Ocular screening in children and young adults at risk for increased intracranial pressure (Pictor Plus)

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Purpose of the Study

The purpose of this study is to evaluate the vision and posterior segment of eyes in children and young adults less than 22 years of age with risk, suspicion, or past medical history significant for elevated intracranial pressure (ICP). Patients will have visual acuity, confrontational visual field, and color vision tested. Assessment of the posterior segment will involve using a non-invasive (non-contact) imaging technique (i.e. a portable fundus camera in clinic and/or hospital settings).

Background & Significance

The need for non-invasive evaluation of ICP is an active area of study. The current gold standard is intraventricular or intraparenchymal catheters but these are invasive, expensive, and require sedation; and thus the need for effective non-invasive screening tools. The utility of funduscopy in identifying processes affecting ICP has long been recognized, i.e. papilledema, ocular venous engorgement, blurring of the optic disk. Studies have demonstrated that funduscopy may have a role in the qualitative assessment of increased ICP as a highly sensitive test. However, conventional bedside funduscopy does not allow for image capture and may necessitate pupillary dilation. Portable fundus cameras address these issues, allowing image capture and storage and the potential for non-mydriatic imaging, i.e. imaging without dilation of eyes. And as demonstrated in a recent study, portable fundus cameras are efficient (median exam time was 3 minutes and 24 seconds in a pediatric Emergency Department).

Additionally, ICP screening in asymptomatic patients remains limited. Patients being treated with medications for acne, specifically tetracyclines (e.g. minocycline and doxycycline), retinol, and isotretinol, are at particular risk for increased ICP but often are not identified until they are symptomatic (i.e. headaches, visual loss, papilledema). Symptom onset has been documented from 2 weeks up to 1 year from drug initiation. The percentage of patients with subclinical asymptomatic disease is unclear. This study would allow us to describe the presence of subclinical disease in our population and the role/utility of routine non-invasive screening methods.

Design & Procedures

We plan to identify patients less than 22 years of age who present to either:

1) The neurosurgery service at Duke University Medical Center (Duke University Hospital, Duke South Clinics, or Duke Children's Health Center) with suspicion or history significant for increased ICP.
2) The dermatology service at Duke Medical Plaza Patterson Place at risk for increased ICP (i.e. those being started on or currently taking high-risk medications).
3) The ophthalmology service at Duke Eye Center who have risk factors consistent with either groups 1) or 2) above.

Patients may be presented with an information sheet providing a brief summary of the research study to help them decide if they want to enroll in the study. Two different information sheets will be created for the two different populations of patients from which we will be recruiting, i.e. neurosurgery

and dermatology patients. Each information sheet will focus on characteristics and risks factors of that specific patient population.

In this study, we will use an FDA-approved portable non-contact, non-mydriatic (i.e. does not require pupil dilation) fundus camera, Pictor™, to image the fundus of both eyes of study participants. There are currently 2 versions of the Pictor camera that will be used. Both versions of the Pictor camera are FDA registered Class II medical devices.

The first generation Pictor camera was registered by 510k premarket notification in 2011.Reference US FDA 510K number: K110986. The Pictor camera is developed together with Volk Optical Inc. partner Optomed and it contains Optomed technology.

The most recent generation of the Pictor camera (trademarked the Pictor Plus) was registered by 510k premarket notification in 2013. Reference US FDA 510K number: K132186. The Pictor plus is manufactured for Volk and is registered as a private label device with the FDA registered under (Smartscope Pro). Therefore its FDA 510K letter is attributable to its private label equivalent device, known as the Smartscope Pro, manufactured by Optomed Oy, from Oulo, Finland. They are exactly the same product, except for their label, thus they use Optomed Oy's K-letter for registration purposes. However, this K-letter is technically no longer applicable per the FDA because the FDA made the Ophthalmic Camera product class 510K-exempt last year.

The FDA classification of this product (Ophthalmic Camera, FDA Product Code: HKI; Regulation #: 21CFR886.1120) no longer requires a pre-market notification 510k. August 2014, the FDA determined that a number of different device classes were considered safe for use based upon a lack of reported adverse events over the years. Thus, as of August, 2014 the FDA made these device groups 510k–exempt (essentially Class I), even though they technically remain Class II. The FDA will plan to change these product groups to Class I the next time they revise the CFR (no time table set for that currently).

