Carbonic anhydrase inhibition: The effect on retinal and optic nerve oxygenation and the mechanisms of action

Daniella Bach Pedersen

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ABSTRACT
Carbonic anhydrase inhibitor (CAI) is a drug widely used in the treatment of glaucoma; it lowers the intraocular pressure (IOP) by inhibiting the production of aqueous humour. It has been shown that systemically administered CAIs increase the optic nerve oxygen tension (ONPO2) in pigs - also when IOP is kept constant. The purpose of this study was to find out whether CAIs have the same effect on the retinal oxygen tension (RPO2) as it has on ONPO2 and to investigate the mechanisms of action of the effect of CAI.

The experiments were carried out on young, healthy pigs, since the porcine eye has similar circulatory properties as does the human eye. Our results are as follows:

1. CAI increases RPO2 as much as it increases ONPO2 when 500 mg dorzolamide is given intravenously.
2. A significant vasodilatation of the retinal arterioles and venules is seen when 500 mg dorzolamide is given intravenously. Vasodilatation is probably the reason why ONPO2 and RPO2 increase.
3. Lowering IOP with another glaucoma drug, timolol (a beta-blocker), did not increase ONPO2, indicating that lowering IOP per se does not increase ONPO2. Thus, CAIs’ increasing effect on ONPO2 is not due to the IOP lowering effect.
4. ONpH decreases during carbonic anhydrase inhibition, metabolic and respiratory acidoses.
5. The ONpH lowering effect of CAI per se is not the cause of the ONPO2 increase.
6. CO2 accumulation imitates the ONPO2 increasing effect of CAI, indicating that CO2 accumulation is a possible mechanism of action in CAIs’ effect on ONPO2.
7. Inhibiting prostaglandin synthesis by giving indomethacin intravenously decreases ONPO2. Additionally it diminishes the effect on ONPO2 of carbonic anhydrase inhibition and CO2 accumulation. It is therefore likely that the effect of CAI is at least partly due to the effect of prostaglandins.

It remains to be shown if CAIs may counter hypoxia and prevent ischaemia by opposing vasoocclusion in ischaemic conditions in the retina and optic nerve. It should be investigated if our results are applicable in clinical settings, eventually offering a pharmacological treatment of retinal ischemia.