Toxicological risk assessment of Acetylsalicylic acid (ASA) in pigeons (columba levia)

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Article Info

ABSTRACT

The current study was aimed to investigate the effect of acetylsalicylic acid on pigeon birds. For this purpose healthy pigeons of different weights were randomly selected from Bio-Park University of Malakand and then placed it in different groups on the basis of their weights. To observe the effect, different doses of acetylsalicylic acid were administered orally to each group of pigeons except one group which was kept as unmedicated (control group). Blood samples were collected from individual pigeon of each group periodically i.e. before medication, during medication and after medication and were analyzed for glucose, cholesterol, alanine amino tranferase (ALT) and uric acid. Blood hematology was also performed for each individual pigeon from all the groups. A significant decrease was observed in glucose and ALT level, while the cholesterol and uric acid level was increased. Likewise to glucose, reasonable increase was observed in total red blood cells count (TRBCs), Hematocrit value (HCT), Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular Hemoglobin concentration (MCHC) and platelets count, while the Hemoglobin (Hb%) and total leukocyte count (TLC) level was decrease. Overall huge toxic effect of acetylsalicylic acid was recorded in pigeons; therefore it should be used carefully in veterinary medicines especially for the treatment of temperature and pain in game birds.

Keywords:
Acetylsalicylic acid, Blood biochemistry, Blood hematology, pigeon, Toxicity

INTRODUCTION

A non-steroidal anti-inflammatory drug (NSAID), Acetylsalicylic acid (ASA) used in veterinary practice normally (Livingston 2010; Miller and Richardson 2011) through some usages in the avian remedy (Machin 2005; Hawkins and Paul Murphy 2011). Acetylsalicylic acid as sodium salt had been administered orally in pigs, calves and chicken 5-300 mg kg⁻¹ per day for not above ten days. Dose and time dependent residues are found in skin, fat, muscle, liver and kidney.

Valuable impact of NSAID like headache medicine on ascites, development and egg generation of chickens during heat stress were valued (Rao et al. 2012; Abdel 2015). Aspirin is utilized every now and again in ducks. At the point when a reovirus disease with tenosynovitis happens. Different uses are for treating locomotor issue, incitement of egg generation and improving eggshell thickness, just as for respiratory and stomach related issues (Balog et al. 2000). In poultry, Aspirin medicine might be utilized as an anti-stress cause (Mc Daniel and Parker 2004).

In nourishment creating animals just as in companion birds, calming drugs are only here and there endorsed because of shortage of essential information and logical research on pharmacokinetic information of veterinary significant NSAIDs. There have been a few examinations concentrated on the pharmacokinetics of Sodium salicylate in poultry (Baert and De Backer 2002; Baert et al. 2004) and its adequacy in treating irritation in feathered creatures (Baert et al. 2005) yet restricted data is accessible on the toxicopathological impacts of acetyl salicylic in pigeons. The advantageous impacts of ASA and its regular use, it was felt important to contemplate the lethal impact of ASA at various portion levels in broiler chicks.
Acetylsalicylic corrosive breaks down quickly in arrangements of ammonium acetic acid derivation/acet acid derivations, carbonates, citrates or hydroxides of the soluble base metals. Acetylsalicylic corrosive is steady in dry air, however step by step hydrolyses in contact with dampness to acidic and salicylic acids. In arrangement with soluble bases, the hydrolysis continues quickly and the reasonable arrangements shaped may comprise totally of acetic acid derivation and salicylate. Aspirin, an acetyl subsidiary of salicylic acid, is a white, crystalline, feebly acidic substance, with a softening purpose of 135 °C (275 °F) (Jenkins et al. 2007).

The adverse effects associated with these drugs result mainly from the impairment of constitutive prostaglandin synthesis (Suleyman et al. 2007). Targets most frequently affected by salicylates are the gastrointestinal tract, haemostasis, kidneys and electrolyte homeostasis (Bergh et al. 2005). It has been reported, that humans tolerate ASA considerably (Leijte et al. 2019). The aim of the present study was to investigate and compare the effects of prolonged administration of high doses of ASA on body weight gain, blood biochemistry, haematological variables and post mortem data, including the liver as well as the kidney to body weight ratio, in pigeons.