Patients will also have visual acuity, confrontational visual field, and color vision tested if able. No eye drops will be given for the purposes of this study. A standard visual acuity assessment, confrontational visual field, and color vision testing will take approximately 5 minutes though patients will be allowed up to 10 minutes. Expected time for imaging each eye is approximately 5 minutes with the non-contact camera.

Study participants will be followed for 1 year from the time of the initial consent. If the patient reaches 18 years of age during the study period, he/she will be reconsented with an adult consent form to continue participation in the study.

Patients enrolled into the study will be added to a customized patient list in Epic. The list will be reviewed weekly in order to keep track of upcoming appointments of enrolled study participants. At each subsequent clinic and hospital encounter, vision testing and imaging will be repeated as described above.

Images will be stored on a secure server and reviewed and evaluated by study team members. The study results will not be provided to the patient or their physician, unless any abnormalities are identified in which case appropriate referrals will be arranged.

The information that will be obtained includes the following:
-Age of study participant
-Demographic information

-Relevant past medical/surgical history (e.g. lumbar punctures, ventriculoperitoneal shunts, hydrocephalus, Idiopathic intracranial hypertension (IIH), acne or dermatology-related conditions)
-Current medications
-Clinical examination findings from medical evaluation for increased ICP (e.g. lumbar punctures, x-rays, fluoroscopy, MRI, CT)
-Clinical examination findings from their standard ophthalmic examination from both eyes (if available) including: visual acuity, pupils; anterior segment (Conjunctiva/Cornea/Anterior Chamber/Iris/Lens); and posterior segment (Vitreous/Optic nerve/Macula/ Vessels/Periphery); refraction results; clinical diagnoses.

We will evaluate:
-Images obtained from fundus photography and their interpretation
-Visual exam findings (visual acuity, confrontational visual field, and color vision testing results)
Selection of Subjects

Inclusion/exclusion criteria

Approximately 200 participants less than 22 years of age with risk, suspicion, or history of elevated ICP will be recruited. We plan to recruit 100 participants with history or suspicion for increased ICP from the neurosurgery service at Duke University Medical Center (i.e. Duke University Hospital, Duke South Clinic, or Duke Children's Health Center) or the ophthalmology service at Duke Eye Center. We plan to recruit 100 participants at risk for increased ICP (i.e. those being started on or currently taking high-risk medications) from the dermatology service at Duke Medical Plaza Patterson Place or the ophthalmology service at Duke Eye Center.

-Inclusion Criteria:
Capable and willing to provide consent
Less than 22 years of age
History of or suspicion for elevated ICP or starting/currently taking high-risk medications associated with increased risk for elevated ICP

-Exclusion Criteria:
Unable or unwilling to give consent
22 years of age and older

Data Analysis & Statistical Considerations

Standard statistical methods will be used in analysis of data collected. Data will most likely be presented as the number of cases in each measured category compared to total number of cases overall, as well as the percentage of the total that each category represents.

The goal is to evaluate if patients less than 22 years old at risk for or with suspicion for or history of elevated ICP demonstrate changes in the posterior segments of their eyes detectable via portable fundus camera and what changes in visual exam are observed. Thus, we will evaluate: The posterior segments (e.g. optic nerve, retina, retinal vessels, and macula) of patients presenting with suspicion for

or history of elevated ICP and visual exam findings (visual acuity, confrontational visual field, and color vision).

Given that this is a descriptive study, we would like to recruit up to 200 patients to ensure that we enroll a wide range of clinical presentations and age ranges.

STATA, SAS, and/or JMP will be used for all statistical analysis along with the assistance of our in-house statistician as needed. Our statistician will only be given a de-identified database, which includes the following data on each subject, without any PHI:

-Age
-Ethnicity
-Relevant past medical/surgical history (e.g. LPs, VP shunts, hydrocephalus, dermatologic diagnoses, medications)
-Posterior segment findings
-Results of visual acuity, confrontational visual field, and color vision testing
-Clinical examination findings from medical evaluation for increased intracranial pressure and eye examination results