PKD: Optimizing Treatment

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Outline

PKD is a form of CKD
ADPKD Specifics
ARPKD Specifics
PKD is a form of chronic kidney disease (CKD)

Blood Pressure	Anemia
Growth	Nutrition
Calcium / Vitamin D	Acidosis
Medication Dosing	Vaccines
Avoiding kidney toxins

ADPKD Specifics

ARPKD Specifics

PKD is a form of chronic kidney disease (CKD)

ADPKD Specifics

Kidney Stones	Cyst Infection
Cyst bleeding	Cyst bursting
Hydration	Hearts
Brains	Livers

ARPKD Specifics
Outline

PKD is a form of chronic kidney disease (CKD)

ADPKD Specifics

ARPKD Specifics
Newborn Care
Hydration

Kidney size
PKD is a Form of Chronic Kidney Disease
Optimizing Treatment

Blood pressure (best evidence, longest discussion)
Anemia
Growth
Nutrition
Calcium / Vitamin D
Acidosis
Medication dosing
Vaccines
Avoiding kidney toxins

Blood Pressure and CKD

Hypertension is bad for the kidneys....

But even within the range of “normal” blood pressure...

lower is probably better
Blood Pressure and CKD

The ESCAPE trial:
- Included more than 300 children with CKD
- Randomized between
  1. treatment to a BP below average (50th percentile)
  2. standard treatment to BP below the 90th percentile

Intense group included an ACE inhibitor (ramipril)
They used 24 hour BP monitoring to define BP


Blood Pressure and CKD

After 5 years:
40% of standard had kidney failure or lost ½ of kidney function (average 2 meds)
30% of intense (average 3 meds) (with ACE inhibitor)

Blood Pressure and CKD

After 5 years...

The intense group was where the standard group was...

at 3 years


Blood Pressure and CKD

What is unknown:

IF doing it 5 years, get 2 years extra kidney function...
Does it mean 10 years = 4 extra, 50 years = 20 extra?

Not clear how to use “casual” BP readings with this information as opposed to 24 hour BP monitor

Does this apply to PKD patients?

There is no consensus guideline to follow the “study protocol” of that study at this point.
Blood Pressure and CKD

What is practical?

Take an ACE inhibitor if you and your labs can tolerate it.

Keep BP on the lower end of the “normal” range…

……but don’t pass out 😊

• Consider season (heat), child activity, and hydration with ACE inhibitors and ARBs (angiotensin receptor blockers)
• Aim for “efficient” BP prescriptions (fewer pills, less often)
• If within the “normal” range, don’t over-worry about small differences in BP percentile if it means adding a medication.
• Use ABPM to recheck over time, but not very frequently.

BP Measurement

What’s the Best Practice?
24 Hour Ambulatory Blood Pressure Measurement (ABPM)

A small BP monitor that allows measurements out of the range of doctors

less “white coat” effect
more measurements
sleep time measures

Correlates better with long term outcomes

Periodic ABPM is Best Practice
ESPECIALLY in CKD

AHA Scientific Statement

Ambulatory Blood Pressure Monitoring in Children and Adolescents: Recommendations for Standard Assessment

A Scientific Statement From the American Heart Association
Atherosclerosis, Hypertension, and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young and the Council for High Blood Pressure Research

Hypertension. 2008;52:433-451
Early in the CKiD study, 1/3 of children had “masked” hypertension. (1/6 had confirmed hypertension)

Complications of Hypertension: End-Organ Damage
HTN and IQ in Hypertensive Children with CKD (CKiD Study)

This is not a very big effect, but it was detectable in the large group of kids. Certainly no sign of lower IQ with better BP control.


Summertime is here!
Anemia in CKD

Kidneys make the hormone that controls red blood cell production

CKD leads to anemia

Anemia can cause fatigue and exercise intolerance, and when severe, worse problems.


Anemia in CKD

Erythropoietin (Epo) and other “ESA’s” are injectable hormone replacements.

Target Hb range is 9-11… unless higher naturally

Don’t forget iron… or other causes of anemia

Epo levels may be higher than expected in PKD ?
….not much evidence– small effect if any
Nutrition & Growth in CKD

A significant issue in CKD.

Growth in CKD

The most common form of malnutrition in N. American children with CKD is... *overweight and obesity*...

....Just as it is for children without CKD.