**MATERIALS AND METHODS**

*Selection of birds and their medication*

Total fifteen healthy pigeons were selected the bio-park of University of Malakand for rearing. Pigeon were classified into five different groups (A, B, C, D, and E) on the basis of their body weights. To each group three number of pigeons were assigned. Group E (281 gm wt.) was kept as un-medicated and named it control group. The rest of the four groups were medicated with different dosage levels of Acetylsalicylic acid. The medication was continued for ten consecutive days to all groups, except control. Group A (214 gm wt.), B (224 gm wt.), C (240 gm wt.) and D (270 gm wt.) were medicated from normal to high doses i.e. 5 mg kg\(^{-1}\) wt, 10 mg kg\(^{-1}\) wt, 15 mg kg\(^{-1}\) wt, 20 mg kg\(^{-1}\) wt, respectively (see in Table 1).

*Collection of blood samples*

Blood sample collection was scheduled before medication and after 5\(^{th}\) and 10\(^{th}\) day of medication. Each time, 5 ml of blood samples were collected from individual member of each group. Of which 3 ml was used for hematology and the remaining 2 ml blood was used for blood biochemistry.

*Isolation of serum*

2 ml blood sample was transferred to the falcon tube and was centrifuged at 4000 rpm for 5 minutes. No anti-coagulant was used. The pellet was settled down and the supernatant was collected as clear serum. The Cholesterol, Glucose, SGPT, Uric acid were analyzed from serum.

*Blood biochemistry and hematology*

A number of biochemical parameters were analyzed for both the medicated and control groups which includes glucose level, cholesterol level, SGPT level and uric acid (Urates). An automatic digital machine (Sysmex Kx-21 Japan) was used for blood profiling. Heparinized blood was used for the complete blood count and the parameters analyzed were: Hemoglobin (Hb %), Total Red Blood Cell Count (TRBC), Hematocrit Value (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Total Leukocyte Count (TLC), Platlets Count, Neutrophils, Lymphocytes, Eosinophils and Monocytes.

*Post mortem examination*

All the birds were slaughtered and blood was collected for hematology and biochemistry. The post mortem was performed and gross pathological findings if any, were recorded. All the data were recorded and the results were statistically analyzed by graph pad prism online. Mean and Standard deviation of each data was obtained in tabulated format.

**RESULTS AND DISCUSSION**

*Blood Biochemistry*

In Group E (control), Blood glucose level was 221.00±4.00 mg dl\(^{-1}\) at 5\(^{th}\) day and 256.00±49.49 mg dl\(^{-1}\) at 10\(^{th}\) day of the experiment which is quite in the range of normal (254 mg dl\(^{-1}\)). For Group A this value was observed in increasing fashion having 312.66±4.04 mg dl\(^{-1}\) at 5\(^{th}\) day and 314.83±79.90 mg dl\(^{-1}\) at 10\(^{th}\) day (Table 2, 3). For group B it was estimated 325.33±4.50 mg dl\(^{-1}\) at 5\(^{th}\) day and 263.80±44.54 at 10\(^{th}\) day of the experiment. For the group C it was estimated 367.33±2.51 mg dl\(^{-1}\) and 227.49±13.90 mg dl\(^{-1}\) at 5\(^{th}\) and 10\(^{th}\) day of the experiment respectively. Almost similar trend was documented for group D. The same results have been found by Nejad 2007 reported that acetylsalicylic acid decrease the glucose level in pigeon.

### Table 1. Groups with level of medication

| S. No | Group | Medication |
|-------|-------|------------|
| 1     | E (Control) | No Medication |
| 2     | A | Dose rate 5 mg kg\(^{-1}\) |
| 3     | B | Dose rate 10 mg kg\(^{-1}\) |
| 4     | C | Dose rate 15 mg kg\(^{-1}\) |
| 5     | D | Dose rate 20 mg kg\(^{-1}\) |
Table 2. Different parameters recorded at 5th day of medication

| Group       | E          | A          | B          | C          | D          |
|-------------|------------|------------|------------|------------|------------|
| Blood glucose level (mg dl⁻¹) | 221.00 ± 4.00 | 312.66 ± 4.04 | 325.33 ± 4.50 | 367.33 ± 2.51 | 327.33 ± 2.51 |
| Blood Cholesterol level (mg dl⁻¹) | 203.66 ± 5.68 | 227.00 ± 3.00 | 208.00 ± 6.55 | 210.00 ± 5.00 | 193.00 ± 3.00 |
| Blood Uric acid level (mg dl⁻¹) | 2.15 ± 0.30 | 3.40 ± 0.45 | 3.46 ± 0.50 | 3.33 ± 0.51 | 3.76 ± 0.30 |
| Blood Haemoglobin level (mg dl⁻¹) | 15.46 ± 1.20 | 18.00 ± 2.00 | 17.10 ± 2.00 | 19.23 ± 1.07 | 17 ± 1.00 |
| Blood TLC level (mg dl⁻¹) | 181.89 ± 133.73 | 211.19 ± 158.91 | 285 ± 100 | 286.00 ± 20.18 | 279.2 ± 10.00 |
| Blood MCH level (mg dl⁻¹) | 58.00 ± 2.00 | 50.33 ± 1.52 | 50.33 ± 1.52 | 70.33 ± 1.52 | 70.67 ± 4.76 |
| Blood MCHC level (mg dl⁻¹) | 37.00 ± 1.00 | 34.00 ± 1.00 | 34.33 ± 1.52 | 70.33 ± 1.25 | 42.00 ± 2.00 |
| Blood Platelets count level (mg dl⁻¹) | 3000.00 ± 1000.00 | 2133.30 ± 1594.80 | 7533.33 ± 251.61 | 5600.00 ± 500.00 | 5000.00 ± 700.00 |

