Anesthesia Does Not Affect Development of Diabetes in ZDF Rats

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1 ABSTRACT

The obese Zucker diabetic fatty (ZDF) rat develops diabetes over time and is an excellent model of late stage type 2 diabetes. The development of diabetes is diet dependent and can be influenced by many environmental factors. Anesthesia has been associated with hormonal changes in blood glucose in rodents. However, long-term effects of anesthesia on regulation of blood glucose levels and development of the diabetic phenotype is not known in rodents. The purpose of this study was to determine whether or not administration of anesthetics agents would alter the development of the diabetic phenotype in these animals. Thirty 8-week-old male ZDF controlled rats were distributed to three groups of 10 animals (ketamine/xylazine, isoflurane and control). Ketamine/xylazine was measured from tail blood samples using a hand-held glucometer. Anesthesia was induced by intraperitoneal injection of ketamine (75 mg/kg) and xylazine (6 mg/kg), or inhalation of isoflurane using a chamber (2 to 4%) and followed by a 15-minute maintenance period (0.5 to 2%). Control animals experienced identical cage changes as the other groups. Immediately post-anesthesia, food was returned to all the animals in each group, while the remaining animals were fasted throughout the acute sampling period. Acute BG was measured every 30 minutes for 4 hours. Chronic BG was measured once every 10 hours (until 26 weeks of age). Fasted BG was estimated 16 hours following collection of the non-fasted blood from all animals treated the study well and showed similar weight gains post-anesthesia. Ketamine/xylazine increased BG immediately following anesthesia in both fasted and non-fasted animals, followed by a decrease compared to controls. BG in isoflurane animals was lower in fasted animals only relative to the control group. Long-term anesthesia of both fasting and non-fasting BG demonstrated no effect on the conversion to the diabetic phenotype in the animals. Based on these data, we concluded that ketamine/xylazine or isoflurane acute exposure does not affect the onset and development of diabetes in male ZDF obese rats.

2 INTRODUCTION

The incidence of obesity and diabetes is an epidemic worldwide. According to Centers for Disease Control and Prevention, an estimated 29.1 million men, women and children in the United States have diabetes. The incidence of obesity and diabetes is an epidemic worldwide. According to Centers for Disease Control and Prevention, an estimated 29.1 million men, women and children in the United States have diabetes. The incidence of obesity and diabetes is an epidemic worldwide. According to Centers for Disease Control and Prevention, an estimated 29.1 million men, women and children in the United States have diabetes.

Studies in appropriate animal models are very important in gaining a better understanding of obesity and diabetes. Historically, rodents have been a model of choice for research. Various mouse and rat models have been found to mimic different aspects of obesity and obesity-driven diabetes. The Zucker diabetic fatty (ZDF) rat is one such model. Because it is obese, hyperinsulinemic and develops diet-dependent diabetes, the ZDF rat embodies many of the facets of human obesity and diabetes.

The ZDF rat has a mutation of the fatty (fat) gene, develops diabetes over time and is an excellent model of late stage type 2 diabetes. The development of diabetes in the ZDF rat is diet dependent and can be influenced by many environmental factors. Anesthesia has been associated with transient changes in blood glucose in rodents. However, long-term effects of anesthesia on regulation of blood glucose levels and development of the diabetic phenotype is not known in rodents. The purpose of this study was to determine whether or not administration of anesthetics agents would alter the development of the diabetic phenotype in obese ZDF rats.

3 MATERIALS AND METHODS

Animals

Thirty 8-week-old male ZDF rats (ZDF-Crl, Charles River Laboratories, Kingston, NY) weighing between 300 and 400 grams were used. They were maintained in polycarbonate cages in a dedicated rodent surgical suite that was kept at 21 ± 2°C with a relative humidity of 55 ± 5% and a 12:12 hour light/dark cycle. Commerically prepared, sterilized feed and water were provided ad libitum. All conditions of animal preparation and care were in accordance with recommendations set forth in the Guide for the Care and Use of Laboratory Animals. The animals were of a VAF®Plus® health status.

Anesthesia procedures

Ketamine/xylazine group: Ketamine (75 mg/kg) and xylazine (6 mg/kg) was injected intraperitoneally. Animals were allowed to recover in a cage placed on a heating pad. Isoflurane group: Isoflurane was induced using a chamber (2 to 4%) and then removed for 15 minutes for maintenance (0.5 to 2%). Animals were allowed to recover in a cage placed on a heating pad.

Control group: Cage changes for the control group mimicked those of the treated groups.

