Histopathological Comparison of Gentamycin and Amikacin Nephrotoxicity in Rabbits

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Abstract: Gentamycin and Amikacin are 2 of the most important antibiotics of Aminoglycosides family. They are most effective on gram-negative bacteria but one problem limiting their usages is their nephrotoxic effects on kidneys. Regarding to the proved higher wide-spread bacteriocidal activity of Amikacin than Gentamycin, researchers were about to compare their nephrotoxicity level so that if Amikacin's lower nephrotoxic effect can be proved, it will be the choice antibiotic between these two. About 48 rabbits were divided in 3 groups based on time (days 3, 7 and 14). In every group, 6 rabbits were injected by Gentamycin, 6 rabbits were injected by Amikacin and 4 as control group. Injections were done once in a day. About 24 h after the last injection, the rabbits were sacrificed and histopathologic slides were provided from their kidneys. The slides were examined on the necrosis severity based on some measures (mentioned in the full text). The results after being statistically analyzed (p<0.05) showed a remarkable and significant difference between 2 groups so that the Amikacin-induced necrosis was dramatically less than Gentamycin-induced necrosis. So because of Amikacin's higher bacteriocidal effect and less nephrotoxic damage, it can be recommended as a choice drug between these 2 considered antibiotics.

Key words: Gentamycin, nephrotoxicity, amikacin, comparison, infection, treatment, Iran

INTRODUCTION

Aminoglycosides are bacteriocidal antibiotics that interfere with protein synthesis by causing misreading of the genetic message and stimulation of faulty production of RNA. Gentamycin is an antibiotic belonging to the aminoglycosides and it is widely used in the treatment of gram-negative infections. However, its nephrotoxic action has limited the extent of its use (Mingeot-Leclercq and Tulkens, 1999). This antibiotic is most used for urinary, respiratory, digestive and soft tissues infections. Amikacin is another member of this family which is famous for its wide-spread affections and is almost used in hospitals whose patients have got resistant to other antibiotics of this family. But just like Gentamycin, its nephrotoxicity is a serious problem limiting its usage. This nephrotoxicity occurs as a result of Reactive Oxygen Species (ROS) (Cuzzocrea et al., 2002). In veterinary treatment especially in Iran, Gentamycin is the choice drug of this family when aminoglycosides are diagnosed to be taken and vet doctors do not intend to use Amikacin and usage of this drug is not common as much among veterinarians. Regarding to the highest Amikacin’s wide-spread influence on different bacteria, researchers are about to prove that if Amikacin-induced nephrotoxicity is dramatically less than Gentamycin-induced one, it will be recommended that Amikacin may be the 1st choice of gram-negative infections treatment so a more effective and less harmful result will be provided.

MATERIALS AND METHODS

This experiment was carried out in Islamic Azad University, Kazeroun Branch in Pathological Department. About 48 rabbits were selected and after being housed under controlled environmental conditions (around 27°C) and being kept in stress-free condition with free access to water and normal diet, they were randomly divided in 3 groups based on time:

Group 1: a-6 rabbits injected intramuscularly by Gentamycin for 3 days (20 mg kg⁻¹), b-6 rabbits injected intramuscularly by Amikacin for 3 days (100 mg kg⁻¹) and c-4 rabbits as control group without any injection.

Group 2: a-6 rabbits injected intramuscularly by Gentamycin for 7 days (20 mg kg⁻¹), b-6 rabbits injected intramuscularly by Amikacin for 7 days (100 mg kg⁻¹) and c-4 rabbits as control group without any injection.

Group 3: a-6 rabbits injected intramuscularly by Gentamycin for 14 days (20 mg kg⁻¹), b-6 rabbits injected
intramuscularly by Amikacin for 14 days (100 mg kg\(^{-1}\))
and c-4 rabbits as control group without any injection.

Every group's animals were anesthetized deeply with ether after 24 h of the last injection and both kidneys were
excised for histopathological studies and fixed in 10% buffered formalin solution and then placed in fresh fixative
solution to pH 7.3 at room temperature for 1 week. After
being processed for paraffin embedding and section
taking were stained with Hematoxylin and Eosin. These
slides were examined by a pathologist with light
microscope. In this stage, all the slides were examined for
tubular necrosis. The seen differences between level of
necrosis and its severity between animals injected by
Amikacin and Gentamycin were statistically significant
(Kruskal-wallis: p<0.05, df = 4, \(\chi^2\) = 44.4).

RESULTS

In examining the slides by a pathologist some grading
levels were provided to be applied on every slide. These
levels include:

**Level 0 (no necrosis):** No tubular necrosis could be seen
in the slide.

**Level 1 (light necrosis):** Average of 1-10 necrosis cells in
10 views of any slide.

**Level 2 (medium necrosis):** Average of 10-30 necrosis
cells in 10 views of any slide.

**Level 3 (severe necrosis):** Average of >30 necrosis cells
in 10 views of any slide.

The kidneys treated by Gentamycin

**Three days injections:** All the slides of 6 rabbits in this
group showed necrosis in medium level.

**Seven days injection:** The necrosis trend showed a
remarkable progress in comparison with the last group.
Four slides showed necrosis in level-3 and two of them
level-2, so a necrosis with level medium to severe (Fig. 1).

**Fourteen days injection:** A lot of necrosis was clear in
these slides so all of them were graded as severe necrosis
(level-3) (Fig. 2).

The kidneys treated by Amikacin

**Three days injection:** Like Gentamycin, coagulative
necrosis was seen in all 6 slides. But their necrosis levels
included five level-1 slides and one level-2 slide. So a light
to medium level (more tendency to light) was determined.

**Seven days injection:** These slides showed a little more
necrosis than the last group but was not as much as
Gentamycin group. Four slides showed medium level and
two slides showed light necrosis (Fig. 3).
In another study on low-dose nephrotoxicity of Gentamycin, Tobramycin and Amikacin, these antibiotics were respectively more nephrotoxic (Gentamycin>Tobramycin>Amikacin) (Hottendorf and Gordon, 1980). Above all in a typical study on some amnoglycosides, Gentamycin has been considered the most nephrotoxic agent and has had the highest degree of net reabsorption (Smith and Lietman, 1983).

It has been proved that animals with pyleonephritic problems are more susceptible to Gentamycin injections because Gentamycin levels in the cortex and medulla of infected animals were significantly higher than in the normal animals and might have been responsible for the increased toxicity noted in the pyleonephritic animals (Beauchamp et al., 1985).

All the given examples prove the findings and between Amikacin and Gentamycin, the former one should be more recommended. On the other hand, in a controlled comparison study of Amikacin and Gentamycin on 174 patients with suspected severe gram-negative infections, the results indicated that Amikacin is effective against severe gram-negative infections and is not more and less otoxic or nephrotoxic than Gentamycin (Smith et al., 1977). Another investigation on some critically ill patients, accumulation of Amikacin and Gentamycin looked similar to each other in the kidneys (French et al., 1981). No significant difference between Amikacin and Tobramycin’s nephrotoxicity has been reported (Gatell et al., 1983).

**CONCLUSION**

As it can be seen none of these studies do not directly prefer Gentamycin as a less nephrotoxic agent rather than Amikacin and in most cases, the results have been almost identical. So totally it can be concluded that Gentamycin is potentially more nephrotoxic than Amikacin and regarding to Amikacin’s more wide-spread antibacterial effects so it is a better choice drug.

**REFERENCES**


