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Original Study

Comparison of Anesthetic Efficacy of Lidocaine and Bupivacaine in Spinal Anesthesia in Chickens

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Abstract: Lidocaine is used for epidural and spinal anesthesia in various animal species. The ideal drug for epidural and spinal anesthesia should have a long effective duration in addition to a fast onset of action, and adequate analgesia and muscle relaxation. Despite the delayed onset of action, bupivacaine provides a longer duration of anesthesia than lidocaine. The purpose of this study was to compare the onset to effect and duration of action between lidocaine and bupivacaine for spinal anesthesia in broiler chickens. Thirty-two, 8-week-old, female Ross broiler chickens were randomly divided into 4 groups of 8: 1) 2 mg/kg lidocaine (L); 2) 0.1 mg/kg bupivacaine (B0.1); 3) 0.25 mg/kg bupivacaine (B0.25); and 4) 0.5 mg/kg bupivacaine (B0.5). After aseptic preparation, a 23-gauge spinal needle was inserted into the synsacrococcygeal space of the chickens with correct needle placement confirmed by a sudden loss of resistance. Spinal anesthesia was performed with the aforementioned doses of lidocaine and bupivacaine. The respiratory rate and cloacal temperature were measured every 10 minutes in each chicken until the anesthetic effect was no longer present. The onset to effect and the duration of action were calculated for each bird based on the pinch test at predetermined time intervals. The results are demonstrated as mean ± SD. The onset of action for bupivacaine (9 ± 1.41, 4.33 ± 1.15, and 3.33 ± 1.23 minutes in B0.1, B0.25, and B0.5 groups, respectively) was significantly delayed compared with that of lidocaine (1.37 ± 0.52 minutes). The duration of action of B0.5 (54 ± 6.08 minutes) was significantly longer than that of any other group (17.87 ± 3.18, 11 ± 1.41, and 18 ± 4.36 min in L, B0.1, and B0.25 groups, respectively). The results showed that a spinal injection of 0.5 mg/kg bupivacaine produces approximately 55 minutes of spinal anesthesia in these broiler chickens, which is much longer than the 18 minutes of anesthesia provided by 2 mg/kg lidocaine. Considering the various disease conditions that affect the cloacal area of birds, one can use each of these anesthetic drugs for either short-term or long-term spinal anesthesia in chickens and possibly other avian species.

Key words: bupivacaine, lidocaine, spinal anesthesia, avian, broiler chicken

INTRODUCTION

For many surgical procedures, general anesthesia is required for the avian patient. For some procedures, including those involving the caudal coelom, local or regional anesthesia may reduce associated pain. Egg retention and dystocia are common reproductive disorders in birds, often requiring critical care and, in some cases, surgery.[1,2] Salpingohysterectomy, cloacopexy, and cloacoplasty are other caudal coelomic surgical procedures that may benefit from regional anesthesia.[3]

A caudal spinal anesthesia technique has been established for chickens, which may eliminate the need for general anesthesia for surgical procedures that involve the caudal coelom or cloaca.[4] The ideal local anesthetic agent should have a short onset to effect, a long duration of action, and provide adequate analgesia and muscle relaxation.

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Although lidocaine is commonly used for local anesthesia in different animal species, its use is limited in lengthy surgical procedures because of its short duration of action. A previous study found that lidocaine has an active duration of 21.3 ± 2.5 minutes after spinal injection in chickens.[4] In contrast, bupivacaine, a derivation from amino amides, although delayed in onset of action, produces a longer anesthetic effect than lidocaine and is used when there is a need for prolonged anesthesia events.[5–7] Bupivacaine has been used with minimal adverse side effects for spinal anesthesia worldwide.[8] Although bupivacaine has been reported to have neurotoxic effects, those adverse effects occur less often than those observed with lidocaine usage.[9,10]

The spinal cord of domestic chickens is enclosed by 3 meningeal layers: the pia mater, the arachnoid, and the dura mater. There is no epidural space caudal to the thoracic region of the coelom because there is a general attachment of the vertebral periosteum to the dura mater.[4] In contrast, the arachnoid space is well developed in the synsacral spinal cord.[11] As a result, epidural injection is not possible in the lumbosacral area of the chickens, but spinal injection is easy to perform.[4]

In the present study, it was assumed that bupivacaine has a dose-dependent, slower onset to effect and a longer duration of action compared with lidocaine when administered into the subarachnoid space of the chicken. Therefore, the purpose of this study was to evaluate and compare the onset to effect and the duration of action for lidocaine and bupivacaine in spinal anesthesia of chickens because the latter anesthetic is not currently used for spinal anesthesia in chickens.