Values of the blood ALT for all the groups were noted in two different stages of medication. High value of ALT has been recorded for heavy weighted group of pigeons on 10th day of medication (76.00±15.55 mg dl⁻¹) followed Group-B and lowest weighted pigeons on 5th and 10th day respectively. Lowest level of blood ALT level was 22.00±2.00 mg dl⁻¹ for control group followed by Group-A (43.00±3.00 mg dl⁻¹) at 5th day of medication supported by Koochaksaraie et al. 2011. LaScalza et al. (2003) have mentioned that acetylsalicylic acid leads to increase in ALT level.

Table 3. Different parameters recorded at 10 days of medication

| Group       | E | A | B | C | D |
|-------------|---|---|---|---|---|
| Blood glucose level (mg dl⁻¹) | 256.00 ± 49.49 | 314.83 ± 79.90 | 263.80 ± 44.54 | 227.49 ± 13.90 | 292.33 ± 24.98 |
| Blood Cholesterol level (mg dl⁻¹) | 288.16 ± 30.87 | 198.49 ± 5.89 | 202.00 ± 4.24 | 240.16 ± 7.30 | 217.33 ± 74.48 |
| Blood Uric acid level (mg dl⁻¹) | 2.86 ± 0.47 | 3.16 ± 0.99 | 2.44 ± 0.68 | 2.46 ± 0.28 | 2.66 ± 0.28 |
| Blood Haemoglobin level (mg dl⁻¹) | 15.66 ± 1.52 | 18.33 ± 1.52 | 16.66 ± 1.52 | 17 ± 1.00 | 15.83 ± 1.60 |
| Blood TLC level (mg dl⁻¹) | 285.66 ± 4.04 | 256.00 ± 100.00 | 296 ± 251 | 31.90 ± 60.20 | 285.3 ± 3.05 |
| Blood MCH level (mg dl⁻¹) | 4.16 ± 1.52 | 0.00 ± 0.00 | 57.67 ± 2.51 | 53.00 ± 2.00 | 51.00 ± 1.00 |
| Blood MCHC level (mg dl⁻¹) | 35.00 ± 5.00 | 0.00 ±0.00 | 37.00 ± 2.00 | 34.33 ± 2.06 | 35.00 ± 1.00 |
| Blood Platelets count level (mg dl⁻¹) | 4000.00 ± 1000.00 | 3400.00 ± 2000.00 | 7533.33 ± 251.66 | 6000.00 ± 1000.00 | 5200.00 ± 1000.00 |

Cholesterol level for control was 203.66±5.68 mg dl⁻¹ at 5th day and 288.16±30.87 mg dl⁻¹ at 10th day of the experiment. In Group-A and B the level of cholesterol was decreased from 5th day of medication to 10th day of medication (Table 2, 3). Luzak (2011) found the increase in cholesterol level. Kassahun (2008) found decrease in cholesterol level in pigeon. This increase in cholesterol level might be due to lack of activities as the pigeons were in the net and having no such facility of long flight.

There was decrease in Uric acid level in pigeon while Spennemann et al. (2107), Omar et al. 2017 support the same results. The reference value for uric acid is 2.6 mg/dl, high concentration of uric acid in blood leads to a type of arthritis known as gout. This chemical is also associated with other medical conditions including diabetes and the formation of ammonium urate kidney stones. Table 2, 3 shows that initially the level of uric acid in blood increases i.e. up to 5th day of medication and later on significant decrease was recorded i.e. from 5th to 10th day of medication.

