the retinal pigment epithelium of normal subjects and patients with retinal dystrophies

G B Arden, J E Wolf, F Singbartl, T E Berninger, G Rudolph, A Kampik

Abstract

Background—Light absorbed by photoreceptors causes oscillations in the voltage across the retinal pigment epithelium (RPE). This is the basis of the clinical test, electro-oculography (EOG). We have previously shown that alcohol causes a sequence of voltage changes which are so precisely the same as those caused by light that they must be produced by the same RPE machinery. There is good evidence that alcohol produces its effect by a direct action on the RPE. Consequently, in diseases associated with loss of photoreceptors, alcohol should continue to produce the voltage changes of the EOG unless secondary changes have occurred in the RPE.

Methods—The alcohol response in patients with retinitis pigmentosa (RP) was investigated using EOG.

Results—In no patient with RP was there any alcohol rise.

Conclusion—In patients with RP secondary abnormalities of function of the RPE must occur.

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The EOG voltage was recorded to standard 30° horizontal eye movements for sighted observers or extreme eye movements (~88°) in blind observers. The absolute voltages expressed as microvolts/degree of eye rotation are shown on the right ordinate. The baseline voltage in normal subjects (grey triangles) is nearly double that in patients. The left hand ordinate shows data normalised to the mean during the 15 minutes before giving alcohol. The grey triangles show the normal alcohol rise and the solid triangles and squares the result in patients with retinitis pigmentosa. The alcohol rise is replaced by a delayed fall. The "peak" voltages are for times 4–8 minutes after the stimulus and the troughs were measured 16–22 minutes after the stimulus. Mean (SE) of patients' normalised responses baseline = 0.9978 (0.0021); mean (SE) "peak" = 1.0126 (0.029); mean (SE) trough = 0.8214 (0.043).

**Discussion**

Much evidence shows that alcohol and light effects only have a final common pathway within the RPE. Thus, the alcohol rise is the same in darkness and in quite strong light although, if alcohol is already present in the bloodstream, a further dose of alcohol does not cause a change in RPE voltage. In the same way, the "light rise" to submaximal illumination is also independent of alcohol levels but is strongly inhibited by low levels of background illumination. Again, brief (1 minute) exposures to light or alcohol produce all the slow oscillatory voltage changes caused by prolonged stimulation, showing that the response is "triggered" or that, once the excitor substance is produced, it desensitises the RPE to further exposure. However, alcohol and light effects sum quantitatively even when one agent is given before or after the other. Thus, for submaximal stimulation, light and alcohol act almost independently. However, when larger amounts are given, the responses to each agent no longer sum but occlude, showing that they act through a final common pathway.

In the myopic patient whose results are given in Figure 1 a markedly reduced light rise occurred with a (near) normal alcohol rise. This may be explained if the retinal degenerative changes of myopia have caused voids, reducing the concentration of the unknown "light substance" in the subretinal space while alcohol, diffusing from retinal and choroidal vessels as from an infinite source, is present in near normal concentration.

In all our cases of RP the normal "alcohol rise" was absent although the EOG voltage fell slowly in a manner reminiscent of the effects of acetazolamide or hyperosmolarity. It would appear that, following the death of rods in patients with RP, there are secondary changes to the RPE which result in the loss of the normal response to alcohol. It would be of interest to determine if this is so for all patients with RP including those who do not suffer from night blindness.

The absence of the normal alcohol response shows that alcohol cannot change the RPE conductances via an action on the surviving inner retina. However, in our patients with RP there are no or few rods, and it might be that alcohol acts directly on rods to cause the RPE changes. However, indirect evidence (summarised above) and experiments in vitro show that alcohol has a direct action on the RPE. The most obvious explanation for the results in Figure 2 is that the RPE mechanism which provokes the stereotyped increase in basal conductance has been lost in RP. The cause of the slower alcohol induced fall in RP remains to be explained. It should be noted that alcohol can reach the RPE from the choroidal circulation.

Since RPE conductance changes are associated with the transport of fluid and specific substances across the tissue, secondary RPE changes could be associated with the loss of RPE function. This could explain the slow
death of cones in dystrophies such as RP which are caused by point mutations in the gene coding for rhodopsin.18 Unless these changes are reversible, our findings could have implications for proposed schemes of retinal rescue since the retina is dependent on the normal functioning of the RPE.

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doi: 10.1136/bjo.84.8.881

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