MATERIALS AND METHODS

Animals

Thirty-two, 8-week-old, female Ross 308 broiler chickens weighing (mean ± SD) 2 ± 0.2 kg were used in this study. The chickens were maintained in custom-made cages (60 × 60 × 40 cm in length, width, and height, respectively, for every 4 chickens) for this investigation and had free access to drinking water and commercial poultry food (Pas Dan 2, Faraz Daneh Avand, Takestan, Iran). The room temperature was set at 21°C (69.8°F), and there was appropriate negative-pressure ventilation. The light and dark cycles were alternated in 12-hour intervals. The birds were provided a 1-week acclimatization period before the study was initiated. Animal use was based on the World Medical Association's statement on the use of animals in biomedical research, and the study was approved by the Research Ethics Committee of the University of Tabriz (approval code: IR.TABRIZU.REC. 1398.007).

Study design and spinal anesthesia

The chickens were randomly divided into 4 groups of 8, with an online random number list (Random Integer Generator. Available at: https://www.random.org/integers) as follows: 2 mg/kg of 2% preservative-free lidocaine hydrochloride (Aburaihan Pharmaceutical Co, Tehran, Iran) as positive control (group L) and 0.1, 0.25, and 0.5 mg/kg of 0.5% bupivacaine hydrochloride (Marcaine Spinal, AstraZeneca AB, Södertälje, Sweden) containing excipients of glucose monohydrate, sodium hydroxide, and water (groups B0.1, B0.25, and B0.5, respectively). The spinal injection was performed as previously described.[4] Under physical restraint, the tail feathers of the animals were cut off with a pair of scissors to make it easier to identify the injection site. The area was prepared aseptically with the povidone-iodine solution. Then, the space between the synsacrum and the first free caudal vertebra was identified by palpation with the spinous process of the first free caudal vertebra as an anatomical landmark. A subcutaneous injection of 2 mg/kg of 2% lidocaine hydrochloride was administered approximately 10 minutes before the spinal injection for local anesthetic effect. A 75-mm, 23-gauge, Quincke-type spinal needle (Vygon, Swindon, UK) attached to a 1-mL insulin syringe (SUPA Medical Devices Co, Tehran, Iran) containing the drug was entered into the synsacrococcygeal space until it passed through the ligamentum flavum, as determined by a sudden loss of resistance. Spinal anesthesia with 2% lidocaine hydrochloride drug or 0.5% bupivacaine hydrochloride at the aforementioned doses was administered, depending on the subject group. The anesthetic volumes were standardized by adding normal saline so that the total volume was 0.2 mL in all birds.

Evaluation of anesthesia and vital parameters

Clinical signs of adverse anesthetic side effects, regional reactions, and recumbency were monitored in all birds for 60 minutes after the spinal injection. A bird was considered recumbent if it was in ventral recumbency and could not stand, even with assistance. The respiratory rate (visual) and cloacal temperature were measured before the spinal injection (time 0) and every 10 minutes until

the anesthetic effect was no longer evident. The cloacal temperature was measured by inserting a digital thermometer (FT 13, Beurer, Ulm, Germany) into the coprodeum of the cloaca for 1 minute. Anesthetic effect was assessed with the pinch test by thumb forceps in pericloacal skin before the spinal injection (time 0), then at 1, 3, and 5 minutes after the spinal injection and every 5 minutes thereafter until the bird responded to the external stimuli. The interval between the spinal injection and the first lack of response to external stimuli was considered as the effective onset of the agent. The duration of action was measured from the onset of effect (no response to external stimuli) to when the bird responded to the external stimuli.

