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Post-unilateral Nephrectomy Administration of Alcohol Escalates Kidney Oxidative Stress of Male Wistar Rats

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ABSTRACT: Alcohol has been used in folk medicine to potentiate some health benefits. Although, alcohol was reported to induce renal dysfunction, its activity on kidney tissues is not fully elucidated. However, whether or not alcohol could be beneficial after unilateral nephrectomy is unknown; thus, the objective of this study was to investigate the impact of post-unilateral nephrectomy administration of alcohol on kidney oxidative stress of male Wistar rats with 150 – 210 g-body weight, randomly grouped into four groups and the oxidative stress biomarkers such as lipid peroxidation (MDA), superoxide dismutase (SOD), Catalase (CAT) and glutathione peroxidase (GPx) determined using kidney tissue homogenates. Nephrectomy and alcohol significantly increased MDA and significantly decreased SOD, CAT and GPx; furthermore, post unilateral nephrectomy administration of alcohol caused advanced significant elevation of MDA as well as advanced significant depletion of SOD, CAT, and GPx of the kidney tissue. This study demonstrated for the first time that post-unilateral nephrectomy intake of alcohol enhances kidney oxidative stress by increasing kidney lipid peroxidation (MDA) and inhibiting its antioxidants (SOD, CAT, GPx); forming basis for campaigning against alcohol intake after unilateral nephrectomy as well as folk treatment with alcohol which may involve an individual that underwent nephrectomy.

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Nephrectomy refers to kidney(s) removal for assay, donation and treatment purpose (Elder *et al.*, 1995; Dols *et al.*, 2010). Nephrectomy could be unilateral nephrectomy (removal of one kidney) (Rojas- Canale *et al.*, 2019), bilateral nephrectomy (removal of two kidneys) (Overman *et al.*, 2021) or partial nephrectomy (removal of small part of the kidney) (Rassweiler *et al.*, 2000). Unilateral nephrectomy is performed when there is damage to one kidney and for donation purpose during renal transplantation (Goldfarb *et al.*, 2001). Bilateral nephrectomy is done when there is damage to two kidneys; patient is sustained by dialysis until a successful kidney transplant is done (Kramer *et al.*, 2009). Partial nephrectomy is performed for removal of tumor or damaged part of a kidney. It is also done to collect small part of a kidney for assay (Rassweiler *et al.*, 2000; O'Connor *et al.*, 2020). Reports suggest that alcohol can have favorable and unfavorable input on kidney function (Schaeffner *et al.*, 2005; Gueye *et al.*, 2007; Schaeffner *et al.*, 2012; Fan *et al.*, 2019; Lee *et al.*, 2021); it is reported to have adverse effects on kidneys and kidney diseases (Schaeffner *et al.*, 2012; Ajuzie *et al.*, 2023). Moderate consumption of alcohol was associated with less renal threat as it potentially alleviates the decline in kidney function and folk medicine uses it for treatments (Gueye *et al.*, 2007; Fan *et al.*, 2019). Nephrectomy was associated with drop in kidney function (Chapman *et al.*, 2010), as one kidney was reported to sustain renal function with

decreased glomerular filtration rate and kidney function (Baudoin *et al.,* 1993; Donckerwolcke *et al.,* 2001). Considering the double-edged effect of alcohol on renal function (Fan *et al.,* 2019); the objective of this study was to investigate the impact of post-unilateral nephrectomy administration of alcohol on kidney oxidative stress of male Wistar rats with 150 – 210 g-body weight randomly grouped into four groups and the oxidative stress biomarkers such as lipid peroxidation (MDA), superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) assessed.

MATERIALS AND METHODS

Ethical statement: This study was a project dissertation approved by Department of Human Physiology, Gregory University Uturu. Laboratory animals received humane care, and procedures were in accordance with the Guide for the use and Care of Laboratory Animals.

Experimental animals: Twenty (20) male Wistar rats (weighing 150 -210g) was purchased from animal house of Faculty of Basic Medical Sciences, Gregory University, Uturu, Nigeria. The rats were housed in standard laboratory cages and maintained at room temperature with alternating 12 h light/dark cycle. The rats had access to their standard chow and clean water *ad libitum*.

Experimental design: Laboratory rats were randomly grouped into four groups (n=5). Group A = (Control: No Alcohol, No Nephrectomy), Group B = 2g/kg of 20% Alcohol, Group C = Unilateral nephrectomy, Group D = Unilateral nephrectomy + 2g/kg of 20% Alcohol. Following 7 days post unilateral nephrectomy; 2g/kg of 20% Alcohol was freshly prepared and administered orally to their various groups (B and D) for 30days.

