**Effect of Curcumin on Biochemical markers and Histopathology examination of LPS induced preeclampsia in experimental rats**

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**ABSTRACT**

**Objective:** The objective of the present study was to evaluate the effect of Curcumin on Biochemical markers and Histopathology examination of LPS induced preeclampsia in experimental rats.

**Materials and Methods:** Biochemical examination was done by manual method of kit. Histopathology was done by pathologist.

**Results:** In the LPS treated group, significant increase in SGPT, Albumin, creatinine and CK-BT levels as compared to pregnant control. Also degenerative changes were seen in kidney and liver tissues. Treatment with curcumin (0.36mg/kg) had significant improvement against LPS induced pre-eclampsia changes in the biochemical markers as well as histopathological examination. The curcumin treatment ameliorates effect that is induced by LPS.

**Conclusion:** The present study concludes that curcumin can be the treatment of pre-eclampsia as it produced significant effect in biochemical examination as well as decreased the degenerative effect in histopathological examination of kidney and liver.

**Keywords:** Curcumin, lipopolysaccharide, pre-eclampsia, histopathology

**INTRODUCTION**

Preeclampsia (PE) is a primary cause of maternal and foetal mortality and morbidity that affects 2-8% of all pregnancies globally [1]. Including conditions like de novo hypertension, proteinuria, renal failure, neurological issues, elevated liver enzymes, and uteroplacental dysfunction [2]. Episodes of hypoxia/reperfusion and reduced uteroplacental perfusion are thought to be brought on by pre-eclampsia’s insufficient placental vasculature [3]. These results in increased inflammatory responses and worsening of the patient’s conditions because cytokines, reactive oxygen species, lipid peroxidases, soluble Fms like tyrosine kinase-1 (sFlt-1), and ET-1 are also produced [4-6].

Preeclampsia still lacks a pharmaceutical treatment that is both efficient and secure. Drug development for pre-eclampsia faces significant challenges due to the condition’s complicated aetiology and strong requirement for safety profiles during pregnancy. Currently, low-dose aspirin is advised for avoiding or delaying the onset of pre-eclampsia due to the anti-platelet and anti-inflammatory effects [7, 8]. Unfortunately, new research suggests that low-dose aspirin’s effectiveness in treating pre-eclampsia is either modest or even non-responsive, while high-dose aspirin is not recommended due to possible side effects such birth abnormalities [9-11]. Faas et al (1994) created a classical animal model for pre-eclampsia (PE) by injecting lipopolysaccharide (LPS) into pregnant rat on gestational day (GD) 14 [12]. Recently, we created a similar model by intravenous administration LPS on GD 5.

Medical herbs and vegetables are now being considered as potential sources for new drugs. Traditional medicine uses curcumin as both a medicinal treatment and a food colouring additive, and it is thought to be harmless [11]. The fat-soluble fragrant phyto-extract curcumin, also known as curcuminoid, was initially found in the aromatic rhizome of...
the Indian plant turmeric (Curcuma longa L.), a member of the ginger family (Zingiberaceae), in 1870. In Asia, it is a typical food additive and natural food colouring. Its antioxidant, anti-inflammatory, anti-cancer, anti-diabetic, and antiviral activities have been shown in numerous in-vitro, in-vivo, and clinical studies undertaken up to this point. The main curcuminoids included in turmeric (Curcuma longa L.) rhizome include dihydrocurcumin, tetrahydrocurcumin, curcumin, bis-demethoxycurcumin, and demethoxycurcumin. Immune system control, cardiovascular and vascular protection, and neuroprotection are just a few of the health advantages of curcumin [13, 14]. Curcumin is used to treat bruises, amenorrhea, hysteria, rheumatic pain, and chest flank pain, according to the Pharmacopoeia of China. It should be emphasised that curcumin, one of turmeric's main active ingredients, has pharmacological properties. Recent research has demonstrated that curcumin acts as a free radical scavenger and has pharmacological effects against hyperlipidemia, diabetes, tumours, inflammation, fibrosis, and oxidation [15]. The aim of this study was to evaluate the effect of curcumin in biochemical markers and histopathology of organs.

MATERIALS AND METHODS

Experimental Animals

Inbred Wistar female rats (180-210g) were used in the study. Rats were housed at a constant temperature of 22 °C under standard laboratory conditions. The animals had free access to food and water throughout the experiment. Care of animals was taken as per guidelines of CPCSEA for use of animals in Scientific Research with approval of Institutional Animals Ethics Committee (IAEC) Sr. No. 2010.

Drugs and Chemicals:
Curcumin, Lipopolysaccharide and other chemicals were procured by SRL Laboratory Pvt. Ltd. Biochemical kits were procured by ERBA Diagonostic Mannheim GmbH.

Biochemical estimation
CK-MB, SGPT, Albumin and creatinine test done by manual procedure that’s available inside each kit.

Experiment procedure
Pre-eclampsia was induced by administration of LPS. Wistar rats were divided into 3 groups. Group-1 served as pregnant control and received normal pellet diet and saline; Group-2 served as pregnant control administered LPS (0.5ug/kg); Group-3 served as pregnant given LPS and curcumin (0.5ug/kg & 0.36mg/kg) [1]. Animals were anesthetized; blood was collected by cardiac puncture, centrifuged and stored at -80°C. After blood collection, animals were sacrificed and liver and kidney was collected for histopathological examination. Total number of rats 24 and in each group 8 rats was included in the experimental study.