Statistical analysis

Statistical analysis was performed with a commercial statistical software (Minitab, version 16.2.0, Pennsylvania State University, State College, PA, USA). The examination of normal distribution was accomplished with the Kolmogorov-Smirnov test and the assumption of equal variance with the Levene's test. Onset and duration of actions of the anesthetics were analyzed between groups with one-way analysis of variance, and the groups were compared with Tukey's post hoc test. Cloacal temperature and respiratory rate data, over time, were analyzed with repeated-measures one-way analysis of variance, and time points within groups were compared with Tukey's post hoc test. Results are shown as mean ± SD. $P < .05$ was considered a significant difference.

RESULTS

General findings

The desired location for spinal injection was easily determined in all chickens, and anesthesia was successfully performed. Clinical signs of adverse side effects, including central nervous system stimulation, mucus cyanosis, and loss of consciousness were not observed at the drug doses used in any of the chickens. During the study, no abnormalities were observed in the skin over the injection site. Four cases (50%) in the B0.5 group experienced ventral recumbency during the anesthesia period, an indication that the locomotor nerves of the feet were affected. Ventral recumbency was first detected in the B0.5 group shortly after sensory loss and was present for 50–60 minutes. All chickens that experienced ventral recumbency stood on their feet once the anesthetic effect was no longer present. No mortality was observed in any bird within any group of this study.

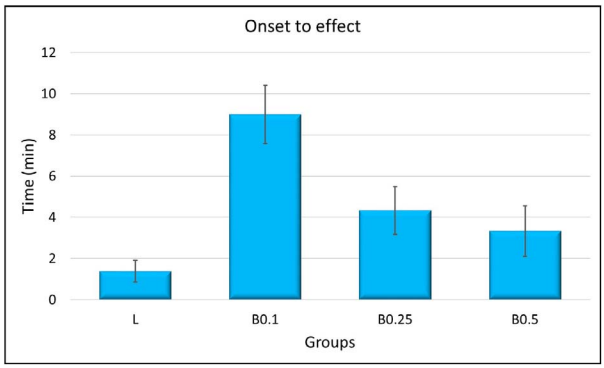

Figure 1. Onset to effect of lidocaine and bupivacaine for spinal anesthesia administered by caudal spinal route (mean ± SD) in 32, 8-week-old, female Ross broiler chickens randomly divided into 4 groups of 8 as follows: 2 mg/kg lidocaine (L), 0.1 mg/kg bupivacaine (B0.1), 0.25 mg/kg bupivacaine (B0.25), and 0.5 mg/kg bupivacaine (B0.5). Generally, the onset to effect of all 3 bupivacaine doses was significantly delayed compared with the effective onset of lidocaine. That time was also significantly different between B0.1 when compared with B0.25 and B0.5 groups ($P < .001$).

Onset to effect and duration of action

Generally, the onset to effect of all 3 bupivacaine doses was significantly delayed compared with the effective onset of lidocaine (1.37 ± 0.52 minutes) (Fig 1). That time was also significantly different between the B0.1 (9 ± 1.41 minutes) and the B0.25 (4.33 ± 1.15 minutes) and B0.5 (3.33 ± 1.23 minutes) groups ($P < .001$).

Bupivacaine at the dose of 0.5 mg/kg (B0.5) (54 ± 6.08 minutes) had a statistically significant difference in the duration of action compared with that of all other groups (17.87 ± 3.18 minutes for L, 11 ± 1.41 minutes for B0.1, and 18 ± 4.36 minutes for B0.25), which resulted in a longer anesthetic event ($P < .001$) (Fig 2).

Changes in cloacal temperature and respiratory rate

The change of cloacal temperatures at all time points among all groups was statistically significant compared with baseline values, except in group B0.1. In general, the spinal injection of the anesthetic agents in all groups, except group B0.1, decreased the cloacal temperature over time (Table 1).

The changes in the respiratory rate between the time of the spinal anesthetic injection and the restoration of sensation in the area of influence are

Table 1. Cloacal temperature changes in °C (°F) presented as mean ± SD from the time after the injection of lidocaine and bupivacaine into the spinal canal of the broiler chickens until initial response to external stimuli, as described in Figure 1. In general, the spinal injection of the anesthetic agents in all groups, except group B0.1, decreased the cloacal temperature over time.

