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CLINICAL RESEARCH ARTICLE

Clinicopathological Studies on Gentamicin Toxicity in White Leghorn Commercial Layers

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ABSTRACT

Gentamicin is an effective and economical drug used to control infectious diseases in poultry but is highly toxic and had slow clearance from the body. This study aimed to report three cases of gentamicin toxicity in three White Leghorn (WLH) layer flocks in different poultry producing areas of Pakistan. In first case, gentamicin was injected in a 9000 WLH layer flock @ 10 mg/kg body weight (BW) for seven times during 9-15 weeks for age. In second case, gentamicin was injected in a flock of 7500 WLH layers @ 25 mg/kg BW for four times during 17-18 weeks of age. In third case, gentamicin was injected in flock of 16000 WLH layers @ 22.22 mg/kg BW three times in 20-21 weeks of age. Flock wise mortality was 8.69, 82.63 and 71.86%, respectively. Birds were dehydrated, emaciated and had prominent keel bone. Clinical signs included dehydration, decreased body weight leading to emaciation, decreased feed intake, increased water intake and watery diarrhea. Necropsy revealed prominent keal bone, shrunken muscles swollen kidneys bulging out from bony sockets. Petechial and echymotic hemorrhages were present on heart and skeletal muscles. Liver was enlarged with hemorrhagic streaks on its surface. Microscopically, hemorrhages and acute tubular necrosis was recorded in kidneys. Liver had hemorrhages, cellular infiltration and vacuolar (fatty) degeneration of hepatocytes. From the results, it could be concluded that overdosing and repeated administration of gentamicin was highly toxic to birds.

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INTRODUCTION

Gentamicin belongs to aminoglycoside group of antibiotics and is an important therapeutic agent used in poultry and animals. It is used in poultry birds for the treatment of different diseases, e.g., collibacillosis, salmonellosis, etc. (Giurov, 1986). Gentamicin use in Pakistan is common as it is economical and effective. It is used in combination with tylosin, lincomycin and other antibiotics. It is also co-administered with inclusion body hepatitis/hydropericardum vaccine for prevention and treatment of different bacterial diseases in broiler and layers (Khan *et al*., 2008). Gentamicin in many regions of the world is unofficially administered to day old chicks to prevent early chick mortality (Saleemi *et al*., 2009). It was retained in muscles and kidneys of turkey birds for 45 and 75 days, respectively which makes it use questionable in birds intended for human consumption (Shem-Tov *et al*., 2003). Experimental gentamicin toxicity has been studied in day old broiler chicks (Saleemi *et al*., 2009) and no observable effect level (NOEL) of single intramuscular injection of gentamicin was 10 mg/kg BW. In an experimental study, Khan *et al*. (2008) found 5-10 mg/kg BW gentamicin I/M injection at the age of 1 and 3 days safe. In this study, we have reported high mortality associated with the treatment of gentamicin in White Leghorn layers.

HISTORY, METHODOLOGY AND RESULTS

Case A

This farm was located in district Vehari of southern Punjab (Pakistan). Total flock size was 9000 commercial WLH layer. Chick mortality up till 10 days of age was

10%. At 8 week of age, ciprofloxacin and tylosin were administered orally for 5 days. After two days of oral therapy birds were injected intramuscularly with gentamicin + Bacolam (Amoxicillin + Colistin) three times on alternate days. Dose rate of gentamicin was 10 mg/kg BW. After three weeks interval (age 12 weeks), gentamicin + Bacolam (Amoxicillin + Colistin) were again injected at the same dose rate for four times on alternate days. During six weeks (starting from 8 week of age) period gentamicin was injected 7 times. Mortality started at 20 days after gentamicin injection at 8 weeks and reached to a maximum at 11th week and remained high upto 14th week of age (Fig. 1). In this flock, overall mortality was 8.69% (Table 1). Morbid birds were depressed, dehydrated and emaciated having prominent keel bone (Fig. 2). Necropsy examination revealed shrunk skeletal muscles that kidneys were hemorrhagic, swollen and bulging out from bony socket. Uric acid crystals were deposited in the kidneys. Liver was swollen, hemorrhagic and friable having light and dark color streaks on its surface. A consistent lesion noticed in many birds was presence of clotted blood and pinpoint hemorrhages on epicardial surface of heart (Fig. 3).

