

OBSERVATIONS

Sulfonylurea Use During Entire Pregnancy in Diabetes Because of *KCNJ11* Mutation: A Report of Two Cases

Mutations of the *KCNJ11* gene are a common cause of permanent neonatal diabetes (PNDM) (1,2) and sometimes result in other diabetic phenotypes (2). Sulfonylureas (SUs) are effective and safe in most diabetic *KCNJ11* mutation carriers (3). However, their application risk is sometimes uncertain. We have previously described glibenclamide use in a pregnant woman with *KCNJ11*-related PNDM (4); for the first time, we report two cases treated with SU throughout the entire pregnancy.

The first case was a Hungarian woman with the E229 K *KCNJ11* mutation resulting in relapsing neonatal diabetes. The patient experienced remission between the ages of 3 and 10 years, at which point insulin was restarted. At the age of 13, after genetic testing, the patient was switched to gliclazide 60 mg/day. The woman became pregnant at the age of 16 years. When she was referred to the clinic in the 11th week of pregnancy, HbA_{1c} was 8.2%. Because diabetes was brittle during the insulin treatment on which she had been earlier, it was decided to continue gliclazide; the Bioethical Committee was informed. She was normoglycemic (HbA_{1c} 5.8, 5.2, and 5.2%) on a stable SU dose. Cesarean delivery was performed in the 38th week. The Apgar score of the baby girl (birth weight 3,010 g) was 10 at the first minute; the neonatal period was uneventful. Genetic testing from the umbilical cord blood showed the E229 K mutation. So far, the baby, currently 18 months old, has not been diagnosed with diabetes and is developing normally.

The second case, a previously reported R201H *KCNJ11* mutation carrier with multiple diabetes complications from Poland (4,5) became pregnant again at the age of 39 years when she was on glibenclamide 45 mg/day. Informed about the risks, she ruled out switching to insulin and decided to continue SU. HbA_{1c} at the

5th month of pregnancy was 5.8%. The amniocentesis in the 16th week showed the fetal DNA without chromosomal abnormalities or the R201H mutation. The woman delivered prematurely in the 33rd week via Cesarean section; the indication was the mother's status: edema, proteinuria, and renal function impairment. The latter was probably responsible for the need for glibenclamide dose reduction (10 mg/day). The Apgar score of the newborn (birth weight 2,720 g, >90 percentile) was 7 at the first minute. The baby girl presented with decreased muscle tension and cyanosis. She was also diagnosed with hypoglycemia requiring intravenous glucose, hyperbilirubinemia (treated with phototherapy), and respiratory acidosis. The latter was initially treated with continuous positive airway pressure and then, for 2 days, noninvasive mechanical ventilation. The recovery was uneventful. No birth defects were recorded. The child's development at the 18th month was normal.

In summary, we provide evidence that SUs constitute an alternative to insulin in pregnant women with Kir6.2-related diabetes, particularly in those refusing standard treatment or not adherent to this approach. The use of SUs did not result in developmental abnormalities. As in the first pregnancy (4), transient complications occurred in the baby of the mother with the R201H mutation receiving glibenclamide. Nevertheless, one should be careful with attributing them to the specific drug because they are common in prematurity.

ZSOLT GAAL, MD¹

TOMASZ KLUPA, MD, PHD²

IRENE KANTOR, MD³

WOJCIECH MLYNARSKI, MD, PHD⁴

LASZLO ALBERT, MD⁵

JUSTYNA TOLLOCZKO, MD, PHD⁶

ISTVAN BALOGH, MD, PHD⁷

KRZYSZTOF CZAJKOWSKI, MD, PHD⁸

MACIEJ T. MALECKI, MD, PHD²

From the ¹4th Department of Medicine, Josa Andras Teaching Hospital, Nyiregyhaza, Szabolcs-Szatmár-Bereg, Hungary; the ²Department of Metabolic Diseases, Jagiellonian University Medical College and University Hospital, Krakow, Malopolskie, Poland; the ³Department of Pediatrics, Josa Andras Teaching Hospital, Nyiregyhaza, Szabolcs-Szatmár-Bereg, Hungary; the ⁴Department of Pediatrics, Medical University of Lodz, Lodz, Lodzkie, Poland; the ⁵Department of Obstetrics and Gynecology, Josa Andras Teaching Hospital, Nyiregyhaza, Szabolcs-Szatmár-Bereg, Hungary; the ⁶Department of Neonatology and Neonatal Intensive Care, Warsaw Medical University, Warsaw, Mazowieckie, Poland; the ⁷Department of Laboratory Medicine, University of Debrecen, Debrecen, Hajdu-Bihar,

Hungary; and the ⁸2nd Department of Obstetrics and Gynecology, Warsaw Medical University, Warsaw, Mazowieckie, Poland.

Corresponding authors: Maciej T. Malecki, malecki_malecki@yahoo.com, and Zsolt Gaal, drgz@josa.hu.

DOI: 10.2337/dc12-0163

Z.G. and T.K. contributed equally to this work.

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Acknowledgments—This study was supported by the EU Framework 7 CEED3 Grant (HEALTH-F2-2008-223211), by funds from the Jagiellonian University Medical College (to M.T.M.), and by the TAMOP 4.2.1./B-091/1/KONV-2010-0007 project (to I.B.).

No potential conflicts of interest relevant to this article were reported.

Z.G. and M.T.M. interpreted data, critically revised the manuscript for important intellectual content, and approved the final version to be submitted. T.K. researched data and contributed to writing the manuscript. I.K., W.M., L.A., J.T., I.B., and K.C. researched data. M.T.M. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

The authors thank the subjects who participated in the study. The authors also acknowledge the editorial assistance of Aleksandra Malecka, Warsaw University, Warsaw, Poland.

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