



## AMINOGLYCOSIDES INDUCED NEPHROTOXICITY AND ITS PROTECTION BY NIGELLA SATIVA

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### ABSTRACT

The major obstacle limiting the use of aminoglycoside antibiotics has been and continues to be the possibility of drug induced ototoxicity and nephrotoxicity. Changes in biochemical parameters related to nephropathy before and after the use of gentamicin and nigella sativa was observed. Ten Rabbits were divided into two groups. Group I was given only gentamicin and its effects on kidney function were observed. Group II was given gentamicin and extract of Nigella Sativa for 11 days and the biochemical changes related to kidney function were estimated. It is suggested that although nigella sativa shows a significant effect on nephrotoxicity induced by gentamicin but its effect on the level of serum calcium and cholesterol may be dangerous. However further research is needed on large number of rabbits to reach on a definite conclusion.

**Key Words:** Aminoglycosides, Nigella Sativa, nephrotoxicity.

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### INTRODUCTION

Aminoglycosides are bactericidal for susceptible organisms by virtue of irreversible inhibition of protein synthesis. These enter the cell, bind to the receptors of the bacterial ribosomes and inhibit protein synthesis. Despite the introduction of several new classes of antimicrobial agents, aminoglycosides are still recognized as first line therapeutic agents in the management of severe gram negative sepsis<sup>1</sup>.

The major obstacle limiting the use of aminoglycoside antibiotics has been and continues to be the possibility of drug induced ototoxicity and nephrotoxicity<sup>2</sup>. Patients at greatest risk for aminoglycoside induced nephrotoxicity include the elderly patients with pre-existing renal disease and those who are volume depleted<sup>3,4</sup>.

Recently the effect of thymoquinone, the main constituent of Nigella Sativa on the nephropathy induced was investigated<sup>5</sup>.

The current study was planned to study the effect of Nigella Sativa on nephrotoxicity induced by gentamicin in rabbits. Changes in biochemical parameters related

to nephropathy before and after administration of nigella sativa is also observed.

### MATERIALS AND METHODS

Study was conducted on 10 rabbits weighing 1 to 1.75 kg and age ranging from 8-10 months. These were housed for 14 days at Pharmacology Department of Fatima Jinnah Medical College, Lahore for acclimatization. The biological clock was maintained. The rabbits were fed on commercial diet, water and libitum.

Rabbits were divided into two groups i.e. Group I and Group II. Group I was given only gentamicin and its effects on kidney functions were observed. Group II was given gentamicin and extract of Nigella Sativa for 11 days and the biochemical changes related to kidney functions were estimated. Gentamicin 60 mg/kg/day was injected intramuscularly in two equally divided doses for 11 days. Extract of Nigella sativa 10 mg/Kg/day was given along with gentamicin for 11 days.

#### Collection of blood sample:

Eight ml of blood was drawn from the vein of shaved ear. Blood sample from both groups were collected according to the following schedule.

- A Before administration of the first dose of drug.
- B On the 11<sup>th</sup> day of experiment.

Biochemical parameters like protein, Albumin, Cholesterol, Calcium, urea and creatinine were estimated by standard chemical methods<sup>6</sup>.

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**Table 1: Variation in biochemical parameters in group I of rabbits**

Biochemical Parameters	Before administration of gentamicin (0 days)	After gentamicin (11 days)
Blood Urea (mg%)	40.5±2.5	68±3.9
Serum Creatinine (mg%)	0.95±0.02	1.2±0.03
Serum Proteins (gm%)	6.7±0.9	5.4±0.85
Serum Albumin (gm%)	4.3±0.21	3.0±0.22
Serum Calcium (mg%)	6.9±0.98	9.7±1.00
Serum Cholesterol (mg%)	155±10.5	33±4.5

**Table 2: Variation in biochemical parameters in group II of rabbits before and after administration of gentamicin+Nigella Sativa**