<table>
<thead>
<tr>
<th>BMI category</th>
<th>Count (Patients)</th>
</tr>
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<tbody>
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<td>≥90th percentile</td>
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More than twice as many CKD participants were overweight than underweight. The average BMI was the 69th (not the 50th) percentile.

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More than twice as many CKD participants were overweight than underweight. The average BMI was the 20th (not the 50th) percentile.

Growth in CKD

Close attention is needed at all ages

Infants and toddlers are at the highest risk of malnutrition and growth failure due to severe CKD

- vomiting
- decreased appetite
- early satiety (large kidneys or peritoneal dialysis)
- altered tastes
- limitations (low phos, Na, K)
Growth in CKD

There is no substitute for calories. supplements tube-feedings gastrostomies Especially infants and toddlers with poor growth

Head size increases 30% in the first year!
Age 1 to 3: 3% yearly
And later about 1% yearly until adulthood

Growth Hormone Issues with CKD

When GFR is moderately low ≈ 75% or less
GH levels are OK
Downstream levels are not.
GH can increase growth in CKD

Guidelines for GH in Children with CKD

Consider GH therapy in patients with:
(a) GFR <75 mL/min/1.73 m² and
(b) Height SDS ≤3rd (3rd percentile), or height velocity SDS ≤-2

Assess and treat complicating factors for poor growth, including:
(a) acidosis, (b) malnutrition, (c) soft-wasting, (d) osteodystrophy, and (e) hypothyroidism

Is Growth Velocity Improved?

NO

Perform baseline assessments for GH therapy:
(a) Recalculate: Height SDS, height velocity SDS, and height velocity
(b) Assess: Prepubertal stage, bone age, hip and knee x-rays, fundoscopic exam, chemistries, PTH, and thyroid studies

Start GH therapy:
0.05 mg/kg/day, SC (0.35 mg/kg/week)

YES

Continue current therapy

There are many years of experience and safety data


Calcium and Vitamin D (and Bones)
Calcium and Vitamin D (and Bones)

If tested, most “healthy” children (and adults) in North America will have low Vitamin D levels

Normal serum 25-hydroxyvitamin D is 20-50 ng/mL

Supplementation is generally advised. Many doctors check levels.

Calcium and Vitamin D (and Bones)

With moderately low kidney function…

• Vitamin D activation falls…
• Required loss of phosphorus in urine falls…
• Parathyroid hormone levels increase to compensate…

Hyperparathyroid bone disease occurs…

Very high doses of regular Vitamin D might work for awhile, but eventually, the required treatment is pre-activated form of Vit D, and sometimes use of other agents that directly lower parathyroid hormone release.

Insurance issues: “vitamin” vs “hormone”
Acidosis

With moderately low kidney function...

- Proximal tubular bicarbonate reclamation may decline
- Less acidification capacity in the distal tubule

Acidosis results (some compensatory respiratory effect)

Oral replacement with sodium bicarbonate or sodium citrate is the standard for many decades

Insurance issues: unintended consequence of FDA saying citrate is not FDA approved to treat...

Vaccinations / Immune Prevention

Adults and Children with CKD are at higher risk of complications of several infectious diseases. Vaccines are proven to reduce the risk of these diseases.

- RSV (antibody dosing): no CKD or PKD specific recommendation but < age 1 maybe age < 2 with lung disease or prematurity
- Influenza (yearly) (CDC Recommendation)
- Pneumococcal vaccines (routine plus Pneumovax > age 2) (CDC recommendation)
- Meningococcal vaccines (consider earlier age but > age 2)
CKD and Medication Use & Dosing

If you drink much from a bottle marked 'poison' it is almost certain to disagree with you, sooner or later.

- Lewis Carroll
- Alice in Wonderland

CKD and Medication Use & Dosing

MANY medications need special “renal” dosing

(usually lower or less frequent or both)
(not the same levels for all medicines)
(not the same at all levels of kidney function)
CKD and Medication Use & Dosing

DOs
Check with your nephrologist
Know your child’s approximate kidney function
…. Or get the NKF’s app

DON’Ts
Hesitate to remind the prescriber!
Expect others to know about child creatinine levels

A few examples of the many medical nephrotoxins

Slow Toxicity:
• “NSAIDs” (ibuprofen, naproxyn, et cetera)

Faster, More Severe Toxicity:
• Certain antibiotics (mainly IV forms)
• Certain medical (radiology, cardiology) contrast
• Certain antiviral medicines
• Certain chemotherapy
Medical Nephrotoxins: DOs and DON’Ts

DOs
Check with your nephrologist
Consider herbal or “natural products” as medicines
“No data” is not the same as “not harmful”

DON’Ts
Hesitate to remind the prescriber!
Hesitate to ask if there are less toxic alternatives
Avoid necessary or emergency treatments!

