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COMPARISON OF FASTING BLOOD GLUCOSE LEVELS OF MALE AND FEMALE MICE POST XYLAZINE HYDROCHLORIDE ADMINISTRATION

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ABSTRACT

This study compared the effect of xylazine on the fasting blood glucose level of male and female mice. Sixteen 9 weeks old mice were assigned to two groups designated groups A and B consisting of 8 male and 8 female mice respectively. After fasting blood glucose determination, mice in both groups were injected with 10 mg/kg Xylazine intramuscularly. Fasting blood glucose levels of mice were re-determined at 30, 60, 120 and 240 minutes post injection. The experiment was repeated; using the same group of mice at 13 and 17 weeks of age. The results obtained showed that 9 and 13 weeks old male mice had significantly ($p < 0.05$) higher fasting blood glucose (FBG) values at 30, 60 and 120 minutes post xylazine injection compared to FBG of female mice of the same age. Blood glucose of 17 weeks old male mice were significantly ($p < 0.05$) lower than the FBG of 9 weeks old male mice at 30 and 60 min post xylazine injection. Fasting blood glucose of 9, 13 and 17 weeks old females were not significantly ($P > 0.05$) different at all time points studied. This study showed more pronounced hyperglycaemia in male mice post xylazine injection compared to female mice. Also the response of male mice to xylazine injection differed in the different ages studied. It was therefore concluded that the use of xylazine hydrochloride in male mice suffering from metabolic disorders such as diabetes should be done with caution.

***Keywords*:** Male, Female, Mice, Xylazine, Hyperglycaemia, Age

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INTRODUCTION

Xylazine, an alpha$_2$-adrenoceptor agonist is commonly used as a pre-anesthetic in many animal species. Use of this drug is highly favoured since it possesses sedative, muscle relaxant and analgesic properties [1]. It is also useful in gastrointestinal surgery and endoscopy since it reduces gastrointestinal motility [2].

Despite its potency and usefulness, xylazine causes cardiopulmonary depression which manifests clinically as bradycardia, hypotension and hypoxaemia [3,4]. Xylazine also interferes with neuroendocrine activity leading to alteration in neurohormonal and metabolic status of healthy anaimals

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[5]. Studies have shown that xylazine suppressed the secretion of nor-epinephrine, insulin and glucagon [5-7]. Some investigators [5,8] had earlier reported the elevation of blood glucose level of xylazine sedated animals. These neuroendocrine effects of xylazine suggest that its use in patients with endocrine or metabolic diseases might be detrimental. Therefore, since most metabolic ailments occur more in aging patients [9-11] and might be sex linked [12], it becomes imperative to compare the effect of xylazine hydrochloride on blood glucose level of male and female animals. This study was designed to investigate and compare the effect of xylazine hydrochloride on the fasting blood glucose levels of male and female mice of different ages.

MATERIALS AND METHODS

Animals

Sixteen (8 males and 8 females) mice constituted the experimental animals. The study animals were acquired from a litter of mice bred in the Department of Veterinary Surgery, University of Nigeria, Nsukka. They were housed in metal cages, fed pelleted growers ration while clean water was supplied *ad libitum*.

Experimental protocol

The 16 nine weeks old mice were assigned to two groups designated as groups A and B consisting of 8 male and 8 female mice respectively. Mice in all groups were fasted for 12 h before fasting blood glucose (FBG) determination. Tails of mice were nipped and blood samples obtained were used for fasting blood glucose determination. Glucose determination was by the glucose oxidase method [13]. After baseline glucose determination, mice in both groups were injected with 10 mg/kg Xylazine hydrochloride (Kepro, Holland) intramuscularly. Fasting blood glucose levels of mice were re-determined at 30 minutes post-injection and subsequently at 60, 120 and 240 minutes post injection. The experiment was repeated using the same group of mice at 13 and 17 weeks of age.

Data analysis

Mean (± standard error) glucose values of both groups were compared using independent sample t-test. Probability levels less than 0.05 were considered significant.

RESULTS

As shown in Tables 1, 2 and 3, fasting blood glucose of both male and female mice of the studied ages, increased post xylazine hydrochloride injection. Nine and thirteen weeks old male mice had significantly ($p < 0.05$) higher FBG values at 30, 60 and 120 minutes post xylazine injection compared to FBG of female mice of the same age (Tables 1 and 2). The FBG of 17 weeks old male mice were significantly ($p < 0.05$) higher than those of female mice of the same age at 60, 120 and 240 minutes post-xylazine injection (Table 3). Blood glucose of 17 weeks old males were significantly ($p < 0.05$) lower than FBG of 9 week old male mice at 30 and 60 min post xylazine injection but was significantly ($p < 0.05$) higher at 240 minutes post-xylazin injection (Table 4). Fasting blood glucose of 9, 13 and 17 weeks old females were not significantly ($p > 0.05$) different at all time points studied (Table 5).

DISCUSSION

The results of this study showed that blood glucose levels of both male and female mice increased post-xylazine injection. Though specific data on effect of xylazine on fasting blood glucose of mice is lacking in available literature, xylazine and other alpha$_2$ agonists (clonidine and medetomidine) have been reported to cause significant increase in blood glucose levels of cattle [8,14], rats[15,16], dogs [5], cats [17] and sheep [6]. According to Benson *et al*. [17], the hyperglycaemic effect of xylazine may be due to its ability to depress insulin release. The net effect of the actions of insulin is to lower blood concentrations of glucose, fatty acids and amino acids and to promote intracellular conversion of these compounds to their storage forms: glycogen, triglycerides and protein, respectively [18].