Blood glucose measurement

Blood glucose was measured using AlphaTRAK® (Abbot Laboratories) portable glucometer. Tail was wiped with alcohol and cauterized. Lateral tail vein was punctured using lancet to collect a drop of blood and placed on glucose test strip. Blood glucose readings from glucometer were recorded.

4 EXPERIMENTAL DESIGN

The 30 rats were randomly allocated into 3 groups consisting of 10 rats each for ketamine/xylazine, isoflurane and control. Ketamine/xylazine was measured from tail blood samples using a hand-held glucometer. Anesthesia was induced by intraperitoneal injection of ketamine (75 mg/kg) and xylazine (6 mg/kg), or inhalation of isoflurane using a chamber (2 to 4%) and followed by a 15-minute maintenance period (0.5 to 2%). Control animals experienced identical cage changes as the other groups. Immediately post-anesthesia, food was returned to all the animals in each group, while the remaining animals were fasted throughout the acute sampling period. Acute BG was measured every 30 minutes for 4 hours. Chronic BG was measured once every 10 hours (until 26 weeks of age). Fasted BG was estimated 16 hours following collection of the non-fasted sample. All the animals tolerated the study well and showed similar weight gains post-anesthesia. Ketamine/xylazine increased BG immediately following anesthesia in both fasted and non-fasted animals, followed by a decrease compared to controls. BG in isoflurane animals was lower in fasted animals only relative to the control group. Long-term anesthesia of both fasting and non-fasting BG demonstrated no effect on the conversion to the diabetic phenotype in the animals. Based on these data, we concluded that ketamine/xylazine or isoflurane acute exposure does not affect the onset and development of diabetes in male ZDF obese rats.

5 RESULTS

Acute effects of anesthesia

Ketamine/xylazine increased BG immediately following anesthesia in both fasted and non-fasted animals, followed by a decrease compared to controls. BG in isoflurane animals was lower in fasted animals only relative to the control group. Long-term anesthesia of both fasting and non-fasting BG demonstrated no effect on the conversion to the diabetic phenotype in the animals. Based on these data, we concluded that ketamine/xylazine or isoflurane acute exposure does not affect the onset and development of diabetes in male ZDF obese rats.

Chronic effects of anesthesia

Ketamine/xylazine increased BG immediately following anesthesia in both fasted and non-fasted animals, followed by a decrease compared to controls. BG in isoflurane animals was lower in fasted animals only relative to the control group. Long-term anesthesia of both fasting and non-fasting BG demonstrated no effect on the conversion to the diabetic phenotype in the animals. Based on these data, we concluded that ketamine/xylazine or isoflurane acute exposure does not affect the onset and development of diabetes in male ZDF obese rats.

6 DISCUSSION

The obese Zucker diabetic fatty (ZDF) rat develops diabetes over time and is an excellent model of late stage type 2 diabetes. The development of diabetes is diet dependent and can be influenced by many environmental factors. Anesthesia has been associated with hormonal changes in blood glucose in rodents. However, long-term effects of anesthesia on regulation of blood glucose levels and development of the diabetic phenotype is not known in rodents. The purpose of this study was to determine whether or not administration of anesthetics agents would alter the development of the diabetic phenotype in these animals. Thirty 8-week-old male ZDF controlled rats were distributed to three groups of 10 animals (ketamine/xylazine, isoflurane and control). Ketamine/xylazine was measured from tail blood samples using a hand-held glucometer. Anesthesia was induced by intraperitoneal injection of ketamine (75 mg/kg) and xylazine (6 mg/kg), or inhalation of isoflurane using a chamber (2 to 4%) and followed by a 15-minute maintenance period (0.5 to 2%). Control animals experienced identical cage changes as the other groups. Immediately post-anesthesia, food was returned to all the animals in each group, while the remaining animals were fasted throughout the acute sampling period. Acute BG was measured every 30 minutes for 4 hours. Chronic BG was measured once every 10 hours (until 26 weeks of age). Fasted BG was estimated 16 hours following collection of the non-fasted sample. All the animals tolerated the study well and showed similar weight gains post-anesthesia. Ketamine/xylazine increased BG immediately following anesthesia in both fasted and non-fasted animals, followed by a decrease compared to controls. BG in isoflurane animals was lower in fasted animals only relative to the control group. Long-term anesthesia of both fasting and non-fasting BG demonstrated no effect on the conversion to the diabetic phenotype in the animals. Based on these data, we concluded that ketamine/xylazine or isoflurane acute exposure does not affect the onset and development of diabetes in male ZDF obese rats.

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