Lifestyle Nephrotoxins…
Lifestyle Nephrotoxins…

DON'Ts:
• Be overweight (more body, more body to clean)
• Smoke (it’s directly bad to the kidney)
• Drink too much alcohol

DOs:
• Stay well hydrated
• Exercise
• Most of the time eat healthy

PKD Specifics
Both ADPKD and ARPKD
PKD and Hydration

Being well-hydrated is the natural way to keep ADH levels low (2-3 Liters/Day for an adult-sized person)

Caffeine “blocks” ADH release by the brain… .... BUT….

1) It leads to increased urination and dehydration so indirectly back to higher ADH
2) It directly interferes with cell processes and leads to increased cyst formation in lab conditions

PKD and Urination

People with PKD generally urinate more than normal.

Toilet training:
Tendency toward later “dry at night”
Not necessarily late toilet training or accidents

School issues:
Increased frequency / bathroom “pass”
PKD and Family Planning / Genetics

ADPKD is very “heritable”
In couples whose child has ARPKD, *the same is true.*

- Clinical genetics is a great resource!
- IVF and pre-implantation genetics are already here
- Women with PKD need special care
- Deliveries of children with severe PKD should be done at a qualified center.

ADPKD Specifics
ADPKD and Kidney Stones

Up to around 30% of people with ADPKD eventually have a kidney stone.

The likelihood parallels the size of the cysts...

... uncommon in children

If there is a family history of stones PLUS the ADPKD, it is probably worth checking a 24 hour urine “stone profile” to see if there are specific things to try.

HYDRATION!

ADPKD and UTI

A severe UTI or one that comes back quickly can be due to cyst infection (acts like an abscess)

Certain antibiotics penetrate the cysts well, others not
ADPKD and Bleeding

Sometimes a cyst can burst and cause bleeding. Often there is pain but not always.

“Trauma” (not usually just a bump) can injure large kidneys more easily than normal sized kidneys

For a first episode of bleeding or any prolonged bleeding some kidney imaging and a doctor’s visit is needed.

ADPKD and the Heart

Affects between 1 in 4 and 1 in 5 people with ADPKD

Most common issues:
  • Mitral valve
  • Aortic valve and “root” of the aorta
  • Tricuspid valve

Usually these mild and do not require any treatment

An echocardiogram (sonogram of the heart) is needed if the heart sounds are not totally normal.

There is a range of opinion as to whether a cardiology consult or echocardiograms is uniformly needed
ADPKD and the “Brain”

Actually the blood vessels IN the brain—
Aneurysms or dissections are more common

The general population has a 1 in 100 baseline risk of an aneurysm in the brain.

The risk is between 1 in 10 and 1 in 20 people with ADPKD, and these occur at a younger (adult) age. (Polycystin 1 and 2 are found in arteries also)

The risk seems to run in certain families, not all people with ADPKD. A family history of stroke or sudden death or aneurysm requires closer attention.

ADPKD Miscellaneous

Pregnancy as well as certain birth control pills can increase cyst formation especially in the liver.

Diverticulosis (an intestinal problem) is more common in ADPKD
ADPKD– in the past some called it “Adult PKD” because most people manifest as adults.

ARPKD Specifics
ARPKD and Newborn Care

Opinion

A prenatal diagnosis of ARPKD should prompt delivery at a center with

- A high level NICU
- Pediatric nephrology

Just in case

ARPKD and Kidney Size

Kidney size can be an issue by itself

Reduced room for breathing

- Lung hypoplasia (underdevelopment) may have occurred
- Increased work of breathing at baseline = less reserve capacity
- Pulmonologists can help minimize effects of inevitable viral infections
ARPKD and Kidney Size

Kidney size can be an issue by itself

Reduced room for breathing

Others may mistake for overweight (body image)
Back pain from muscle stress
Increased susceptibility to injury
Increased abdominal fullness / reduced hunger

ARPKD: Uniformly Severe?

A relatively new recognition....

“mild” ARPKD
“mostly liver” ARPKD
“adult onset” ARPKD

.... has yet to permeate the medical field