Effect of Trans Fatty Acid on Glucose Level and Pancreatic β Cell in Rats

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Abstract: A high intake of trans fatty acids can cause inflammation and lipid peroxidation of cell membranes which, in turn, damage cells and tissues. The purpose of the current study was to investigate the effects of dietary trans fatty acids on blood glucose levels and pancreatic β cells. Our randomized pre-post test control group study design included two groups of Wistar rats fed either a diet containing 2% trans fat or a control diet containing no trans fat for 10 d. The results showed that blood glucose levels were not significantly different between the two groups. There was no obvious damage to pancreatic β cells, but the number of normal cells in the treatment group was less than that in control animals.

Key words: Trans fatty acid, blood glucose, pancreatic β cell

INTRODUCTION
Fats are composed of fatty acids and glycerol. Fatty acids consist of two saturated (single bonds) and/or unsaturated fatty acids (double bond) hydrocarbon chains of varying lengths. Chemically, hydrogen atoms on trans fatty acid chains bind hydrogens on the opposite chain, but bind adjacent hydrogens in cis fatty acids. Trans fatty acids were thought to be metabolized similarly to saturated forms due to their conformational similarity (Hunter et al., 2010).

Intake of high-fat foods, including trans fatty acids, may have an impact on the formation of free radicals which can induce oxidative stress, inflammatory responses and destruction of pancreatic β cells. In addition to their effect on membranes and blood glucose levels, trans fatty acids are also associated with systemic inflammation (Mozaffarian, 2006). Muller et al. (2001) concluded that a high intake of trans fatty acids may increase insulin resistance.

Blood glucose levels are fundamental to the diagnosis of hyperglycemia. An epidemiological study by Salmeron et al. (2001) showed that intake of trans fatty acids is a risk factor for type 2 diabetes mellitus. Zapolska-Downar et al. (2005) concluded that trans fatty acids induce apoptosis in endothelial cells. Therefore, the objective of the present study was to determine the effect of dietary trans fatty acids on blood glucose levels and pancreatic β cells in rats.

MATERIALS AND METHODS
The current study had a randomized pre-post test control group design and compared two groups of male Wistar rats (200-300 g each) fed a standard diet (control, n = 6) or a diet containing 2% trans fatty acids (treatment, n = 6) for 10 d. Blood glucose levels and pancreatic β cells were examined before and after treatment.

Rats were housed individually in plastic cages with a stainless steel cover and acclimatized for 1 week at room temperature under a 12 h light/12 h dark cycle, 40% minimum relative humidity and distilled water ad libitum. Any rats that developed diarrhea characterized by unformed stools, a weight change of >10% and/or that died during the study period were excluded. Animals included in our study were healthy with no anatomical abnormalities, active and had an initial fasting blood glucose level of <110 mg/dL.

After a 12-h fast, blood was sampled from all rats using a microhematocrit and capillary tube. Approximately 5 mL of blood was collected from each rat in collection tubes containing potassium oxalate as an anticoagulant agent. Plasma was separated by centrifugation (400 x g) for 15 min at 4°C. Plasma glucose was determined spectrophotometrically using a Hitachi 902 automatic analyzer (Hitachi, Tokyo, Japan). Examination of serum glucose levels was done by Prodia Laboratory (Yogyakarta, Indonesia) in accordance with laboratory-based protocols (ISO-15189). After the 10 d treatment period, rats were sacrificed pancreatic tissue removed for histopathological examination. Pancreatic endocrine cells in the islets of Langerhans were observed using hematoxylin and eosin staining. Observation was performed descriptively by calculating the number of β cells.

All breeding phases and experiments conformed to rules outlined by the Integrated Analysis and Research Laboratory and Pathology Laboratory, Faculty of Veterinary Medicine, University of Gajah Mada (Yogyakarta, Indonesia) and were conducted with approval of the Faculty of Public Health Ethics Committee of the University of Indonesia (Depok, Indonesia).

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Results were presented as means±standard deviation of treatment and control groups. A Student’s t-test was used for all analyses and p<0.05 was considered statistically significant. The data were analyzed using the SPSS software.

