Influence of *Phyllanthus niruri* Linn. Extract Therapy on Renal and Uterus in 2% NaCl -induced Fibrotic Scarring Rodents

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Abstract

Background

Phyllanthus niruri (english name : leafflower) extract is used in therapy of renal and uterus fibrotic scarring disease. Influence of alcohol extract of *P. niruri* on renal and uterus of 2% NaCl- induced fibrotic scarring rodents had been researched.

Aim of Study

Purpose of this research to study the influence of leafflower (*Phyllanthus niruri* Linn.) therapy on renal and uterus in 2% NaCl - induced fibrotic scarring rodents.

Methods

Wistar rodents were stimulated with 2% NaCl in drinking water to induce fibrotic scarring renal and uterus. *Phyllanthus niruri* extract (200 mg/kg) was given orally for 4 weeks. Matrix extracellular expression was determined by HE Staining and calculated by METAVIR fibrosis scarring score. The data of this study were analyzed by SPSS 16.

Results

P. niruri extract was able to decrease the matrix extracellular in 2% NaCl-induced rodent compared to control group ($p<0.05$).

Conclusion

P. niruri extract was able to decrease the matrix extracellular in the renal and uterus of the rodents.

Keywords : *Phyllanthus niruri* extract, fibrosis, matrix extracelluer

Background

Non-infectious diseases (NIDs) are the leading cause of death worldwide, causing 36 million deaths each year, 6% of all deaths worldwide. Three number one NIDs (malignancy, cardiovascular disease, and diabetes) and three risk factors (inadequate diet, disproportionate physical tactics, and tobacco use and hazardous alcohol use).[1] Increasing prevalence of NID, including long-term sequelae of blood pressure, diabetes mellitus and obesity, with surveillance for persistent renal disease increasing steadily by about 8% year-on-year.[2] In 2005, approximately 1 billion people (14%) worldwide suffered from high blood pressure. Elevated blood pressure is the greatest threat of cardiovascular, cerebrovascular and renal diseases related to fibrotic contamination in certain parts of the body which include the heart, kidneys, liver and cardiovascular system.[3,4]

In particular, the increase in blood pressure occurs under the influence of many factors. Epidemiological statistics show that the body's genetics, stress from activity and the field cause prolonged blood pressure,[5] However, overuse of mineral salts such as sodium chloride (NaCl) is the main problem leading to improvement in blood pressure, cardiovascular disease and kidney disease worldwide.[6] The hypertensive system caused by excess mineral salts is still incomplete, but it has been found that the kidneys are impeded in excreting the full amount of sodium chloride.[7] The link between misrepresented mineral salts and blood pressure also remains insufficient and, in fact, is still denied by some social media. Sodium chloride renal destruction techniques, reflexive nerve motion (SNA) produced by the baroreflex instrument, and collagen accumulation have recently been reviewed by numerous analysts (Blaustein et al., 2012).[3]

With regard to the previous test in animal models, 8% NaCl was shown to improve heart rate in rodents with hypertension (SHR) and normotensive Wistar-Kyoto rodents (NWKY).[8] Challenge methods are presented by angiotensin II challenge method by methods for Na in the form of aldosterone → endogenous oabain (EO).[9] Angiotensin II triggers vasoconstriction and causes the adrenal gland to produce aldosterone. Thereafter, aldosterone activates the distal tubule for reabsorption of Na and H2O.[10,11] In addition, angiotensin II stimulates the proselyte from fibroblasts to myofibroblasts via the developmental factor beta1 (TGF-β1) switch pathway. The myofibroblast connects the extracellular structure (ECM), therefore the ECM accumulates in the interstitial region of the tubule.[12]

Phyllanthus niruri extract (local name: Meniran) is used to treat kidney and uterine diseases. It contains quercetin, which can increase the expression of PPAR-γ. Activation drives the heterodimer of PPAR-γ forms with retinoid X receptors (RXRs) to synthesize a corepressor that can block TGF-β1 expression.[13]

Based on the description above, treatment with Phyllanthus niruri extract in rats induced with 2% sodium

chloride is most likely antifibrotic when describing the extracellular matrix stained with HE stain in kidney and uterus. 2% NaCl is able to induce fibrotic organ in rats.[14]

Methods

The research design was an experimental study conducted only after testing with a control group design. The study was endorsed by Ethics Approval Number 41/EC/FK-06/UNIZAR/X/2020, Faculty of Medicine, Al-Azhar Islamic University, Mataram, NTB.

Preparation Extract of *Phyllanthus niruri*

P. niruri plants were collected from Alung Village, Mekar Damai Residence, Praya District, Central Lombok Regency, West Nusa Tenggara Province, Indonesia. Next to. It was determined by the Herbal Science Study Center of the Faculty of Health Sciences at Nahdlatul Wathan Mataram University. PThe Niruri plants were extracted in 70% ethanol by maceration methods.

Procedure of Experimental

Wistar rats (3 months old) received normal (CTRL; n=8) or high (2% NaCl in drinking water) salt intake (n=16) for 4 weeks. Rats in the high-salt group received vehicle (SALT; n=7) or Phyllanthus extract (PE) (200 mg/kg) (SALT-PE; n=8) for the last week of the high-salt diet. Salt. 14.15 The extracellular abundance of the matrix was determined by HE staining and measured using the METAVIR Fibrosis Score. The results of this study were analyzed by SPSS 16.

