



Neonatal Diabetes: The Rewards and Challenges

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AV Presentation

- Presented with diabetes at 42 days of life
- Increased thirst
- Increased urination/ diarrhea
- Weight loss
- Irritability

AV Presentation Labs

- Glucose: > 900 mg/dl
- Bicarb: 11
- Sodium: 138
- Urine Ketones: large

Hospital Course

- Seizures secondary to cerebral edema
- IV insulin for 3 days 0.08-0.1 unit/kg/hour
- Teaching

AV Initial Management

- Diluted NPH insulin
 - 10 units/ cc
 - To give 0.1 units draw up 1 unit
 - NPH U-10 2.2 units every 6 hours
- Frequent blood glucose testing
- Structured feeding schedule:
 - 4a, 8a, 12n, 4p, 8p

AV and Diabetes

- Family coping
- Structured lifestyle
- Daycare

AV gets an Insulin Pump

- December of 2004- age 5 years
- AV started on a Medtronic insulin pump

The Phone Call

- A different type of diabetes
- Hattersly's article on KCNJ11 Neonatal Diabetes
- We Dr. Stanley, myself and Susan Becker called mom with a proposal

Neonatal Diabetes

- Genetic form of diabetes
- Develops within the 1st months of life
- Estimated prevalence 1:100,000- 300,000 live births
- Heterozygous / homozygous mutations in KCNJ11 or ABCC8
 - Encoding 2 subunits
 - Kir 6.2
 - SUR1

Permanent Neonatal Diabetes

- The most common cause of Permanent Neonatal Diabetes (NDM) is a mutation in KCNJ11
- Patients with KCNJ11-related NDM are at increased risk for delays in learning, social-emotional and behavior development, ADHD and sleep difficulties

Transient Neonatal Diabetes

- Mutations less strongly activating
- Develops in the first few weeks of life, resolves within a few months of age
- May recur in adolescence
- Caused by imprinted region of 6q24

Genetics

- Athena Genetics
- ABCC8: p.L225p
- De Novo mutation
- Reported as a “gain of function” mutation

Ordering Genetic Testing

🌐 University of Chicago

🌐 University of Pennsylvania

🌐 Athena

What do the genetic mean?

🌐 Loss of function mutation in ABCC8

🌐 Increase activity in the KATP Channels

🌐 Decrease insulin secretion since the membrane does not depolarize normally

Transitioning from Insulin to Glyburide

🌐 In December 2006, following the protocol by Hattersley, we transitioned AV from his insulin pump to glyburide

🌐 Initial dosing was Glyburide 7.5 mg/ day, we gradually increased to Glyburide 15 mg/day= 0.6 mg/kg/day

Glycemic Control on Glyburide

- A1C levels were maintained less 6 % until 2012 when adolescence and puberty came into play

Glyburide Side Effects

- Glyburide is generally used for older adults with Type 2 Diabetes
- Side effects typically seen with Glyburide are also complications seen in the elderly population

The Importance of Sulfonylurea therapy

- Neonatal Diabetes is associated with learning and behavior issues. Sulfonylurea therapy is important for learning issues

Illness and Glyburide

- AV experienced very minimal hyperglycemia
- Family monitored closely during times of illness
- AV has not required any insulin since initiation of glyburide

Growing up on Glyburide

- Without glyburide AV would experience elevated blood sugars
- Its difficult to impress upon a teen that pills are just as crucial as injections

Diabetes Management

- As time went on mom began to realize that we were correct- blood glucose levels did not need to be monitored 6-8 times / day
- As AV got older we were asking for blood sugars to be tested

Food Choices

- 🌐 Sweetened Beverages
- 🌐 Junk food
- 🌐 Eating like a teen

A1C Creeping up

- 🌐 6-7% range
- 🌐 7/2015- A1C 7.4% - intervention needed

Januvia (Sitagliptin)

- 🌐 DPP- 4 Inhibitor. Believed to exert its actions by slowing the inactivation of incretin hormones
- 🌐 Starting dose- Januvia 25 mg each morning (lowest dose)

Why does Januvia work?

🌍 Januvia inhibits the enzyme that degrades GLP1 (incretine), thus as a result GLP1 has a more prolonged half life and its actions on stimulating insulin secretion is extended