Case B

White Leghorn commercial layer pullets of 17 weeks of age were injected gentamicin (10% solution) four times @ 25 mg/kg BW on alternate days during two weeks period at a layer farm, Arifwala, district Sahiwal. Total flock size was 7500. Mortality started 21 days post gentanmicin injection. Overall mortality in this flock was 82.63% with a peak during week 21-23 (Fig. 1). Dead birds upon necropsy showed emaciated pectoral muscles, swollen and hemorrhagic kidneys having urates (Fig. 4). Swollen and friable liver and hemorrhages present on epicardial surface were frequent gross lesions.

Case C

A total of 16000 commercial WLH layer (Sheikhupura) at 20 weeks of age were intramuscularly administered gentamicin @ 22.2 mg/kg BW. The same treatment was repeated three times on alternate days. Mortality started three weeks after the treatment. Mortality increased gradually from week 24 and remained high during weeks 25-27 (Fig. 1). Overall mortality in this flock was 71.86% (Table 1). Birds were depressed, emaciated having lesser feed intake and more water intake. The postmortem examination of dead birds revealed emaciation, swollen and hemorrhagic kidneys with urates. Liver was swollen and friable having streaks of light and dark color, hemorrhages were also present on epicardial surface (Fig. 3).

Microscopic lesions

In all three cases, liver and kidneys were collected during postmortem examination, fixed in 10% neutral buffered formalin and processed for histopathological examination by paraffin embedding method. Sections of 5 µm thickness were cut and stained with hematoxylin and eosin (Bancroft and Gamble, 2007).

Kidneys of all birds from three cases had condensed and shrunken nuclei of epithelial cells of convoluted tubules indicating acute tubular necrosis. In some birds these changes were more severe involving extensive areas of tubular necrosis (Fig. 5). Glomeruli were congested having pinkish material in the urinary spaces. At few places congestion was also present in renal parenchyma. Liver of birds showed vacuolar degeneration characterized by vacuoles of different sizes present in the cytoplasm of hepatocytes. These vacuoles were clear in appearance, round in shape and had sharp boundaries suggesting fatty change (Fig. 6). Individual cell necrosis of hepatocytes was present. The congestion was present throughout the parenchyma of liver. At many places cellular infiltration was also present.