	Time, min		
Groups	0	10	20
L	41.79 ± 0.18 (107.22 ± 0.32)	41.17 ± 0.14 (106.11 ± 0.25)	41.19 ± 0.08 (106.14 ± 0.15)
B0.1	41.25 ± 0.07 (106.25 ± 0.13)	41.25 ± 0.07 (106.25 ± 0.13)	41.25 ± 0.21 (106.25 ± 0.38)
B0.25	41.56 ± 0.40 (106.81 ± 0.73)	41.20 ± 0.20 (106.16 ± 0.36)	41.20 ± 0.20 (106.16 ± 0.36)
B0.5	41.43 ± 0.35 (106.57 ± 0.63)	41.30 ± 0.26 (106.34 ± 0.47)	41.13 ± 0.31 (106.03 ± 0.55)

Abbreviations: L, lidocaine at 2 mg/kg; B0.1, bupivacaine at 0.1 mg/kg; B0.25, bupivacaine at 0.25 mg/kg; B0.5, bupivacaine at 0.5 mg/kg.

Table 1. Extended.

	Time, min			
Groups	30	40	50	60
L	41.34 ± 0.12 (106.41 ± 0.21)	—	—	—
B0.1	—	—	—	—
B0.25	40.90 ± 0.17 (105.62 ± 0.31)	—	—	—
B0.5	40.97 ± 0.37 (105.75 ± 0.66)	40.97 ± 0.37 (105.75 ± 0.66)	41.00 ± 0.34 (105.80 ± 0.61)	41.20 ± 0.20 (106.16 ± 0.36)

shown in Table 2. In the lidocaine group, the respiratory rate significantly increased after 20 minutes. Conversely, in the B0.25 and B0.5 groups, there was a downward trend in the respiratory rates; however, those changes were not statistically significant.

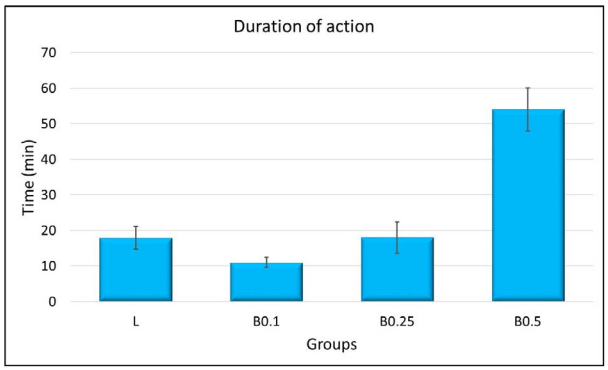

Figure 2. Duration of action of the drugs and chickens as described in Figure 1 (mean ± SD) of 2 mg/kg lidocaine (L), 0.1 mg/kg bupivacaine (B0.1), 0.25 mg/kg bupivacaine (B0.25), and 0.5 mg/kg bupivacaine (B0.5). Bupivacaine at the dose of 0.5 mg/kg (B0.5) had a statistically significant difference in the duration of action against all other groups and resulted in a longer anesthetic event ($P < .001$).

DISCUSSION

Because of reluctance to use local anesthetic agents in poultry, there is little information regarding their use in these avian species.[12] In a few published studies on birds, lidocaine and bupivacaine have been investigated for possible use as local or regional anesthetic agents.[13,14] A brachial plexus nerve block was performed in adult female mallard ducks (*Anas platyrhynchos*) with a combination of lidocaine (15 mg/kg) and epinephrine (3.8 μg/kg) or bupivacaine (2–8 mg/kg).[13] However, variable results were obtained, indicating that the local anesthetics used, their concentration, or volume were not effective in producing local anesthesia.[13] In a similar study with chickens, the results were also disappointing because the drugs had a high failure rate in local anesthetic effect.[14] In addition, intra-articular administration of bupivacaine in chickens at doses of 2.7 to 3.3 mg/kg resulted in adverse side effects, recumbency, abnormal standing, and distress.[15] Others have

Table 2. Respiratory rate changes in breaths per minute presented as mean ± SD from the time after the injection of lidocaine and bupivacaine into the spinal canal of the broiler chickens until initial response to external stimuli, as described in Figure 1. In the lidocaine group, the respiratory rate significantly increased after 20 minutes ($P < .001$). Conversely, in the B0.25 and B0.5 groups, there was a downward trend to their respiratory rate; however, these changes were not statistically significant.

