Animal study suggests that newborn period may be crucial time to prevent later diabetes

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Pediatric researchers who tested newborn animals with an existing human drug used in adults with diabetes report that this drug, when given very early in life, prevents diabetes from developing in adult animals. If this finding can be repeated in humans, it may become a way to prevent at-risk infants from developing type 2 diabetes.

"We uncovered a novel mechanism to prevent the later development of diabetes in this animal study," said senior author Rebecca A. Simmons, M.D., a neonatologist at The Children's Hospital of Philadelphia. "This may indicate that there is an important developmental window, a period of time in which we can intervene to permanently protect the body's insulin-producing cells."

Simmons and lead author Sara E. Pinney, M.D., a pediatric endocrinologist at Children's Hospital, published the study in the October issue of *Diabetologia*.

The research may be relevant to children with intrauterine growth retardation (IUGR), a common complication during the mother's pregnancy. Simmons' previous research showed that IUGR, which is associated with decreased availability of nutrients and hormones to the developing fetus, permanently alters gene expression and impairs the function of insulin-producing cells in the pancreas. These defects have been shown to cause type 2 diabetes to develop in adulthood.

The study team used exendin-4 (Ex-4), a drug recently approved for use

in adults with type 2 diabetes—a condition in which a patient produces insufficient insulin, or is unable to process insulin normally. Although the drug's mechanism is not known, it has a hormone-like effect, raising insulin secretion in adults.

In their study, Simmons and Pinney used rats with an induced form of IUGR. They found that after being given to newborn rats, Ex-4 had epigenetic effects—modifying gene function without changing the underlying DNA sequences. Ex-4 increased the expression of a gene called Pdx1 that is necessary for beta cells to function properly. Beta cells produce insulin in the pancreas of mammals, including humans.

"In our study, giving exendin-4 during the newborn period had permanent beneficial effects on beta cells," said Pinney. "This could be important for people, in whom abnormal changes in infancy may irreversibly alter beta cells and lead to adult-onset diabetes. If we can establish that treating at-risk human babies with exendin-4 or a similar compound has corresponding effects, we may have a new preventive approach for type 2 diabetes."

Simmons and Pinney cautioned that much follow-up research remains to be done, such as investigating more of the basic biology and evaluating the genome-wide effects of exendin-4, before their research findings could translate into clinical use in children.

More information: "Exendin-4 increases histone acetylase activity and reverses epigenetic modifications that silence Pdx1 in the intrauterine growth retarded rat," Diabetologia, October 2011 print issue. doi: 10.1007/s00125-011-2250-1

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