

Glaucoma

New York Certification Course
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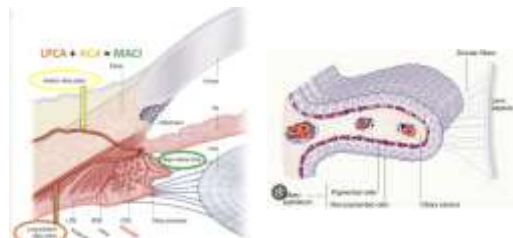
Learning Objectives

- To understand aqueous production and the management of aqueous production
- To understand the use of and indications for oral agents that lower IOP

Aqueous Humor Function Blood surrogate for lens/cornea

- Removes excretory products from metabolism
- Transports neurotransmitters
- Permits circulation of
 - inflammatory cells and mediators when needed
 - drugs to be distributed to ocular structures
- Stabilizes the ocular structure
- Contributes to the regulation of tissue homeostasis

Ciliary Body Anatomy

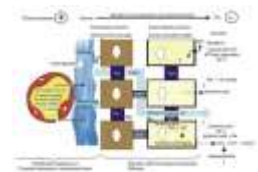


Aqueous Humor Formation and Composition

- Three mechanisms are involved in aqueous humor formation
 - Diffusion
 - Ultrafiltration
 - Active secretion
- The first two processes are passive and do not entail active cellular participation

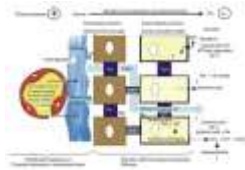
Active Secretion

- 80% - 90% of the total aqueous humor formation
- Non-pigmented epithelial cells
 - main site for active transport
- Active transport takes place through selective trans-cellular movement of anions, cations, and other molecules across a concentration gradient in blood-aqueous barrier
- This is mediated by protein transporters distributed in the cellular membrane



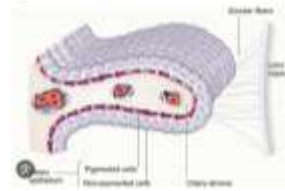
Energy Source

- ATP → ADP
- Activated by Na⁺-K⁺
- Mediated by Na⁺-K⁺-ATPase
 - Enzyme in the (non)pigmented ciliary epithelium
- Inhibited by acetazolamide (via pH changes?)

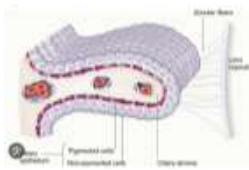


Aqueous Production

- Most plasma substances pass easily from the capillaries of the ciliary processes across the stroma and between the pigmented epithelial cells before accumulating behind the tight junctions of the nonpigmented epithelium

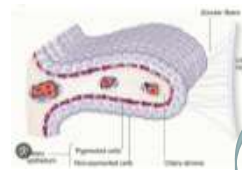


Transport Across Blood-Aqueous Barrier



- Mediated by transferring NaCl from the stroma to the posterior chamber with H₂O passively following
- 3 steps (more detail to come)
 - Electroneutral transporters
 - Passage of NaCl from pigmented to nonpigmented cells
 - Release of Na⁺ and Cl⁻ through Na⁺, K⁺ activated ATPase and Cl⁻ channels

Role of Carbonic Anhydrase



- Inhibit CA in Ciliary Epithelium
- CA mediates the transport of bicarbonate across the ciliary epithelium through a rapid interconversion between bicarbonate and CO₂
- Bicarbonate formation influences fluid transport through its effect on Na⁺, possibly by regulating the pH for optimum active transport of Na⁺
- 3 steps
 - Electroneutral transporters
 - Passage of NaCl from pigmented to nonpigmented cells
 - Release of Na⁺ and Cl⁻ through Na⁺, K⁺ activated ATPase and Cl⁻ channels