Unilateral nephrectomy procedure: Unilateral nephrectomy was performed on anesthesia (Ketamine, 40mg/kg and Xylazine, 10mg/kg, i.p.) with midline incision of epigastric region using a forceps. Following the opening of the epigastric region; one kidney was removed, precaution was taking to avoid damage to neighboring tissues, organ or/and vessels. Catgut was used to suture the injury and the laboratory animals were returned to their cage for them to regain consciousness. Post-surgery treatment with ampicillin sodium (22 mg/kg im) was done for 7days (Seifi et al., 2011). After 7days of unilateral nephrectomy complete healing of the surgery injury was observed and then administration of freshly prepared 2g/kg of 20% alcohol started immediately for 30 days.

Preparation of 20% alcohol: Pure (99.99%) alcohol was purchased from the Biochemistry Department, Gregory University, Uturu, in Nigeria. 20% of alcohol was prepared by diluting 20ml of the alcohol with 80ml of distilled water (v/v).

Sample collection and determination of kidney oxidative stress: After 30 days post unilateral nephrectomy administration of alcohol, the experimental animals were sacrificed on anesthesia (Ketamine, 40mg/kg and Xylazine, 10mg/kg, ip) and kidney was harvested, homogenized on phosphate buffer solution as described by Kaur et al., (2012) and assayed for kidney oxidative stress biomarkers (lipid peroxidation (MDA), superoxide dismutase (SOD), Catalase, (CAT) and Glutathione peroxidase GPx) as described by (Ige *et al.,* 2019; Nwosu *et al.,* 2022).

Statistical analysis: Data obtained was statistically analyzed using GraphPad Prism version 8, One way analysis of variance was used to determine the difference among various groups; multiple comparisons among groups was done using Boneferroni post hoc test and significance was considered at $p<0.05$.

RESULTS AND DISCUSSION

Post unilateral nephrectomy impact of alcohol on lipid peroxidation (MDA) of kidney tissues: Whether alcohol would restore or induce oxidative stress in the kidney of laboratory rats that underwent unilateral nephrectomy was determined by measuring changes in the kidney lipid peroxidation (MDA). Lipid peroxidation in control group of Wistar rats was decreased compared to the group that underwent unilateral nephrectomy as well as the group that was administered alcohol. Lipid peroxidation (MDA) was greatly increased in the group of the laboratory rats that was administered alcohol following 7 days post unilateral nephrectomy (Figure 1); suggesting that alcohol consumption increases lipid peroxidation and alcohol consumption after undergoing unilateral nephrectomy can escalate kidney lipid peroxidation.

Post unilateral nephrectomy impact of alcohol on superoxide dismutase (SOD) of kidney tissues: Superoxide dismutase (SOD) was investigated in kidney homogenates to ascertain its activity in the kidney of Wistar rats that was administered alcohol after undergoing unilateral nephrectomy. The results showed that unilateral nephrectomy and alcohol caused decrease in the superoxide dismutase level. Apparently, administration of alcohol following 7 days post unilateral nephrectomy greatly depleted superoxide dismutase level (Figure 2). This suggests that alcohol consumption after undergoing unilateral

nephrectomy could impair kidney superoxide dismutase activity; this could predispose the kidney to oxidative stress.

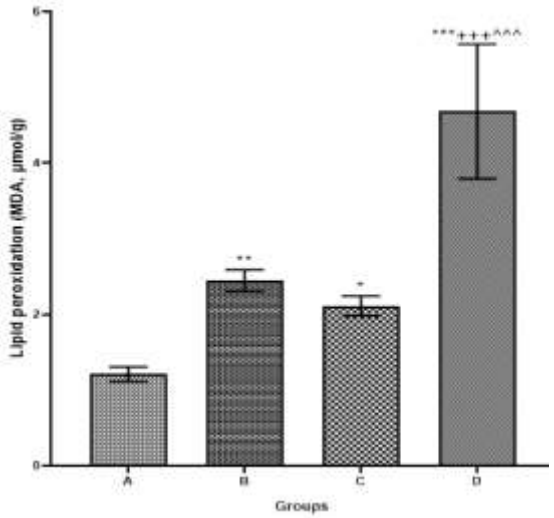

Fig 1: Lipid peroxidation (MDA, µmol/g) levels in all experimental groups. Values are expressed as mean ± standard error of mean. * indicate significant difference on comparing Group B, C, D to Group A (***P<0.001, **P<0.01, *P<0.05). +++ indicate significant difference between Group B and D, P<0.001. ^^^ indicates significant difference between Group C and D, P<0.001. Group A = (Control: No Alcohol, No Nephrectomy), Group B = 2g/kg of 20% Alcohol, Group C = Unilateral nephrectomy, Group D = Unilateral nephrectomy + 2g/kg of 20% Alcohol.