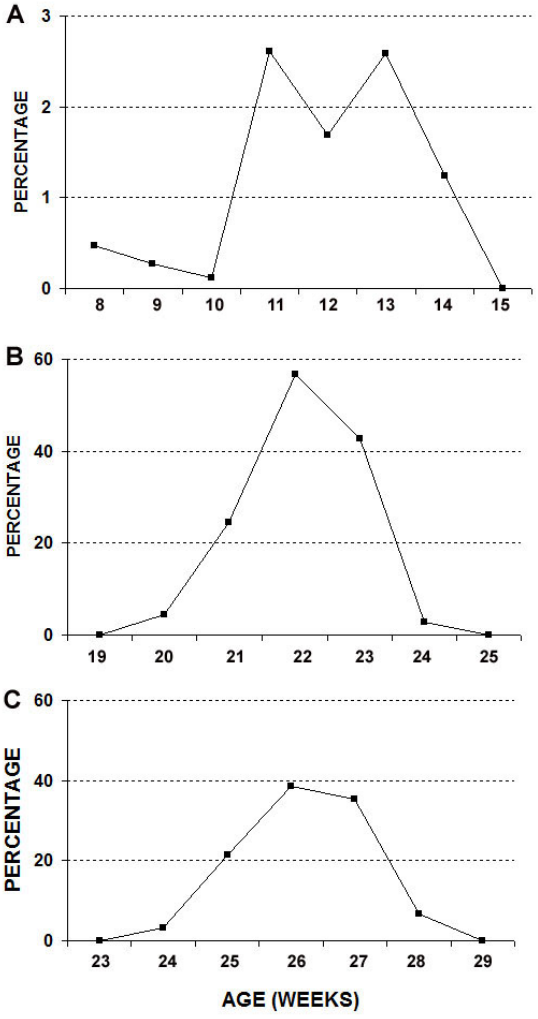

Fig. 1: Mortality pattern in WLH layers in three flocks (Case A-C).

DISCUSSION

There is scanty information available about toxicopathological effects of gentamicin in chicken. Experimentally produced pathological effects of gentamicin have been reported in growing cockerels of 5-6 weeks of age (Khan *et al*., 2008), day old broiler chicks

(Saleemi *et al*., 2009), growing broilers (Javed *et al*., 2008) and owls (Bauck and Haigh, 1984). In these studies the safe dose of gentamicin has been reported as 10 mg/kg BW in day old broilers (Saleemi *et al*., 2009) and growing *al*., 2009) and growing White Leghorn cockerels (Khan *et al*., 2008).

Table 1: Overall mortality recorded in White Leghorn layer due to gentamicin treatment

Case	Age of flock (weeks)	Total flock	Mortality	
			No	%
A	8-15	9000	782	8.69
B	19-25	7500	6197	82.63
C	23-29	16000	11497	71.86
Overall		32500	18476	56.85

Fig. 2: Photograph showing prominent keel bone with smaller pectoral muscles in layer birds repeatedly injected with gentamicin**.**

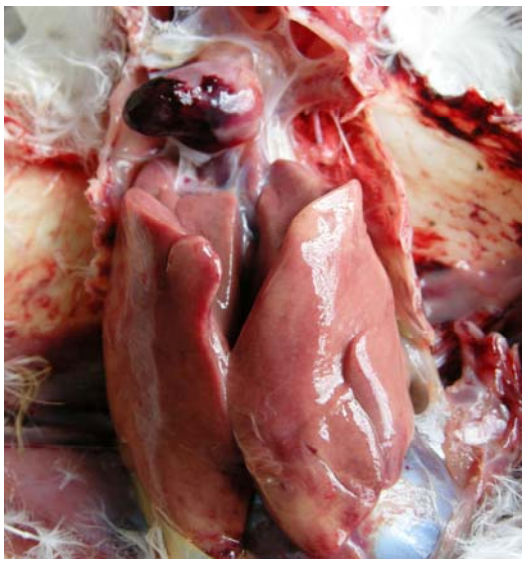

Fig. 3: Photograph showing hemorrhages on heart surface and swollen liver.

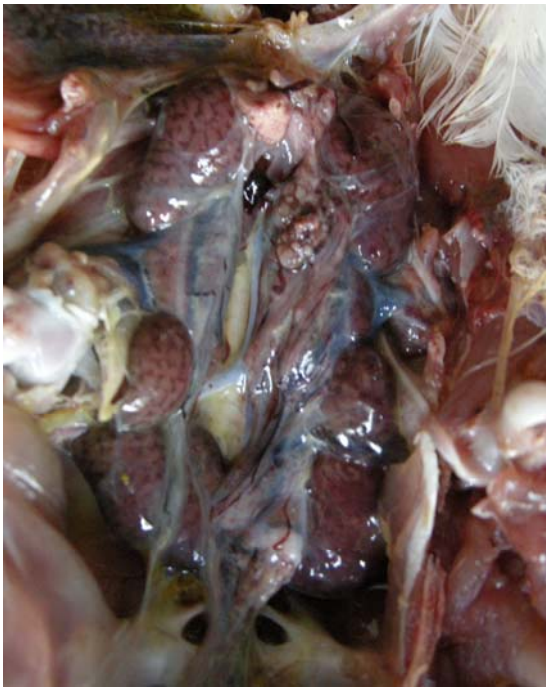

Fig. 4: Photograph showing swollen and congested kidneys with urates.

