Effects of Acetazolamide on intracranial pressure in glaucoma

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The primary objective is to evaluate changes in ICP due to acetazolamide using a noninvasive method of ICP measurement and to compare this with changes in IOP. Healthy controls will be used to control for any effect of diurnal fluctuations.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glaucoma and ocular hypertension
Study type	Observational non invasive

Summary

ID

NL-OMON48559

Source
ToetsingOnline

Brief title
Acetazolamide and Glaucoma

Condition

- Glaucoma and ocular hypertension

Synonym
Glaucoma; POAG

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,European committee and Uitzicht

Intervention

Keyword: Acetazolamide, Glaucoma, Intracranial pressure, Intraocular pressure

Outcome measures

Primary outcome

Peak and trough values of ICP (phase shifts of DPOAEs) and IOP for patients and

controls, for patients measured before and after taking their acetazolamide.

Secondary outcome

N/A

Study description

Background summary

Glaucoma is a chronic, progressive disease of the optic nerve in which there are detrimental effects on field of vision and visual acuity which, if left untreated, can lead to blindness. Historically, an elevated intraocular pressure (IOP) was deemed to be the key factor in the pathophysiology, but, recently, it was found that the relationship between IOP and intracranial pressure (ICP) may be a crucial aspect (Berdahl et al. 2008; Ren et al. 2010). This theory posits that alterations in IOP, ICP, or both can lead to a change in the pressure gradient across the lamina cribrosa (LC) and cause it to bulge and damage the nerve fibers.

The main treatment for glaucoma is IOP lowering medication. Acetazolamide is given to glaucoma patients to lower their IOP, however, it is also given to patients in neurology to lower ICP. If the difference between these two pressures is important in the cause and progression of glaucoma, then lowering both ICP and IOPx may not be the most successful means of treatment, and lowering ICP more than IOP during a significant part of the day could even be harmful.

A recent study determined that there is a linear relationship between distortion product otoacoustic emissions (DPOAEs) and invasive ICP (METc 2016/599, submitted for publication). DPOAEs are sounds emitted by the inner ear in response to tones at specified levels and frequencies. These emissions

represent ICP because there is a connection between the cranium and inner fluids via the cochlear and endolymphatic aqueducts. Previous research has also shown that DPOAEs can accurately represent changes in ICP (Büki et al. 1996; Voss et al. 2006; Williams et al. 2016; Bershad et al. 2014).

The proposed study investigates how ICP is affected in glaucoma patients who are taking acetazolamide. Peak IOP changes have been shown to occur at 1-2 hours after ingestion but the time course for ICP changes has not been properly assessed. Plasma levels peak at 1 hour post ingestion and continue to be raised for at least 7 hours (Friedland, Mallonee, and Anderson 1977). ICP will therefore be measured non-invasively using DPOAEs before the patient takes their prescribed medication, and then intermittently for 2 hours following ingestion to be sure we can characterize the changes in both ICP and IOP. Healthy subjects will be used as a comparison to control for any changes that are occuring due to diurnal fluctuations (Wostyn et al. 2011). To the best of our knowledge, the effect of acetazolamide on ICP in glaucoma patients has never been tested. We aim to gain better insight into the use of this drug in the treatment of glaucoma.

Study objective

The primary objective is to evaluate changes in ICP due to acetazolamide using a noninvasive method of ICP measurement and to compare this with changes in IOP. Healthy controls will be used to control for any effect of diurnal fluctuations.

Study design

cross-sectional, observational

Study burden and risks

Patients will have one visit to the ophthalmology department to perform the experiment. They will first be tested to detect the presence or absence of DPOAEs. Subjects who meet the selection criteria will then undergo the DPOAE testing. The test is completely non-invasive and will cause no discomfort for the patients. It is important to note that only patients already taking oral acetazolamide will be invited to participate and they will only be asked to take their prescription as they normally would. Patients and healthy subjects will spend 10 minutes for reception, additional questions, and DPOAE screening and, if they meet the selection criteria, 2.5 hours for the experiment. The total time will therefore be about 2 hours and 40 minutes, however only a fraction of this time will be used for measurements as much of the allotted time is waiting for the drug to enact changes. If abnormal eye screening results are obtained for healthy subjects, they will be referred to their GP.

Detection of signs of glaucoma may cause psychological stress, however, an early diagnosis will allow treatments to be initiated and therefore more preservation of visual functioning. Glaucoma patients will not perform any ophthalmological screening tests; therefore there is no risk of identifying any other eye conditions.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700VB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700VB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

*50-70 years of age
*Presence of DPOAEs in at least one ear
*Written informed consent.
*For patients only: taking acetazolamide as part of their regular IOP-lowering medication

Exclusion criteria

*No presence of DPOAEs
*Any other medications that may influence ICP
*For healthy controls, glaucoma or family history of glaucoma. This will be determined by form F1a and the ophthalmologic screening described in section 3.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-05-2019
Enrollment:	35
Type:	Actual

Ethics review

Approved WMO Date:	14-06-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-03-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL66015.042.18