Biochemical Parameters	Before administration of drug (0 days)	After gentamicin+ Nigella Sativa (11 days)
Blood Urea (mg%)	37.8±0.98	32.4±1.20
Serum Creatinine (mg%)	1.0±0.03	0.8±0.02
Serum Proteins (gm%)	5.9±1.02	6.3±1.00
Serum Albumin (gm%)	3.8±0.2	4.0±0.15
Serum Calcium (mg%)	8.1±0.85	10.2±0.91
Serum Cholesterol (mg%)	217±11.21	54±8.50

## RESULTS

Blood samples were taken from group I of rabbits before administration and then 11 days after the administration of gentamicin. A variation in biochemical parameters was observed. Level of serum proteins, albumin and cholesterol were decreased after the administration of gentamicin but significant difference was only observed in case of cholesterol when compared with the level of cholesterol before the administration of gentamicin. On the other hand the level of blood urea, serum creatinine and serum calcium was increased, but significant difference was only observed in case of serum calcium when compared with the level of calcium before the administration of gentamicin. (Table 1).

In group II of rabbits, gentamicin along with Nigella

Sativa was given for 11 days and biochemical parameters were estimated at 0 and 11 days. Level of blood urea, serum creatinine and cholesterol were decreased after the administration of gentamicin and Nigella Sativa (at the 11<sup>th</sup> day of administration) but significant difference was only observed in case of serum cholesterol. On the other hand the level of serum protein and serum calcium were non-significantly increased, whereas the level of serum albumin remained the same (Table 2).

## DISCUSSION

Progression of tubular dysfunction results from accumulation of high concentration of antibiotics in renal parenchyma due to tubular filtration and secretion of drug by tubular epithelial cells<sup>7</sup>.

It was observed that gentamicin administration causes a decreased level of serum proteins, albumin and cholesterol. The current study is confirmed by Wilson SE<sup>3</sup> who also observed a disturbed level of protein. He concluded that altered metabolism of proteins and amino acids is due to altered activity of aminotransferase activity that may be one of the factors of nephrosis. In the present study a decreased level of cholesterol was calculated. The current study is in contrast to a report of Steyer E et al<sup>8</sup> who observed that in kidney dysfunction there is an increased level of cholesterol due to a decreased activity of LCAT. Due to deficiency of this enzyme the free cholesterol is not converted into esterified cholesterol.

Level of blood urea, serum creatinine and serum calcium were increased due to gentamicin. A number of studies confirmed these findings Potapova AV et al<sup>7</sup> and Levin ML<sup>9</sup>. These studies reported that the kidneys are the primary site of aminoglycoside (gentamicin) clearance: any factor that permits renal parenchymal accumulation increases the risk of aminoglycoside nephrotoxicity that may increase the level of blood urea and serum creatinine.

A study by Ascencio C et al<sup>4</sup> also confirmed our findings and showed an increased level of serum calcium. They reported that increased calcium inhibits hormone stimulated cAMP level that may effect on cellular process going on in cells.

Effect of Nigella Sativa on nephrotoxicity induced by gentamicin was also studied. In group II of rabbits, gentamicin along with Nigella Sativa was given for 11 days and biochemical parameters were estimated at 0 and 11 days. Level of blood urea, serum creatinine and cholesterol were decreased after the administration of gentamicin and Nigella Sativa (at the 11<sup>th</sup> day of administration). The current study is confirmed by Badary OA et al<sup>15</sup> who stated that the kidney functions become normal due to thymoquinone. Another study by AL-Tahir KE<sup>10</sup> reported



that the volatile oil of *Nigella Sativa* has an effect on hypertension and may be related with renin-angiotensin system and may effect on level of cholesterol.

On the other hand the level of serum protein and serum calcium were increased whereas the level of serum albumin remained the same. It was reported by Badary OA<sup>5</sup> and AL-Tahir KE<sup>10</sup> that thymoquinone significantly suppressed drug induced proteinuria. An increased level of serum calcium and decreased level of

serum cholesterol was observed in both groups of rabbits. This shows that the increased level of serum calcium may result in stone formation.

**Conclusion:** It is therefore concluded that although *Nigella Sativa* shows a significant effect on nephrotoxicity induced by gentamicin but its effect on the level of serum calcium and cholesterol may be dangerous. However further research is needed on large number of rabbits to reach to a definite conclusion.

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