	Time, min						
Groups	0	10	20	30	40	50	60
L	42.38 ± 5.40	44.00 ± 4.96	43.38 ± 5.83	52.37 ± 1.59	—	—	—
B0.1	33.00 ± 4.24	35.50 ± 0.70	35.50 ± 0.70	—	—	—	—
B0.25	38.67 ± 9.02	38.33 ± 9.07	38.00 ± 8.89	35.33 ± 7.58	—	—	—
B0.5	44.00 ± 5.29	40.00 ± 6.00	38.00 ± 8.54	36.67 ± 8.26	36.00 ± 9.17	35.33 ± 7.02	34.67 ± 7.02

Abbreviations: L, lidocaine at 2 mg/kg; B0.1, bupivacaine at 0.1 mg/kg; B0.25, bupivacaine at 0.25 mg/kg; B0.5, bupivacaine at 0.5 mg/kg.

used subcutaneous bupivacaine at doses of 2–10 mg/kg in male spectacled eiders (*Somateria fischeri*) and king eiders (*Somateria spectabilis*).[16] The investigation by Brandão et al[17] suggests that, despite the fact that 4 mg/kg of lidocaine is proposed by some reports as the maximum usable dose in chicken, intravenous (IV) injection of 6 mg/kg of lidocaine is well tolerated by the chicken and is not associated with adverse cardiovascular effects. A more recent study by DiGeronimo et al[18] determined that 1.94 mg/kg is the IV effective dose for 50% of the study population (ED_{50}) of bupivacaine in broiler chicken. In contrast, the ED_{50} of IV lidocaine was approximately 3 times greater than that of IV bupivacaine. In this study, lidocaine was injected at a dose of 2 mg/kg, based on the previous study,[4] and bupivacaine at doses of 0.1, 0.25, and 0.5 mg/kg. The convulsive dose of IV lidocaine in chickens has been reported to be 30.52 ± 5.15 mg/kg, which is close to a lethal dose.[19] Based on the information above, all injections in this study were under lethal doses.

Although measuring physiological parameters for nociception is not always consistent and useful in birds, withdrawal behaviors in response to noxious stimuli, including escape reactions, noise, reduced head movements, or vigorous jumping are considered more reliable, and were used in this study.[20] Sedation was not performed in this study to investigate the effects of the anesthetic agents alone because sedated birds may not show an obvious withdrawal response to the painful external stimuli. However, sedation is recommended before local anesthetic administration to minimize stress. Stress causes catecholamine and corticosteroid elevation, as well as behavioral changes in birds.[21,22] Currently, sedation through the intranasal or intramuscular administration of midazolam is widely used for avian patients. Intranasal midazolam or diazepam can provide adequate sedation for diagnostic and minor therapeutic procedures in choughs (*Pyrrhocorax pyrrhocorax*).[23] When administered to pigeons (*Columbia livia*), a midazolam-dexmedetomidine combination resulted in effective immobilization.[24]

The anesthetic drug of choice to be given by spinal injection should have a faster effective onset, a longer duration of action, and provide appropriate analgesia and muscle relaxation. Lidocaine is the most common anesthetic drug administered by spinal injection in animals, and although it has a rapid onset, its usefulness in long-term surgeries is limited. Moreover, there are concerns regarding the development of transient neurologic clinical signs.[25] In contrast, bupivacaine has a longer duration of action but a slower effective onset and produces poor muscle relaxation.[5] The ultimate effect of an injectable anesthetic agent is not only related to its solubility in fat but also to its physicochemical properties, such as the acid dissociation constant, the pH of the solution and tissue, and the ability to bind to proteins. The infiltration of lidocaine and bupivacaine into tissue has been reported to be similar, despite differences in fat solubility, and the onset of action of the 2 drugs in the motor nerves is similar, approximately 3 to 4 minutes.[26] Nevertheless, as previously stated, the maximum time to effect of bupivacaine was clinically slower, and this was verified in a low-dose study that investigated its use as a spinal anesthetic agent in humans.[27,28] The onset to effect of bupivacaine is also dependent on concentration.[26] In this study, the onset to effect was statistically significant only in group B0.1, which was the lowest dose and concentration of bupivacaine. According to Covino,[29] the difference in the onset to effect of various anesthetics, when administered epidurally, is reduced compared with that of local administration. Therefore, it can be concluded

that, if a proper dose of bupivacaine is used, the onset to effect will not be a limitation.

