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Mortality and Success Rates of the Neonatal Rat Model of Type 2 Diabetes Mellitus

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Description

Suitable models of Type 2 Diabetes Mellitus (T2DM) are being sought to investigate various treatment options. The neonatal streptozotocin (nSTZ) model has been explored and this study investigated the success and mortality rates of the nSTZ T2DM model. Following ethical approval by the University Hospital of the West Indies/University of the West Indies/Faculty of Medical Sciences Ethics Committee, two- and three-day old neonatal rat pups (n=66) were injected intraperitoneally with 60 mg/kg STZ (Sigma, France). Normal control pups (n=9) received equivalent volume of citrate buffer. Weaned animals were allowed free access to chow and water and kept at a constant light cycle of 12 hours on/12 hours off. Following an eight-hour fast, tail vein blood glucose was assessed weekly using Accu Chek Advantage glucometer (Roche Diagnostics, Germany). Oral glucose tolerance test was used to assess the type of diabetes in hyperglycaemic animals.

Type 2 diabetes mellitus (T2DM) can be induced in neonatal rat pups using streptozotocin in various concentrations, and the model simulates the characteristics of T2DM well. This paper highlights the lengthy duration for development of T2DM in the neonatal model (up to 14 weeks) and its associated potential high mortality rate of up to 32.6 % (with range 0 to 100 %). It calls into question whether the nSTZ model in its current form is worthwhile, and points to greater impetus to perfect the technique of successful induction of T2DM with significantly lower mortality. Neonatal mortality occurred within 10 days of STZ injection and successful diabetes development occurred mostly between 8 and 10 weeks post-STZ at a rate of 40.9 % of the total number of pups injected with STZ (or 81.8 % of pups that survived STZ injection).

Diabetes mellitus (DM) is a group of metabolic disorders that is characterized by hyperglycaemia, polydipsia, polyphagia, polyurea, and glycosuria as well as pruritis and slow healing of wounds [American Diabetes Association (ADA). The main types are type 1 and type 2 DM. Type 1 DM generally results from an autoimmune destruction of pancreatic beta cells or islets of Langerhans and produces a reduced quantity of insulin that is unable to properly regulate blood glucose. Type 2 DM (T2DM) typically results from tissue insulin sensitivity. In both types, accumulation of glucose results and this can in turn lead to a myriad of deleterious effects including neuropathy (tingling, ocular problems), renal complications, brain and cardiovascular problems, especially if the condition is chronic or untreated (ADA, 2020).[1] Diabetes is confirmed when non-fasting glucose exceeds 11.0 mmol/L (200 mg/dL) or fasting glucose is equal to or exceeds 7.0 mmol/L (126 mg/dL) on at least two occasions. There is an extreme paucity of reports on the success and mortality rates of the neonatal and other models of diabetes mellitus. Arulmozhi et al. (2004)[4] reviewed various neonatal models of T2DM and concluded that the nSTZ model was suitable based on its resemblance to T2DM secretory characteristics.

Description of Neonates

Neonates on the day of birth had a portion of their umbilical cord still intact or just a black mark where the umbilical cord was previously attached. These marks disappeared between days 6 and 9 of birth. Their eyes were closed until 11-14 days old and ears were folded downward, covering the orifice. The ears began to unfold as early as day 1 and was completed by day 5, but the orifices were not clearly defined until day 10-11 of birth.

Bodies were hairless and red to reddish pink in colour at birth, whiskers were present, and tails were approximately 1 inch long. Paws were unseparated and gender differentiation was not possible. By day 2 of birth, their body colour began to take on a pink colour in appearance. At 5 days old, a white hue started to emerge, representing hair growth, and their paws began to part with completion by day 10. Gender differentiation was evident as early as day 9 of birth, with females displaying nipples. Rat pups weighed between 6 and 13 g on the day of injection (2-3 days old).

References

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