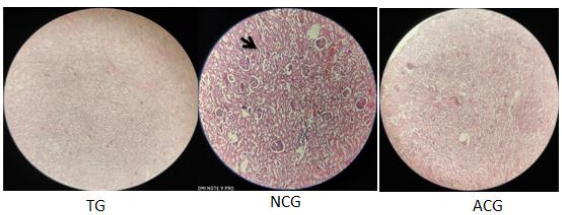
Analysis of Data

The result of this study was tested with SPSS 16. The data were examined bivariate. The bivariate test was the Kruskal-Wallis test ($p<0.05$).

Result

HE Staining of Kidney

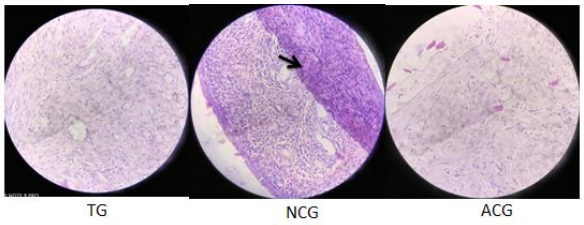
Figures 1 and 2 show the differences in extracellular matrix in the treatment group versus the control group. This means that Phyllanthus extract was able to reduce extracellular matrix abundance in kidney and uterus in rats with sodium chloride-induced fibrosis.



TG (treatment group) = induced by 2% NaCl + 200 mg/Kg *P.niruri* extract; NCG (NaCl-control group) = induced by 2% NaCl without treatment; ACG (aquadest-control group) = no induction and treatment. → = matrix extracelluler.

Figure 1. HE staining of kidney

HE Staining of Uterus



TG (treatment group) = induced by 2% NaCl + 200 mg/Kg *P.niruri* extract; NCG (NaCl-control group) = induced by 2% NaCl without treatment; ACG (aquadest-control group) = no induction and treatment. → = matrix extracelluler.

Figure 2. HE staining of uterus

Tables 1 and 2 show the METAVIR fibrosis score for kidney and uterus in the treatment group compared to the control group. The bivariate test was the Kruskal-Wallis test, which gave the p-value < 0.05. This means that there were significant differences between the treatment group and the control group. Therefore, phyllanthus extract was more effective in reducing extracellular matrix in sodium chloride-induced fibrotic rats.

Table 1.
METAVIR Kidney Fibrosis Score of treatment group

Group	Fibrosis score Mean	P value
Treatment group (TG)	0.4±0.16	0.001
NaCl-control group (NCG)	3.9±0.18	
Aquadest-control group (ACG)	0.7±0.52	

TG = induced by 2% NaCl + 200 mg/Kg *P.niruri* extract; NCG = induced by 2% NaCl without treatment; ACG = no induction and treatment

Table 2.
METAVIR Uterus Fibrosis Score of treatment group

Group	Fibrosis score Mean	P value
Treatment group (TG)	1±0.00	0.04
NaCl-control group (NCG)	3.9±0.2	
Aquadest-control group (ACG)	1.5±0.7	

Discussion

Based on Figures 1 and 2 and Tables 1 and 2 of this study, the difference between the treatment and control groups was clear ($p<0.05$). They indicated that P. niruri is effective in reducing the amount of extracellular matrix in the kidney and uterus that causes fibrosis. Taking 2% NaCl went with a 2nd5-fold increase in collagen abundance in the aorta and reduced sensitivity of aortic explants to the vasorelaxant effects of SNPs after endothelin-1-induced constriction.[14]

The effects of P. niruri aqueous extract on the kidney, liver and testes of CCl4-induced hepatotoxic rats have been previously studied. High levels of malondialdehyde (MDA) were found within the CCl4 testing organization, with significant reductions in MDA levels in all companies that administered P. niruri extract. The highest levels of glutathione (GSH) are found in P.Niruri organization. The activities of the enzymes alanine transaminase, aspartate transaminase and alkaline phosphatase were significantly reduced within the healing organization (P. niruri agents after CCl4 injection). Liver histopathology confirmed a low level of irritation in all cells treated with P. niruri, while renal and seminiferous tubules confirmed eosinophilic protein casts with signs and symptoms of tubular damage and degeneration.The testes also showed a reduced number of mature sperm. The effects suggest that P. niruri has antioxidant and hepatoprotective activity with associated deleterious effects on the kidneys and testes.[16]

Phyllanthus niruri extract helps maintain renal function and halt histopathological changes by improving oxidative stress, inflammation, fibrosis, and apoptosis while improving renal proliferation in diabetes mellitus.17 Phyllanthus sp extract administration reduced collagen levels significantly. and tissue inhibitors of matrix metalloproteinases (TIMPs); and definitely modulated the expression of matrix metalloproteinases (MMP).[18]

Conclusion

The P. niruri extract was effective in reducing extracellular matrix in rat kidney and uterus.

Acknowledgments

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