Statistical analysis
The data were expressed as mean ± Standard error mean (SEM). Statistical analysis was done by using one-way analysis of variance (ANOVA) followed by post hoc Tukey’s test for intergroup comparisons. A p-value< 0.05 was used as the level of significance in all statistical tests. Software GraphPad Prism 5.0 was used.

RESULTS

Biochemical markers
In the pregnant LPS (PE) group 2, a single dose (0.5ug/kg) was given on G5 day which resulted in a significant increase in SGPT, Albumin, Creatinine and CK-MB level in serum (p<0.01 & p<0.001) as compared to that in the pregnant control group 1. In group 3 (pregnant + LPS + curcumin), which was given LPS (0.5ug/kg) followed by treatment with curcumin(0.36mg/kg), a significant decrease (p<0.01) was seen in the SGPT, Albumin, Creatinine and CK-MB level after the administration of curcumin. Results are summarized in figure 1.
Histopathological examination

On examination of H&E stained pregnant control kidney tissue, renal tubular epithelium shows normal histology. Very few areas show autolytic changes. There is no inflammation, malignancy, necrosis seen. Overall impression shows normal appearance of kidney tissue. Pregnant LPS (PE) tissue, renal tubular epithelium shows degenerative changes with few cells showing vacuolations, presence of epithelial cell shedding and pyknotic cells, few isolated areas show hyperemia. Pregnant LPS with curcumin treatment tissue, renal tubular epithelium shows degenerative changes with very few cells showing vacuolations, few areas show hyperemia. No inflammatory cells and malignancy seen Overall impression of renal tissue shows no major pathological effect (figure 2).

On examination of H&E stained pregnant control liver tissue, overall hepatocytes shows normal architecture. Very few areas show autolytic changes. There is no inflammation, malignancy, necrosis seen. Overall impression shows normal histological appearance of hepatic tissue. Pregnant LPS (PE) tissue, some hepatocytes shows degenerative changes, few hepatocytes show necrosis, few isolated areas show low inflammatory cellular infiltration. Pregnant LPS with curcumin treatment tissue slide, hepatic tissue shows no major pathological effect. Few hepatocytes show binucleation and pyknosis. Central view shows dilation. No hyperemia/congestion, inflammatory cells and malignancy seen. Overall impression of hepatic tissue shows no major pathological effect (figure 3).
DISCUSSION

In this study, we showed that curcumin reduced the PE-like effect generated by the injection of LPS on GD 5 in a rat model. Our findings showed that curcumin attenuated histological analysis and biochemical indicators. Following curcumin treatment, the LPS-induced functional and morphologic damages to the kidneys and liver were reduced. A low-dose LPS infusion procedure is thought to be the standard method for creating a PE rat model [12].

A promising model for examining the pathophysiology of preeclampsia and assessing therapies for this illness is the Wistar rat model of preeclampsia caused by LPS. In rats, LPS administration led to elevated levels of CK-MB, SGPT, Albumin, and Creatinine as well as poor pregnancy outcomes, dysregulated liver enzymes and cardiac abnormalities. Despite significant scientific efforts, relatively little is understood about its intricate and convoluted aetiology. Since PE only develops spontaneously during human pregnancies, it has been up for debate for a long time whether an animal model could be helpful for PE research. As a result, rather than being exact, the symptoms in animal models can only be approximated [16]. Such changes in ECG records indicate heart injury, which the cardiac biomarker CK-MB later confirmed. When compared to the pregnant control group, we saw that PE groups’ CK-MB levels were considerably greater. We have found that the biochemical levels of the enzymes SGPT, Albumin, and Creatinine are significantly higher in PE rats as compared to the biochemical reports of all other groups. Hepatic dysfunction and PE are linked [17]. According to one theory, in PE, different mediators are released from the liver and blood vessel endothelium, leading to hepatic hypoxia and vasoconstriction, which in turn cause other systemic disorders such as edema and cardiovascular disease.

Our histological analysis revealed that kidney tissue from pre-eclampsia caused by LPS exhibits degenerative changes, with a small number of cells exhibiting vacuolations, the presence of epithelial cell shedding and pyknotic cells, and a small number of isolated locations exhibiting hyperemia. Following treatment with curcumin and LPS, the degenerative alterations improved and no significant adverse effects were observed. Additionally, liver tissue has degenerative alterations, little necrosis in hepatocytes, and little inflammation in isolated places. Few hepatocytes were observed in the hepatic tissue following the curcumin administration, which had no significant pathogenic effects.

CONCLUSION

Pre-eclampsia was induced in experimental rats by lipopolysaccharide, as shown by modifications in biochemical markers and histological analyses. In rats exposed to LPS-induced pre-eclampsia, curcumin therapy was found to drastically lower pre-eclampsia-related indicators. In conclusion, curcumin may be used to treat pre-eclampsia.

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CONTRIBUTION OF THE AUTHORS

Muzammil Muzaffar conducted experiment, dosage, data collection and manuscript design. Arifa Hassan also helps during experiment and dosage. Mohd Rafi Reshi participated in the study’s conception, design as well as analysis, and article drafting. The final draft of the work was approved by all authors.

CONFLICT OF INTEREST

There is no conflict of interest.

REFERENCES