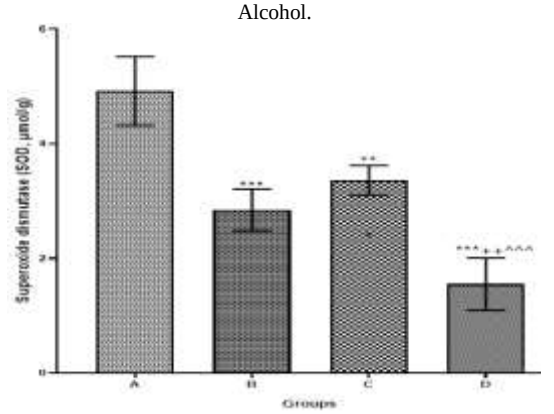

Fig 2: Superoxide dismutase (SOD µmol/g) levels in all experimental groups. Values are expressed as mean ± standard error of mean. * indicate significant difference on comparing Group B, C, D to Group A (***P<0.001, **P<0.01, *P<0.05). ++ indicate significant difference between Group B and D, P<0.01. ^^^ indicates significant difference between Group C and D, P<0.001. Group A = (Control: No Alcohol, No Nephrectomy), Group B = 2g/kg of 20% Alcohol, Group C = Unilateral nephrectomy, Group D = Unilateral nephrectomy + 2g/kg of 20% Alcohol.

Post unilateral nephrectomy impact of alcohol on catalase (CAT) of kidney tissues: Oxidative stress neutralization impact of catalase (CAT) on the kidney of Wistar rats administered alcohol following 7days post unilateral nephrectomy was determined by evaluating the changes in its level. The result showed that alcohol and unilateral nephrectomy inhibited catalase in the laboratory rats. Alcohol administration following 7days post unilateral nephrectomy further inhibited catalase (Figure 3), indicating that alcohol consumption after undergoing unilateral nephrectomy escalates kidney oxidative stress by reducing the tissue catalase level.

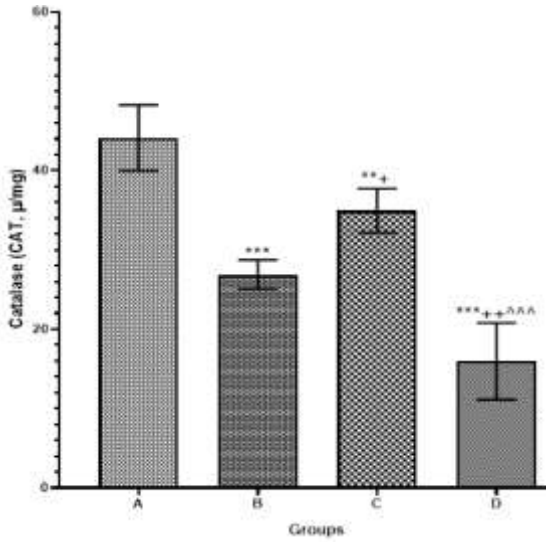

Fig 3: Catalase (CAT, µ/mg) levels in all experimental groups. Values are expressed as mean ± standard error of mean. * indicate significant difference on comparing Group B, C, D to Group A (***P<0.001, **P<0.01, *P<0.05). +indicate significant difference on comparing Group C and D to B, ++P<0.01, +P<0.05. ^^^ indicates significant difference between Group C and D, P<0.001. Group A = (Control: No Alcohol, No Nephrectomy), Group B = 2g/kg of 20% Alcohol, Group C = Unilateral nephrectomy, Group D = Unilateral nephrectomy + 2g/kg of 20% Alcohol.

Post unilateral nephrectomy impact of alcohol on glutathione peroxidase (GPx) of kidney tissues: Levels of glutathione peroxidase (GPx) were measured on kidney homogenates to ascertain the impact of post unilateral nephrectomy administration of alcohol on kidney tissue with respect to kidney oxidative stress induction. Glutathione peroxidase of the kidney was reduced in groups of Wistar rats that was treated with alcohol and underwent nephrectomy. Furthermore, administration of alcohol following 7 days post unilateral nephrectomy caused more reduction in the kidney glutathione peroxidase (Figure 4). This finding suggests that alcohol enhances kidney oxidative stress of laboratory rats that underwent unilateral nephrectomy by depleting the levels of glutathione peroxidase which in turn reduces its activity.

Considering the double edged activity of alcohol suggesting that alcohol could be beneficial or deleterious to kidney tissues (Schaeffner *et al.*, 2005; Gueye *et al.*, 2007; Schaeffner *et al.*, 2012; Fan *et al.*, 2019; Lee *et al.*, 2021), there was curiosity on the

impact of alcohol on kidney tissues following unilateral nephrectomy. This is to ascertain whether or not alcohol could be beneficial to kidney tissue of individuals that underwent unilateral nephrectomy. Hence, the study evaluated post unilateral nephrectomy impact of alcohol administration on oxidative stress of kidney in laboratory rats.