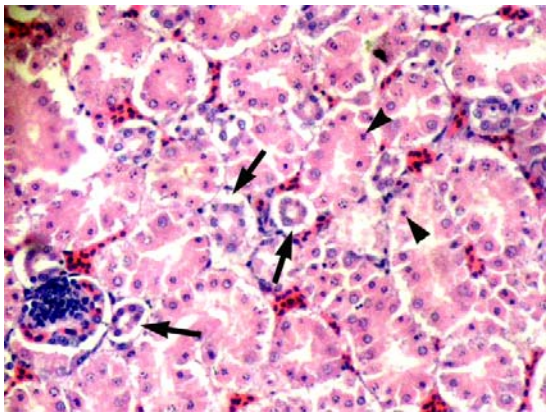

Fig. 5: Photomicrograph of kidneys showing karyorrhectic changes indicating acute tubular necrosis and congestion. H&E. 400X.

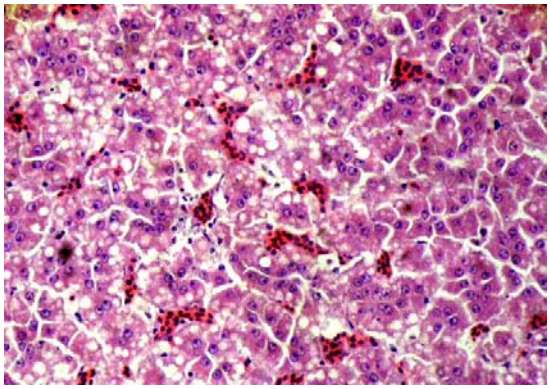

Fig. 6: Photomicrograph liver showing vacuolar degeneration, individual cell necrosis and congestion. H&E. 400X.

Gross and histopathological alterations observed in these cases were similar to those reported in experimental studies in birds (Khan *et al*., 2008; Saleemi *et al*., 2009), humans (Bourguignon *et al*., 2010; Beger *et al*., 2010) and other animals (Faraq *et al*., 1996; Lakshmi and Sudhakar, 2010). In present cases another persistent finding was hemorrhagic lesions on epicardial surface. No such lesions have been reported by previous workers. The variation in mortality of the birds in the reported cases could be due to the doses of gentamicin administered over multiple times and age of the birds. However, the pattern of mortality in all three cases was similar to each other. In the present case studies all the flocks were administered higher than safe dose level of gentamicin (10mg/kg BW) and the treatment was repeated many times. Gentamicin is a known nephrotoxic antibiotic for human (Ali, 1995; Selby *et al*., 2009; Lv *et al*., 2010), farm animals (Godber *et al*., 1995), rats (Bibu and Jor, 2010; Ozaki *et al*., 2010; Yaman and Balikci, 2010; Manali *et al*., 2011) and pet birds (Bird *et al*., 1983). It was assumed that repeated injections of gentamicin might have resulted in the severe nephrotoxicity in these cases. The history of these multiple overdose injection of gentamicin, gross and histopathological lesions and pattern of mortality had close resemblance with those of earlier reported experimental studies. These findings along with the absence of any other clinically apparent toxicity or infection were the basis of diagnosis of gentamicin toxicity in these cases.

It has been concluded from findings of present field and previous experimental studies that depending upon the type of birds, age, dose and frequency of treatment, gentamicin clinical toxicity starts after 2-3 weeks of administration and may continued upto five weeks. It is suggested that gentamicin should not be administered above the safe dose level (10 mg/kg BW) and its repeated use should be avoided.

REFERENCES

Ali BH, 1995. Gentamicin nephrotoxicity in human and animals: some recent research. Gen Pharmacol, 26: 1477-1487.

Bancroft JD and M Gamble, 2007. Theory and Practice of Histological Techniques. 5th Ed; Churchill Livingstone, London, UK, pp: 125-138.