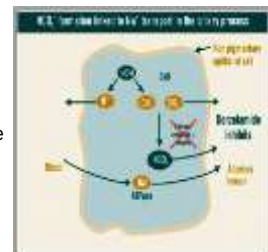
Carbonic Anhydrase

- Mediates transport of HCO₃⁻ across the ciliary epithelium by the reversible hydration of CO₂
- HCO₃⁻ influences fluid transport by affecting Na⁺
 - ?possibly by regulating the pH for optimal active ion transport
- Forms HCO₃⁻ and protons through the following reaction:

$$\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{HCO}_3^- + \text{H}^+$$

CAI's

- CAI's blocks the transformation of carbon dioxide (CO₂, a well-known vasodilator) to bicarbonate and therefore, has two beneficial effects.
- Increased CO₂ in the eye improves ocular blood flow
- Less bicarbonate in the eye reduces aqueous humor production, thus lowering IOP as well.



Carbonic anhydrase inhibitors

- Therapeutic prototype: acetazolamide
- Sulfonamide
- Inhibits excretion of hydrogen ion from the kidney
- Can induce a metabolic acidosis

Acetazolamide

- Reduces rate of aqueous humor formation by direct inhibition of enzyme carbonic anhydrase (CA) on secretory ciliary epithelium, causing, in turn, a reduction in IOP
- More than 90% of CA must be inhibited before IOP reduction can occur
- May reduce IOP by 40-60%
- Effects are seen in about an hour, peak in 4 h, and trough in about 12 h
- Derived chemically from sulfa drugs
- IV administration of this medication may be used for rapid relief of increased IOP

Acetazolamide

- Adult Dose
 - 500 mg IV stat, followed by 500 mg PO
- Pediatric Dose
 - 5-10 mg/kg/dose IV/IM, then 0-15 mg/kg/d PO divided q6-8h

Acetazolamide

- Contraindications
 - Documented hypersensitivity
 - Hepatic disease
 - Severe renal disease
 - Adrenocortical insufficiency
 - Severe pulmonary obstruction

Acetazolamide

- Interactions
- Can decrease therapeutic levels of lithium
- Can alter excretion of drugs by alkalinizing urine
 - Amphetamines
 - Quinidine
 - Phenobarbital
 - Salicylates

Acetazolamide

- Pregnancy
 - Safety for use during pregnancy has not been established
- Precautions
 - Patients with impaired hepatic function may go into coma; may cause substantial increase in blood glucose level in some diabetic patients

Methazolamide

- Reduces aqueous humor formation by inhibiting enzyme carbonic anhydrase, which results in decreased IOP
- Adult dose
 - 50-100 mg PO bid/tid
- Pediatric Dose
 - Not established

Methazolamide

- Interactions
 - Documented hypersensitivity; renal impairment
- Contraindications
 - May increase toxicity of salicylate, digoxin; coadministration with other diuretics may induce hypokalemia; decreases effects of lithium and alter excretion of other drugs by alkalinizing urine

Methazolamide

- Pregnancy
 - Safety for use during pregnancy has not been established
- Precautions
 - Caution in respiratory acidosis and diabetes mellitus; impairs mental alertness and/or physical coordination; hematuria, glycosuria, polyuria, hepatic insufficiency, bone marrow suppression, thrombocytopenia/purpura, agranulocytosis, urticaria, pruritus, and rash may occur

Hyperosmotic agents

- Reduces vitreous volume, which decreases IOP
- Decreased IOP reverses iris ischemia and improves its responsiveness to pilocarpine and other drugs
- Osmotic agents cause an osmotic diuresis and total body fluid reduction. They should not be administered in cardiovascular and renal patients.

Primary Angle Closure Attack aka: Acute Angle-Closure Crisis

- Presence of at least two of the following symptoms:
 - ocular or periorbital pain
 - nausea and/or vomiting
 - an antecedent history of intermittent blurring of vision with halos.
- Presenting IOP of >21 mm Hg (Goldmann)
- Presence of at least three of the following signs
 - conjunctival injection
 - corneal epithelial edema
 - mid-dilated unreactive pupil
 - shallow anterior chamber.