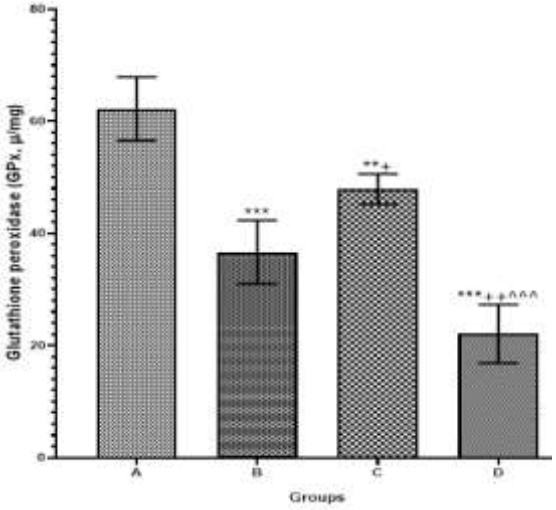

Fig 4: Glutathione peroxidase (GPx, µ/mg) levels in all experimental groups. Values are expressed as mean ± standard error of mean. * indicate significant difference on comparing Group B, C, D to Group A (***P<0.001, **P<0.01, *P<0.05). +indicate significant difference on comparing Group C and D to B, ++P<0.01, +P<0.05. ^^^ indicates significant difference between Group C and D, P<0.001. Group A = (Control: No Alcohol, No Nephrectomy), Group B = 2g/kg of 20% Alcohol, Group C = Unilateral nephrectomy, Group D = Unilateral nephrectomy + 2g/kg of 20% Alcohol.

This is because oxidative stress is a biomarker of tissue or organ damage that results from imbalance between free radicals and antioxidants (Onwuka *et al.,* 2022). Oxidative stress biomarkers include lipid peroxidation (MDA), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), glutathione (GSH), total antioxidant capacity (TAC) and others (Giribabu *et al.,* 2017; Ige *et al.,* 2019; Nwosu *et al.,* 2022). Thus, this study evaluated post unilateral nephrectomy impact of alcohol on kidney oxidative stress biomarkers such as MDA, SOD, CAT and GPX. The study demonstrated for the first time that alcohol administration following 7 days post unilateral nephrectomy escalates kidney oxidative stress by enhancing MDA and depleting SOD, CAT and GPx. Lipid peroxidation is an indicator of the activity of free radicals in a tissue, which involves tissue damage (Owada *et al.,* 2010); findings from this study reports that alcohol consumption after undergoing unilateral nephrectomy enhances deleterious activity of free radicals on the kidney as there was clear evidence of increase MDA of the tissue. Superoxide dismutase constitute antioxidant defense against oxidative stress as it is a first line of defense against free radicals (reactive oxygen species) (Fujita *et al.,* 2009). This study reported depletion of superoxide dismutase level in the kidney tissue as a result of alcohol administration after unilateral nephrectomy, suggesting that oxidative stress induced in the kidney was an evidence of impaired SOD defense against free radicals (Kitada *et al.,* 2020). The neutralization role of catalase against free radicals was impaired in the study as post unilateral administration of alcohol caused decrease in kidney catalase level indicating oxidative kidney damage as a result of depleted activity of the catalase; since reports has it that declined catalase level is an indicator of oxidative damage to kidney (Iman *et al.,* 2011).

Decrease in glutathione peroxidase a potent antioxidant (Kishido *et al.,* 2007) was also observed in laboratory rats administered alcohol after unilateral nephrectomy. Thus, this study has demonstrated that alcohol consumption after unilateral nephrectomy can be dangerous to the remaining kidney which followed the trend of reported adverse impact of alcohol on kidneys and kidney disease (Schaeffner *et al.,* 2012; Okerulu *et al.,* 2022); forming basis for campaigning against alcohol consumption after unilateral nephrectomy. The kidney is an essential organ controlling vital physiological and biochemical processes such as homeostasis, detoxification, elimination of metabolites and drugs (Tousson *et al.,* 2019); further studies are recommended to investigate and link up the observed adverse effects with other tissues, organs and systems.

Conclusion: This study demonstrated that alcohol as well as unilateral nephrectomy can induce oxidative stress on kidney tissue and post unilateral nephrectomy intake of alcohol escalates kidney oxidative stress caused by unilateral nephrectomy by increasing kidney MDA and inhibiting its antioxidants (SOD, CAT, GPx). Thus, this study formed basis for campaigning against alcohol intake after unilateral nephrectomy as well as professional advisory to be used by medical/health practitioner on patients that underwent unilateral nephrectomy.

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