Bauck LA and JC Haigh, 1984. Toxicity of gentamicin in great horned owl (*Bubo virginianus*). J Zoo Wildlife Med, 15: 62–66.

Beger RD, J Sun and LK Schnackenberg, 2010. Metabolomics approaches for discovering biomarkers of drug-induced hepatotoxicity and nephrotoxicity. Toxicol Applied Pharmacol, 243 (SI): 154-166.

Bibu K J and AD Jor, 2010. Protective effect of *Mangifera indica* Linn. on gentamicin induced nephrotoxicity in rats. Indian J Anim Sci, 80: 965-968.

Bird JE, MM Walser and GE Duke, 1983. Toxicity of gentamicin in red tailed hawks. Am J Vet Res, 44: 1289–1293.

Bourguignon L, S Goutelle, JB De Saint-Martin and P Maire, 2010. Evaluation of various gentamicin dosage regimens in geriatric patients: a simulation study. Fund Clin Pharmacol, 24: 109-113.

Faraq MM, M Mikhail, R Shehata, E Abdel Mequid and S Abdel Tawab, 1996. Assessment of gentamicin induced nephrotoxicity in rats treated with low doses of ibuprofen and diclofenac sodium. Clin Sci, 91:187-1891

Giurov B, 1986. Drug sensitivity of Salmonella strains isolated from poultry in 1980-1984. Vet Med Nauki, 23:10-17.

Godber LM, RD Walker, G Stein, JG Hauptman and FJ Derksen, 1995. Phramackinetics, nephrotoxicosis and in vitro anti-bacterial activity associated with single versus multiple (three times) daily gentamicin treatments in horses. Am J Vet Res, 56: 613-618.

Javed U, MK Saleemi, MZ Khan, A Khan and I Javed, 2008. Pathological effects of gentamicin in growing broilers. Proc 15th Congress of FAVA-OIE Joint Symposium on Emerging Diseases, pp: 17-18.

Khan I, MZ Khan, MK Saleemi, I Javed and A Khan, 2008. Pathological and biochemical effects of intramuscular gentamicin administration in chicken. Turk J Vet Anim Sci, 32: 345-351.

Lakshmi, BVS and M Sudhakar, 2010. Protective effect of zingiber officinale on gentamicin-induced nephrotoxicity in rats. Int J Pharmacol, 6: 58-62.

Lv, HT, LA Liu, YZ Zhang, T Song, JA Lu and X Chen, 2010. Ingenuity pathways analysis of urine metabonomics phenotypes toxicity of gentamicin in multiple organs. Mol Biosys, 6: 2056-2067.

Manali BP, S Deshpande and G Shah, 2011. Evaluation of Efficacy of Vitamin E and N-Acetyl Cysteine in Gentamicin-Induced Nephrotoxicity in Rats. Renal Fail, 33: 341-347.

Ozaki N, KA Matheis, M Gamber, T Feidl, T Nolte, A Kalkuhl and U Deschl, 2010. Identification of genes involved in gentamicin-induced nephrotoxicity in rats - A toxicogenomic investigation. Exp Toxicol Path, 62: 555-566.

Shem-Tov M, N Gabor, M. Suth and P Kormoczy, 2003. Depletion of gentamicin and its major components from various tissues of turkeys. Am J Vet Res, 64: 1234-1236.

Saleemi MK, MZ Khan, A Khan and I Javed, 2009. Pathological effects of gentamicin administered intramuscularly to day old broiler chicks. Exp Toxicol Path, 61: 425-432.

Selby NM, S Shaw, N Woodier RJ Fluck and NV Kolhe, 2009. Gentamicin-associated acute kidney injury. QJM Int J Med, 102: 873-880.

Yaman I and E Balikci, 2010. Protective effects of *Nigella sativa* against gentamicin-induced nephrotoxicity in rats. Exp Toxicol Path, 62: 183-190.