Treatment

- Acetazolamide 250 mg, 2 TABS PO (non-extended release)
 - Assuming no contra-indications



X2

Treatment

- Topical aqueous suppressants
- Let's alternate these every 15-20 minutes



Treatment

- Anti-inflammatory
- Often overlooked



Pilo 1 or 2% will help especially when the iris is less ischemic

- Should we wait?
- IOP has to be 35-40 mmHg before it will work?
- < effective if 2ndary pupillary block
 - Intraocular gas/oil
 - Phakomorphoc



Mydriatic would be better

Oral or IV hyperosmotic agents

- ~ reserved for failure of other treatments
- Mannitol is effective but contraindicated in renal failure and can cause hypotension in the volume depleted patient
- Mannitol: 1-2 g/kg IV given over 45 minutes to minimize cerebral effects (most common)
- 50% Glycerin (Osmoglyn)-Not for Diabetics, OR 45% Isosorbide (Ismotic): 1.5 mL/kg PO, ok for Diabetics (rarely used)



Acute Primary Angle Closure Glaucoma Treatment Summary

- Management
 - Acetazolamide 500 mg IV once or 2x 250 mg tabs PO then topical beta blocker 0.5% and apraclonidine or brimonidine, COMBO
 - AQUEOUS SUPPRESSANTS
 - Pred Forte
 - Pilocarpine 1-2%
 - Hypo-osmotics
 - Indentation gonioscopy

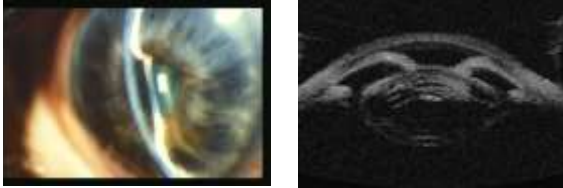


Case Report

- 64 y/o female presents with acute onset of pain and photophobia in her OD ~ 3 hours s/p a DFE in your office



Iris Bombe



Acute Primary Angle Closure Glaucoma

- An ophthalmic emergency
- Immediate goal: lower IOP
- Follow with LPI to prevent recurrence
- No standard drug therapy



Acute Primary Angle Closure Glaucoma

- Epidemiology
 - More common in:
 - Women
 - Hyperopes
 - Patients with shallow anterior chambers
 - Flatter corneal curvature
 - Increased intraocular lens thickness
 - Older Chinese men

Acute Primary Angle Closure Glaucoma

- Attacks commonly occur in low light conditions or generalized states of excitement when the pupil is mid-dilated (2nd relative pupillary block)
- Signs and Symptoms
 - Acute onset unilateral brow ache, eye pain, reduced VA, conjunctival injection, cornea may be edematous, pupil usually mid-dilated and non-reactive. IOP is usually > 50 mm Hg.
 - If cornea clear: may see cells in the AC without KP's, glaukomflecken.
 - Systemic symptoms: nausea, vomiting, generalized weakness

Acute Primary Angle Closure Glaucoma

- Evaluation
 - Gonio (Posner, Zeiss, Sussman) confirm angle closure, + indentation gonioscopy
 - Examine the fellow eye!

Case

- A 61 y/o male is referred to your clinic with a history of endstage glaucoma, s/p trabeculectomy and subsequent tube shunt OU.
- VA's 20/30 OU (accounted for by several applications of focal grid laser for CSDME)
- IOP's on maximum tolerated ophthalmic gtts is 34 mm Hg OD, 42 OS

- His medical history is significant for diabetic ketoacidosis, myocardial infarction, and renal insufficiency for which he is taking furosemide, potassium, and metoclopramide.
- You Rx Acetazolamide 250 mg PO QID and ask the pt to RTC in 2 weeks or PRN

- 10 days later, the patient returns, accompanied by his daughter who complains that her father seems “mentally out of it” and appears to be short of breath
- Your assessment reveals that the patient seems lethargic and that he is rapidly and deeply breathing as if he has just aggressively exerted himself.