Haemoglobin (Hb or Hgb) is the iron-containing oxygen-transport metaloprotein in the red blood cells of all vertebrates (Renjie et al. 2010). In comparison to control group, the level of haemoglobin significantly increased with treatment of acetylsalicylic acid. The increase in haemoglobin level jumps initially with medication but later on the increased becomes slow (Table 2, 3). Haemoglobin level was documented at peak (19.23±1.07 mg dl⁻¹ at 5th day and 17±1.00 mg dl⁻¹ at 10th day) for Group-C in comparison to all other groups. The Haemoglobin level was reported by Dumaro et al. (2014) the same result. White blood cells or leucocytes (TLC) are cells of the immune system involved in defending against both infectious disease and foreign materials (Martinez-Martin et al. 2001). In group E (control), TLC level was 181.89±133.73 mg dl⁻¹ at 5th day and 285.66±4.04 mg dl⁻¹ at 10th day, while for group A it was 211.19±158.91 mg dl⁻¹ at 5th day and 256.00±100.00 mg dl⁻¹ at 10th day of the experiment.
experiment (Table 2, 3). TLC level in pigeon were decrease during using the use of acetyl salicylic acid (Bosetti et al. 2006).

Red blood cells or erythrocytes (TRBC), are the most common type of blood cells and in vertebrate organism’s the principal means of delivering oxygen (O$_2$) to the body tissues via the blood flow through the circulatory system (Jensen 2004). In group E (Control), TRBC level was 2.60±0.55 mg dl$^{-1}$ at 5th day and 3.00±1.00 mg dl$^{-1}$ at 10th day, while for group A it was 3.21±1.66 mg dl$^{-1}$ at 5th day and 3.17±1.13 mg dl$^{-1}$ at 10th day of the experiment. The hematocrit (Ht or HCT), the control group (E) was 43.00±1.00 mg dl$^{-1}$ at 5th and 45.33±5.05 mg dl$^{-1}$ at 10th day. Similar pattern was recorded for group C and group D while decrease in HCT was noted for group A. Unlike to all other groups (i.e. medicated and non-medicated), It was group B in which there was no change observed in HCT level throughout the experiment. The mean corpuscular volume, or “mean cell volume” (MCV), is a measure of the average red blood cell size that is reported as part of a standard complete blood count (Schrier et al. 2011). MCV in all groups was recorded and presented in table 2, 3, which flows in the range of 131.33±3.21 to 165.00±1.0 mg dl$^{-1}$. There is no dramatic change in the level MCV, which indicates that acetylsalicylic acid have very minor effect on overall MCV level. The mean corpuscular hemoglobin, or “mean cell hemoglobin” (MCH) in control group E was 58.00±2.00 mg dl$^{-1}$ at 5th day and 4.16±1.52 mg dl$^{-1}$ at 10th day. For the group A it was 50.33±1.52 mg dl$^{-1}$ at 5th day and 0.00±0.00 mg dl$^{-1}$ at 10th day, while group B was 50.33±1.52 mg dl$^{-1}$ at 5th day and 57.67±2.51 mg dl$^{-1}$ at 10th day and group C was 70.33±1.52 mg dl$^{-1}$ at 5th day and 53.00±2.00 mg dl$^{-1}$ at 10th day of the experiment. The MCH level of group D was 70.67±4.76 mg dl$^{-1}$ at 5th day and 51.00±1.00 mg dl$^{-1}$ at 10th day of the experiment (Table 2, 3).

The mean corpuscular hemoglobin concentration, in group E (control) level was 37.00±1.00 mg dl$^{-1}$ at 5th and 35.00±5.00 mg dl$^{-1}$ at 10th day. While for group A it was 34.00±1.00 mg dl$^{-1}$ at 5th day and 0.00±0.00 mg dl$^{-1}$ at 10th day of the experiment. Group B was 34.33±1.52 mg dl$^{-1}$ at 5th day and 37.00±2.00 mg dl$^{-1}$ at 10th day (Table 2, 3). For group C it was 70.33±1.25 mg dl$^{-1}$ at 5th day and 34.33±2.06 mg dl$^{-1}$ at 10th day, while for group D it was 42.00±2.00 mg dl$^{-1}$ at 5th day and 35.00±1.00 mg dl$^{-1}$ at 10th day of the experiment. Morgan et al., 2005 previously reported that the using of acetyl salicylic acid was lead to increase the RBC level in pigeon birds. Notarbartolo et al. (1995) reported the increase in HCT level in pigeon birds while during our experiment we also noted the same results about HCT. Carella et al. (1988) previously reported the increase in MCV level in pigeon birds as our result. However Fonseca et al. (2007) has mention that acetyl salicylic acid decrease the RBC level, the results are not in correlation with present findings and Meloni et al. (1988) report the reason for the deviation may be the use of different experimental subjects and difference in diagnostic tools. Cruz (2004) has mentioned that acetyl salicylic acid decrease in MCH level. Brattstrom et al. (2010) has mentioned that acetyl salicylic acid decreases the MCHC level in pigeon birds. Megginson (2017) reported increase the Platelet count in pigeon as our results.

