

## Abstract

### Background

Vancomycin is a glycopeptide antibiotic which is considered as indispensable antibiotic for the treatment of methicillin resistant staphylococcus aureus. It has many side effects and the most harmful one is nephrotoxicity. The incidence of vancomycin induced nephrotoxicity is increased with increasing the dose, duration and the concomitant use of other nephrotoxic drugs. The exact mechanism by which vancomycin induces its harmful effect to the kidney is not fully known but studies indicated the oxidative stress, inflammation and cell apoptosis in the kidney tissues as the main mechanisms. *Nigella sativa* was known to have an antioxidant activity and a protective effect against the nephrotoxicity of many drugs like methotrexate and others. These effects make it attractive to investigate its protective effect against .vancomycin induced nephrotoxicity

### Aim of study

This study was designed to evaluate the nephroprotective effect of .*nigella sativa* in an animal model of vancomycin induced nephrotoxicity

### Methodology

The study was conducted between November 2017 and February 2018. 28 male adult albino rats were randomly divided into four groups, seven rats in each. Group 1 (Control) were given normal saline orally and intraperitoneally (2 ml/kg). Animals in group 2 were treated with vancomycin (2ml/kg; 400 mg/kg/day) intraperitoneally. Group 3 were treated with oil of *nigella sativa* orally (2 ml/kg/day) and the animals in group four were treated with the oil of *nigella sativa* given orally and vancomycin intraperitoneally. The animals were sacrificed at day 8 after 7 days of treatments. Blood samples were collected directly from the heart and serum was obtained. Serum samples were analyzed

to evaluate the levels of serum urea and serum creatinine. Renal tissue specimens were analyzed in order to evaluate glutathione, malondialdehyde and neutrophil gelatinase associated lipocalin levels. Histopathological examination was also done for kidney specimens

## Results

Treatment with vancomycin intraperitoneally for 7 days resulted in a significant increase in the levels of serum urea and serum creatinine to  $184.61 \pm 77.1$  and  $2.41 \pm 0.1$  mg/dl respectively. In addition, the levels of malondialdehyde and neutrophil gelatinase associated lipocalin in kidney tissues were also increased to  $27.9 \pm 4.3$  ng/ml and  $1026.84 \pm 682.17$  pg/ml respectively. On the other hand the level of renal tissue glutathione was significantly reduced as compared to control from  $4.6 \pm 1.2$  mg/ml to  $2.11 \pm 0.5$  mg/ml. The above changes were accompanied by a number of morphological changes like swelling of the kidney and turning its color to faint gray, as well as histopathological changes like dilatation in renal tubules with cast and cyst like formation and hemorrhage in all treated animals. Treatment with nigella sativa oil orally for 7 days concomitantly with vancomycin intraperitoneally resulting in the reduction of serum levels of urea and creatinine significantly as compared to vancomycin treated group to  $59.00 \pm 19.5$  and  $0.44 \pm 0.11$  mg/dl respectively. The levels of renal tissues malondialdehyde and neutrophil gelatinase associated lipocalin were also reduced to  $25.3 \pm 8$  ng/ml and  $844.64 \pm 308.53$  pg/ml respectively. On the other hand the level of glutathione in renal tissues was significantly increased as compared with vancomycin treated group to  $4.15 \pm 0.1$  mg/ml. At the same time treatment with nigella sativa oil resulted in amelioration of the renal histopathological and morphological changes in all vancomycin treated animals

## III

## Conclusions

NS oil has a nephroprotective activity against vancomycin induced nephrotoxicity probably through its scavenging effect to reactive oxygen species produced by vancomycin in kidney tissues