Table 1: Mean ± SEM blood glucose levels of 9 weeks old male and female mice after xylazine injection.

Time post injection (minutes)	Mean ± SEM Fasting blood glucose (mg/dl) Group A (Male)	Group B (Female)
0	95.9±7.02[a]	95.1±3.2[a]
30	231.88±51.2[a]	149.6±24.0[b]
60	197.75±27.7[a]	143.7±17.1[b]
120	168.5±5.8[a]	117.8±7.1[b]
240	93.7±7.8[a]	94.8±9.1[a]

[ab]Different superscripts in a row indicate significant ($p < 0.05$) difference in blood glucose levels of B groups A and.

Table 2: Mean ± SEM blood glucose levels of 13 weeks old male and female mice after xylazine injection.

Time post injection (minutes)	Mean ± SEM Fasting blood glucose (mg/dl) Group A (Male)	Group B (Female)
0	94.25±19.45[a]	87.0±11.1[a]
30	200.25±15.7[a]	178.25±54.0[b]
60	227.5±52.8[a]	144.0±15.1[b]
120	173.3±29.7[a]	103.5±10.3[b]
240	99.25±6.8[a]	107.5±18.8[a]

[ab]Different superscripts in a row indicate significant ($p < 0.05$) difference in blood glucose levels of groups A and B.

Table 3: Mean ± SEM blood glucose levels of 17 weeks old male and female mice after xylazine injection.

Time post injection (minutes)	Mean ± SEM Fasting blood glucose (mg/dl) Group A (Males)	Group B (Females)
0	98.5±3.9[a]	88.5±8.5[a]
30	167.3±11.8[a]	144.3±4.6[a]
60	169.5±14.9[a]	136.3±12.3[b]
120	158.8±13.1[a]	103.8±11.1[b]
240	112.8±3.7[a]	72.0±7.5[b]

[ab]Different superscripts in a row indicate significant ($p < 0.05$) difference in blood glucose levels of B groups A and.

The findings in the present study showed that fasting blood glucose readings of male mice were significantly higher than those of females post-xylazine injection is in agreement with the fact that sex hormones (testosterone and estrogen) play major roles in glucose metabolism [19,20]. Studies have also demonstrated that estrogen treatment improved insulin resistance [21], lowered fasting insulin levels [22.23], improved carbohydrate metabolism as well as caused hyperglycaemia [19,24,25]. Thus, since the hyperglycaemic effect of xylazine is due to its ability to cause insulin resistance, it is possible that

estradiol in experimental female mice might have improved insulin resistance post xylazine injection; hence lowering the glucose readings recorded in the female mice.

Table 4: Mean ± SEM blood glucose levels of 9, 13 and 17 weeks old male mice after xylazine injection.

Time post injection (minutes)	Mean ± SEM Fasting blood glucose (mg/dl) Week 9	Week 13	Week 17
0	95.9±7.02[a]	94.25±19.45[a]	98.5±3.9[a]
30	231.88±51.2[a]	200.25±15.7[ab]	167.3±11.8[b]
60	197.75±27.7[a]	227.5±52.8[b]	169.5±14.9[c]
120	168.5±5.8[a]	173.3±29.7[a]	158.8±13.1[a]
240	93.7±7.8[a]	99.25±6.8[a]	112.8±3.7[b]

[abc]Different superscripts in a row indicate significant ($p < 0.05$) difference in blood glucose levels of groups A and B.

Table 5: Mean ± SEM blood glucose levels of 9, 13 and 17 weeks old female mice after xylazine injection.

Time post injection (minutes)	Mean ± SEM Fasting blood glucose (mg/dl) Week 9	Week 13	Week 17
0	95.1±3.2[a]	87.0±11.1[a]	88.5±8.5[a]
30	149.6±24.0[a]	178.25±54.0[a]	144.3±28.6[a]
60	143.7±17.1[a]	144.0±15.1[a]	136.3±12.3[a]
120	117.8±7.1[a]	103.5±10.3[a]	103.8±11.1[a]
240	94.8±9.1[a]	107.5±18.8[a]	72.0±7.5[a]

[abc]Different superscripts in a row indicate significant ($p < 0.05$) difference in blood glucose levels of groups A and B.

Earlier studies had shown that glucose and energy metabolism diminished with the process of aging [26]. The present study was conducted using young mice aged between 9 - 17 weeks with the expectation that their response to xylazine injection would differ. Contrary to our expectation, the response of female mice in the age groups studied did not differ significantly. In contrast, fasting blood glucose levels of older males (aged 17 weeks) were lower than FBG of younger male mice (aged 9 weeks). The finding is in contrast to earlier reports [26] that showed that the rate of glucose disappearance is faster in young male mice compared to the elderly ones.

CONCLUSION

The results obtained in this study showed more pronounced hyperglycaemia in male mice post xylazine injection compared to females. Also the response of males to xylazine injection differed in the different ages studied. It is therefore recommended that the use of xylazine hydrochloride in males suffering from metabolic disorders such as diabetes may be done with caution.

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