MORPHOLOGICAL CHANGES PRODUCED BY AMINOGLYCOSIDE INDUCED NEPHROTOXICITY - AN EXPERIMENTAL STUDY

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Aminoglycosides are very commonly used antibiotics to treat life threatening infections because they display many highly desirable properties. The major limitations to their uses being their adverse effects, such as nephrotxicity. The purpose of present study was to see and compare the morphological changes in kidneys caused by use of aminoglycosides in animal model. The study was conducted on eighteen male local breed rabbits weighing 1 to 1.75 Kg and age ranging from 8 to 10 months for the period of 20 days. These animals were divided in three groups at random with 6 animals in each group. Two groups (G & A) were given Aminoglycosides namely Gentamicin and Amikacin in doses 10 times larger than corresponding human clinical dose to produce experimental nephrotoxicity while third group being control was injected only isotonic saline. After sacrificing the animals the histological examination of the kidneys revealed morphological changes mainly involving the renal tubules which show patchy necrosis along with hyaline and granular casts in their lumina. Dropped out tubular cells were also seen in the lumina of some of the renal tubules. The lining epithelial cells show hydropic changes with cytoplasmic vacuoles at some areas while regeneration at others. The glomerulae showed mild hypercellularity and congestion in most of the sections. The renal interstitium showed infiltration by polymorphonuclear leukocytes, lymphocytes, plasma cells and macrophages while the renal vascular changes were limited to focal congestion only but the changes were more pronounced in gentamicin treated group. It is concluded that Aminoglycosides cause nephrotoxicity by producing damaging effects on renal tubules especially at higher does, so their administration should carefully be monitored for early detection and prevention of toxic effects.
RESULTS
The histological sections of kidneys of the rabbits which were administrated with heavy doses of
Aminoglycosides revealed morphological changes mainly involving the renal tubules which show
patchy necrosis along with hyaline and granular casts in their lumina. The extent of necrosis was
more in gentamicin treated animals than amikacin group. Dropped out tubular cells were also seen in
the lumina of some of the renal tubules. The lining epithelial cells show hydromic changes with cyto-
plasmic vacuoles at some areas while regeneration at others. The regenerating cells were recognized
by enlarged nuclei. The changes in glomerulae were not very marked. The glomerulae showed
mild hypercellularity and congestion in most of the sections. The renal interstitium showed infiltration
by polymorphonuclear leukocytes, lymphocytes, plasma cells and macrophages particularly around
the necrotic tubules. The renal vascular changes were limited to focal congestion only. The sections
from control group showed normal morphology.

DISCUSSION
Over the years many classes of highly potent and
wide spectrum antibiotics have been introduced
but still aminoglycosides are mainstay to treat life
threatening infections because they display many
highly desirable properties, but, such an extensive
and common use is still thought to be limited in
the face of their usefulness; the major limitations
to their uses being their adverse effects, such as
nephrotoxicity, bringing about kidney damage via a
direct dose dependant mechanism. This study
was carried out to examine the morphology of kidney in experimental animals after adminis-
trating the high doses of two aminoglycosides. In
our study the most common morphological effects
occurred on the kidney tubules which showed
patchy necrosis. Some of the tubules also showed
hyaline and granular casts while others exhibited
dropped out tubular epithelial cells in their
lumina. At some sites the tubular epithelial cells
also showed hydromic change with cytoplasmic
vacuolization. These findings are almost consistent
with many other studies. Another change seen in
some of our cases was tubular regenerating activity recognized by enlargement of lining epithelial
cell nuclei, prominent nucleoli and baso-
philic cytoplasm. Several other studies on renal
effects of aminoglycoside reveal almost similar
results. In our study the tubular necrosis was
more marked in those administrated with genta-
mycin than amikcin. This is attributed to the fact
that toxic potential of individual aminoglycoside
agents is directly related to its ability to bind and
disrupt plasma membrane. Considering the glo-
merular changes, in our study many of the glo-
merulae showed focal hypercellularity and congestion
while no glomerular change was described in
other studies as the toxic effects of aminoglycosides are mainly on tubules. In almost all of
our cases renal interstitial tissue revealed infiltration by lymphocytes, plasma cells and macrophages. Similar results were also described by Lee and Michael (1985) and Vecchi et al (1988). Our findings are also similar to the findings of Lerma et al (2006). Vascular changes in the kidneys were limited to mild congestion only while Vecchi et al described focal thrombosis of the vessels along with congestion.

It is concluded that Aminoglycosides can produce nephrotoxicity via dose dependant me-
chanism. The morphological changes observed
with amikacin were lesser than gentamicin, so the administration of aminoglycosides should not only
be carefully monitored for early detection and
prevention of toxic effects but risk factors and / or
concomitant administration of other nephrotoxic
agents should also be avoided.

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