Combinations of short (or medium) and long-acting local anesthetics are sometimes used in peripheral nerve blocks to get both faster time to effect and longer duration of action. Some studies have shown that the combined use of local anesthetic drugs in this way may only reduce the onset to effect whereas the duration of action may be decreased compared with the use of bupivacaine alone.[30,31] In that regard, the combination of lidocaine and bupivacaine for spinal anesthesia in chickens should be reconsidered because the observed delayed onset to effect for bupivacaine in this study was insufficient for adverse reactions to occur in a clinical setting.

The duration of action depends on the local anesthetic agent's ability to bind protein. Local anesthetic drugs (eg, lidocaine and mepivacaine), with lower binding abilities (65%–75%), have a duration of action of about 1.5–4 hours. Bupivacaine and ropivacaine have high protein binding (99%), thus a longer duration of action of approximately 3–6 hours.[32] In the present study, the duration of action of bupivacaine was directly dose related. Bupivacaine administered at a dose of 0.5 mg/kg (B0.5) significantly induced a longer duration of anesthesia than the other groups evaluated.

Drugs used for local anesthesia can affect the sensory, motor, and sympathetic nerves; therefore, hypotension and foot weakness may be caused by spinal anesthesia.[33,34] Temporary paralysis of the hindlimbs in large animals can be an unintended consequence of the use of local anesthetic agents. Half of the chickens in group B0.5 became ventrally recumbent. If the animal is unable to stand and remains in ventral recumbency, it may indicate an effect of the anesthetic on the locomotor nerves, most notably, the ischiadic nerve, which is within the chicken sacral plexus.[35,36]

In the present study, after the spinal injection of the anesthetic drug, the cloacal temperature decreased over time. Reports emphasize that spinal anesthesia has a physiological effect on body temperature and increases the risk of hypothermia.[37] In the caudal aspect of the anesthetized area, the vasomotor tone and body shivering cease with sympathetic and somatic nerve blocking, respectively. Shivering is one of the physiological mechanisms to counteract hypothermia. Therefore, the risk of hypothermia increases when a higher dose and volume of anesthetic drug is injected for spinal anesthesia because it spreads further in the spinal canal and affects more spinal nerve roots. In a study on human patients, for each dermatome that was anesthetized, the body temperature dropped 0.15°C (0.27°F).[38,39] The lack of change in cloacal temperature in the B0.1 group may be due to the anesthetic effective onset in that group being significantly longer than other groups and thus having no influence on physiological parameters (eg cloacal temperature); therefore, this finding is consistent with the results of the onset to effect. Nevertheless, further studies are required to determine whether the body core temperature also decreases during spinal anesthesia in birds. Because of the lack of a negative control group in this study, it cannot be excluded that there was a decrease in core body temperature because a decrease in regional temperature may have been the result of cloacal sphincter relaxation.

Respiratory rate changes after the spinal injection of the anesthetic agent in the L and B0.1 groups increased during the first 10 minutes, but in the B0.25 and B0.5 groups, there was a downward trend of the respiratory rate. An increased respiratory rate can be an indication of incomplete anesthesia in which the external stimuli lead to pain and increased respiratory rate without any obvious behavioral reflex. In fact, respiratory and hemodynamic impairment are among the complications when more spinal nerves are affected by high doses of the anesthetic drugs.[39]

One of the major limitations of this study was the lack of a cardiovascular assessment. This was due to the lack of access to monitoring devices suitable for domestic chickens at the time of study. Bradycardia is the main cardiovascular effect of bupivacaine-induced spinal anesthesia in dogs with hypotension being another sequela.[40] Restraining chickens results in significant changes to the heart rate, and the measured rates can mislead the researcher in attributing those changes to the physiologic effects of the anesthetic agent.

The results of this study showed that subarachnoid injection of 2 mg/kg lidocaine or 0.5 mg/kg bupivacaine produced effective anesthesia in the caudal coelomic area of chickens for approximately 20 and 55 minutes, respectively. In addition, there is a significant difference between both drugs when the anesthetic effect is initiated. Depending on the surgical procedure required, these anesthetic drugs at the doses found to be effective in this study, can be used for short- or long-term anesthesia in chickens and possibly other avian species after further research investigations.

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