Based upon this clinical scenario, which of the following best explains the etiology of these findings

- Metabolic acidosis resulting in cerebral hypoxia
- Metabolic alkalosis resulting in constriction of the cerebral arteries
- Increased ammonia production resulting in hepatic encephalopathy
- An allergic reaction to acetazolamide
- Ethylene glycol poisoning

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Which of the following best explains the purpose of this patient's rapid and deep breathing

- To increase the amount of oxygen to the pancreas in an effort to increase insulin production
- To increase the amount of carbon dioxide exhaled in an effort to lower serum carbon dioxide
- To increase the amount of oxygen to the kidneys in an effort to facilitate renal function
- To increase the amount of oxygen to the heart to prevent an MI
- To relieve his anxiety

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Which of the following lab tests is essential for the diagnosis of this condition

- a. Complete Blood Count (CBC)
- b. Urinalysis
- c. Arterial blood gases
- d. Antinuclear antibody (ANA)
- e. Blood Urea Nitrogen (BUN) and Creatinine

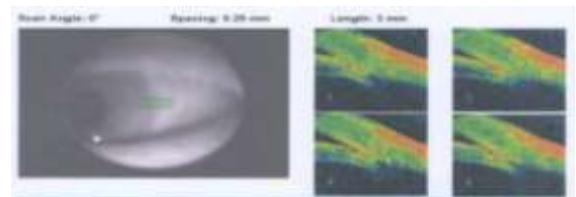
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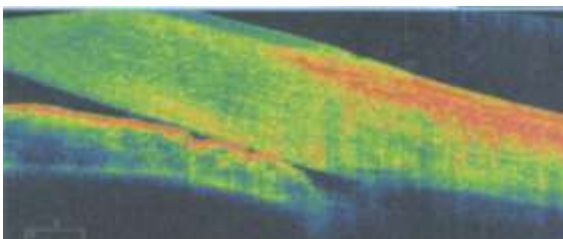
Case

- SL: Narrow angle (VH)
- <http://www.gonioscopy.org/vanHerick.html>
- Gonioscopy Only anterior TM visible with tilt OD, Only anterior TM visible with indentation gonioscopy OS.
- 4 clock hours of apposition OS
- No synechia present OU

Anterior Segment OCT OS



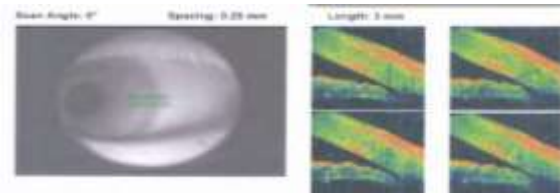
Anterior Segment OCT OS



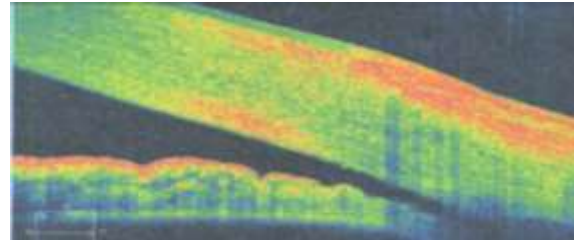
Case Assessment and Plan

- Primary Narrow Angle
 - Intermittent Angle Closure (glaucoma)
- Refer for LPI ASAP

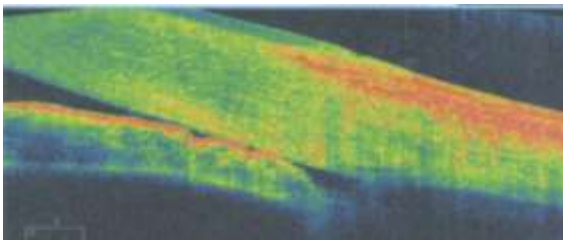
Anterior Segment OCT OS
s/p LPI



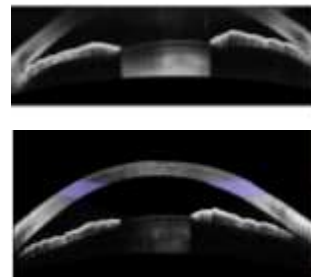
Anterior Segment OCT OS
s/p LPI



Anterior Segment OCT OS
Pre-LPI



65 y/o Pakistan



FIN