Platelets or thrombocytes, in group E (control) platelet count level was 3000.00±1000.00 mg dl$^{-1}$ at 5th day and 4000.00±1000.00 mg dl$^{-1}$ at 10th day, while for group A it was 2133.30±1594.80 mg dl$^{-1}$ at 5th day and 3400.00±2000.00 mg dl$^{-1}$ at 10th day, and for group B it was 7533.33±251.61 mg dl$^{-1}$ at 5th day and 7533.33±251.66 mg dl$^{-1}$ at 10th day of the experiment. The platelet count level of group C was 5600.00±500.00 mg dl$^{-1}$ at 5th day and 6000.00±1000.00 mg dl$^{-1}$ at 10th day, while for group D it was 5000.00±700.00 mg dl$^{-1}$ at 5th day and 5200.00±1000.00 mg dl$^{-1}$ at 10th day of the experiment (Table 2, 3). Short-term acetyl-salicylic acid treatment - less than or equal to 50 mg kg$^{-1}$ dose is safe in every examined bird species. Nevertheless the five day long application of this agent can cause lesions in the intestinal mucosa as well as severe congestion and hemorrhages in the small intestine (Mohan 2012), furthermore the long-term application of acetyl-salicylic acid can lead irreversible degenerative changes in bone.

Table 4. Post mortem examination of pigeons

| Group                  | Weight (g) | Chest Muscles | Heart | Liver | Lungs | Kidney | Gizzard | Brain       |
|------------------------|------------|---------------|-------|-------|-------|--------|---------|-------------|
| Group E (Control)      | 294        | Normal        | 4mg,  | 8mg   | Yellow| 2 mg   | Detachable, Green | Detachable, Green | Normal       |
| (No medication)        |            |               | Rigged|       |       |        |         |             |
| Group A (Dose rate 5 mg kg$^{-1}$) | 237        | Normal        | 3mg,  | 5mg   | Yellow| 1mg   | Detachable, Green | Detachable, Green | Hemorrhage |
|                        |            |               | Flabby|       |       |        |         |             |
| Group B (Dose rate 10 mg kg$^{-1}$) | 230        | Normal        | 4mg,  | 5mg   | Yellow| 1mg   | Detachable, Green | Detachable, Green | Hemorrhage |
|                        |            |               | Flabby|       |       |        |         |             |
| Group C (Dose rate 15 mg kg$^{-1}$) | 248        | Normal        | 2mg,  | 3mg   | Yellow| 1mg   | Detachable, Green | Detachable, Green | Hemorrhage |
|                        |            |               | Flabby|       |       |        |         |             |
| Group D (Dose rate 20 mg kg$^{-1}$) | 284        | Normal        | 4mg,  | 3mg   | Yellow| 1mg   | Detachable, Green | Detachable, Green | Hemorrhage |
tissues (Derakhshanfar 2013).

Pozniak et al. (2010) reported that an increase in kidney size was evident in chickens treated with ASA at the dose of 200 mg/kg, which was the highest dose used in that experiment. This is consistent with the effect on rats treated with ASA for 3 months when an increase in kidney size occurred after doses of 50, 150 or 500 mg/kg were administered daily. Mohan et al. (2012) found significant decrease in serum total protein concentration. Total erythrocyte count, hemoglobin concentration. PCV and platelet after oral administration of ASA (10 mg kg⁻¹) daily for a period of five days. Derakhshanfar et al. (2012) who found decrease in AKP level in the serum of broiler chicks given ASA at the dose rate of 400 mg L⁻¹ for 21 days.

CONCLUSIONS

Pozniak et al. (2010) reported that an increase in kidney size was evident in chickens treated with ASA at the dose of 200 mg kg⁻¹, which was the highest dose used in that experiment. This is consistent with the effect on rats treated with ASA for 3 months when an increase in kidney size occurred after doses of 50, 150 or 500 mg kg⁻¹ were administered daily (Anonymous, 1999). Mohan et al. (2012) found significant decrease in serum total protein concentration. Total erythrocyte count, hemoglobin concentration. PCV and platelet after oral administration of ASA (10 mg kg⁻¹) daily for a period of five days. Derakhshanfar et al. (2012) who found decrease in AKP level in the serum of broiler chicks given ASA at the dose rate of 400 mg L⁻¹ for 21 days.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

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