Effect of high saturated free fatty acids feeding on progression of renal failure in rat model of experimental nephrotoxicity

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ABSTRACT

The current study evaluates the impact of high saturated free fatty feeding in rat model of experimental nephrotoxicity induced by gentamicin. Sprague-Dawley rats weighing 200 g were randomized into four groups; the first group received the standard rodents chow for 8 weeks and was treated as control, the second group (HFD) received an experimental high fat diet rich in palm kernel oil (46% of Calories as fat) for the same period. The third group (HFDxG) was given 80 mg/kg (body weight)/day gentamicin 3 times per week through intraperitoneally during the last 24 days of the feeding period while the fourth group was given gentamicin as above along with the standard rodents chow. Renal function was assessed through measuring serum creatinine, creatinine clearance and absolute and fractional excretion of both sodium and potassium. At the end, rats underwent a surgical procedure for blood pressure measurement. Renal function study showed a stronger nephrotoxicity for HFDxG group. Hypertension was observed in HFD group while the pressure declined after gentamicin co-administration. Overall, changing the feeding behavior toward using more SAFAs for rats injected with gentamicin promotes the progression of renal failure.

KEY WORDS: nephrotoxicity, blood pressure, hypertension, creatinine clearance, high fat diet.

INTRODUCTION

Gentamicin is a widely used aminoglycoside antibiotic to treat various Gram +ve and Gram -ve infections. Its nephrotoxic action is attributed to its potential to damage the proximal convoluted tubules (PCT) and glomerular basement membrane [1]. Oxidative stress mediated damage is the main character of its nephrotoxicity [2, 3]. Substituting the elementary dietary constituents by fats rich in saturated free fatty acids (SAFAs), has a negative impact on the ability of the body to cope with various patho-physiological conditions [4]. In spite of that, these fats are used extensively in food industry. This is due to their physicochemical properties that give food products the sought after texture [5]. SAFAs induce their deleterious effects through several mechanisms [1]. They stimulate a specific type of immune system related receptors called TLRs (toll like receptors). TLRs are expressed in most body cells including myocytes, hepatocytes and adipocytes [6]. Their activation triggers the inflammatory pathway related to insulin resistance [6, 7]. From the other hand, SAFAs induce visceral obesity. When the visceral adipose tissue is engorged with fats, it does not merely act as a fat depot but it also acts as an endocrine gland releasing the inflammatory cytokines related to insulin resistance [8]. Disposition of the source of cellular energy from carbohydrates to fats rich in SAFAs increases the release of free radicals during mitochondrial internal respiration. This results in higher oxidative stress [9]. Our study aimed to find the impact of replacing the essential dietary elements in food by SAFAs on progression of renal damage in rats model of gentamicin induced nephrotoxicity.

MATERIALS AND METHODS

Animals and diet
Male Sprague-Dawley rats, weighing 180–205 g obtained from animal house of Universiti Sains Malaysia, were used in the study. They were housed at the animal transit room with 4 animals per cage at room temperature with 12:12-h light-dark cycle. All the procedures were performed according to guidelines of the Animal Ethics Committee, Universiti Sains Malaysia for the use of animals in research. Time dependent effect for nephrotoxicity induction and the required sample size was estimated according to a prelimi-