RESULTS AND DISCUSSION
Blood glucose level: Although blood glucose levels were not significantly different between the two groups before or after the 10-d experimental feeding period, they tended to be higher in rats fed the high trans fat diet (16.17 mg/dL) versus the control diet (2.5 mg/dL) (Table 1). These results are similar to those reported by Aronis et al. (2012) in which trans fatty acid intake did not significantly alter glucose or insulin levels. Glucose is a major regulator of transcription and translation in β cells, an effect that is necessary for long-term maintenance of their highly differentiated state and the secretory requirements imposed by prolonged elevation of glucose (Schuit et al., 2002). Our results showed that glucose levels ranged from 99.00 to 115.17 mg/dL in rats fed the high trans fat diet (Table 1). An increase in blood glucose levels causes an increase in insulin secretion, which increases the transport of glucose into liver, muscle and other cells, thereby reducing blood glucose concentrations back to normal values.

Although treatment rats were fed a diet high in trans fatty acids (2%), it is possible that 10 d is an insufficient amount of time to induce a significant increment in blood glucose levels in male Wistar rats. A study by Huang et al. (2009) also reported that Wistar rats fed a diet containing 4.5% trans fats for 16 weeks did not show significant changes in plasma glucose levels, insulin levels, or the insulin sensitivity index. This result is presumably due to unpredictable metabolic and hormonal factors associated with rats. Rats have endogenous homeostatic mechanisms that keep blood glucose levels within the normal range; liver, extrahepatic tissue and several hormones (insulin, glucagon, cortisol, and catecholamine) play important roles in the regulation of blood glucose levels (Rosen and Spiegelman, 2006).

Table 1: Mean concentration of blood glucose in the treatment and control group

<table>
<thead>
<tr>
<th>Blood glucose level</th>
<th>N</th>
<th>Mean±SD (mg/dL)</th>
<th>p-value (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before intervention</td>
<td>Treatment group</td>
<td>99.00±10.69</td>
<td>0.246 (-6.184; 21.516)</td>
</tr>
<tr>
<td></td>
<td>Control group</td>
<td>97.33±10.84</td>
<td></td>
</tr>
<tr>
<td>After intervention</td>
<td>Treatment group</td>
<td>115.17±14.30</td>
<td>0.097 (-3.262; 27.928)</td>
</tr>
<tr>
<td></td>
<td>Control group</td>
<td>99.63±9.45</td>
<td></td>
</tr>
</tbody>
</table>

*Not statistically significant (p>0.05); SD: Standard deviation

Table 2: Mean number of pancreatic β cell in the treatment and control group

<table>
<thead>
<tr>
<th>Pancreatic β cell 'normal'</th>
<th>N</th>
<th>Mean±SD</th>
<th>p-value (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cells</td>
<td>Treatment group</td>
<td>67.80±14.29</td>
<td>0.384 (-7.519; 29.452)</td>
</tr>
<tr>
<td></td>
<td>Control group</td>
<td>74.83±11.15</td>
<td></td>
</tr>
</tbody>
</table>

*Not statistically significant (p>0.05), SD: Standard deviation
pancreatic β cells, but rats with higher glucose levels tended to have fewer normal pancreatic β cells. Ferrannini (2010) stated that hyperglycemia is associated with β cell failure, including cell number and function. A 60% decrease in β cell mass has been reported in type 2 of diabetes in humans (Butler et al., 2003). Generally, free fatty acids have complex effects on β cell function. Although the mechanism by which this occurs is still hotly debated, it has been suggested to involve impaired glucose metabolism, reduced insulin biosynthesis and β cell loss (Poitout and Roberston, 2008).

Conclusion: Our experimental findings indicated that eating a 2% trans fat diet for 10 d did not significantly increase blood glucose levels of male Wistar rats. Though the amount of normal pancreatic β cells in the treatment group was less than controls, this change was not significant. Other studies with different doses of trans fats and longer experimental periods may better explain the mechanisms by which dietary trans fatty acids affect blood glucose levels and pancreatic β cells.

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