

Hypersensitivity in Chicken (*Gallus gallus domesticus*) due to the Association of Lidocaine and Bupivacaine in Neural-Guided Femoral and Sciatic Nerve Block

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ABSTRACT

Background: Osteosyntheses, orthopedic surgeries that cause highly painful stimulation, are increasingly common in veterinary medicine. Epidural anesthesia is used to provide intraoperative and postoperative analgesia in mammals undergoing pelvic limb surgery. In birds, the synsacrum, the bone originating from the fusion of the lumbar and sacral vertebrae, makes this route inapplicable, thus peripheral nerve block is an easier option in this species. This report describes a case of local hypersensitivity following the association of lidocaine and bupivacaine in anesthetic blocks of the femoral and sciatic nerves in chickens (*Gallus gallus domesticus*).

Case: A study was conducted in chickens evaluating the effectiveness of anesthetic sciatic and femoral nerve blocks, guided by a neural stimulator. Thirty-two 42-day-old male chickens of the species *Gallus gallus domesticus*, double breasted, weighing 1.86 ± 0.5 kg, were randomly divided into four groups: control (CG), lidocaine (LG), bupivacaine (BC) and the association of lidocaine and bupivacaine (LBG). The doses used were 4 mg/kg of 2% lidocaine and 2 mg/kg of 0.5% bupivacaine, without vasoconstrictor. For CG, 0.9% NaCl solution was used, respecting the total volume of 1 mL/kg. Only one bird from the LBG showed side effects, presenting sensory and motor loss for 24 h after the administration of these drugs, before euthanasia was performed using anesthetic induction with isoflurane through a face mask, followed by the intravenous administration of propofol and then potassium chloride. The chicken was submitted to a necropsy and macroscopically, soft, irregular, brownish lesions with a grayish focus were observed, indicating areas of necrosis in the muscles adjacent to the femoral and sciatic nerves. Histopathological examination showed mild, active inflammatory migration with perivascular organization, highlighting the presence of lymphocytes, plasmacytes, segmented heterophiles, and areas of hemorrhagic foci. The pairs of nerves evaluated showed edematous areas, but no inflammatory infiltrate, a histopathological finding that is considered to be nonspecific.

Discussion: In the case of the chicken with side effects, histopathological examination showed vasculitis and hemorrhagic areas, which were correlated with ischemia and focal tissue necrosis, together with edematous lesions in the nerves evaluated, and extremities that showed an inflammatory response. These changes are related to acute hypersensitivity lesions, the drug response and drug hypersensitivity. Local anesthetics have been widely used in birds, but there are reports of reactions, including neurotoxicity and local myotoxicity, and bupivacaine is the drug that shows the highest cytotoxicity. However, long-term, repeated applications of bupivacaine on the sciatic nerve do not induce degenerative neural lesions in rats, rabbits, and dogs. The reactions described here are proportional to the concentration of the anesthetic injected, and in the case reported, the recommended dose for birds of 4 mg/kg of 2% lidocaine and 2 mg/kg of 0.5% bupivacaine, without vasoconstrictor, was adhered to. These findings suggest a reaction specific to the bird described; however, further studies regarding the local adverse effects of these anesthetics in birds should be conducted to make the practice of peripheral nerve block safer by testing different concentrations, associations and doses of the variety of drugs available.

Keywords: birds, local block, drug hypersensitivity.

DOI: 10.22456/1679-9216.109636

Received: 12 December 2020

Accepted: 22 March 2021

Published: 24 May 2021

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INTRODUCTION

The recent introduction of exotic and wild bird species as companion animals and the consequent increase in interest in the legal breeding and commercialization of captive animals is of clinical interest. Veterinarians need to accompany this trend, improving their knowledge and care practices related to these animals, particularly regarding their physiology and behavior, which is very different from their usual patients [12].

Osteosyntheses are surgeries that cause highly painful stimulation and are increasingly common in veterinary medicine, corresponding to about 30% of consultations related to birds [2]. Epidural anesthesia between the L7 and S1 vertebrae is used to provide intraoperative and postoperative analgesia in mammals undergoing pelvic limb surgery [4]; however, birds have the synsacrum, a fusion of lumbar and sacral vertebrae, which makes it impossible to use this technique. An alternative adopted for pelvic limb surgery in birds is the association of general anesthesia with femoral and sciatic nerve block [11].

Although simple, low cost and requiring minimal equipment, this technique still raises questions regarding possible adverse effects, the drugs of choice, their doses, and the duration of neural block. Therefore, the purpose of this study was to describe a case of local hypersensitivity following the association of lidocaine and bupivacaine in anesthetic block of the femoral and sciatic nerves in a chicken (*Gallus gallus domesticus*).

CASE

An essay evaluation was developed for studying the effectiveness and duration of sciatic and femoral nerve block, guided by neurostimulator, in chickens (*G. domesticus*) anesthetized with isoflurane.

Thirty-two 42-day-old, double-breasted male chickens of the species *G. domesticus*, weighing $1.86 \pm 0.5\text{kg}$, were divided into four groups: Control group (CG): 1 mL/kg of physiological solution¹ [2]; lidocaine group (LG): 4 mg/kg of lidocaine² [3]; bupivacaine group (BG): 2 mg/kg of bupivacaine³ [4] and the association of lidocaine and bupivacaine group (LBG): 4 mg/kg of lidocaine plus 2 mg/kg of bupivacaine [6].

After anesthetic induction with isoflurane⁴, each chicken was placed in the lateral position. The feathers at the application site were removed and the skin was cleaned with 70% alcohol. The positive pole of the neurolocator⁵ [6] was placed 10 cm away,

cranially to the needle insertion site⁶ [7], the current was adjusted to 1.0 mA, for 0.1 ms, at a frequency of 1 Hz. To confirm the injection site, contractions of the quadriceps femoris muscle and knee extension were observed for the femoral nerve, and contraction of the caudal muscles of the thigh were observed for the sciatic nerve. The current was then adjusted to 0.4 mA, if the contractions continued, this indicated the correct location of the nerves, and the anesthetic was applied. Next, isoflurane administration was stopped, and the chicken was placed in a comfortable position when it awoke.

After awakening, the chickens were monitored for up to 2 h, evaluating sensory and motor stimuli. All the birds recovered limb reflexes after a few minutes. Only one chicken, assigned to the LBG, lost all sensory and motor response when it awoke and remained so for the following 24 h. During this period, the bird was kept in a cage with water and food available. It was then euthanized by anesthetic induction with isoflurane using a face mask, followed by intravenous administration of propofol⁷ [8] and, subsequently, potassium chloride⁸ [9]. The chicken was sent to necropsy, which included collecting samples for histopathological evaluation.

During necropsy, hematoma was observed in the pectoral muscle, caused by sternal decubitus positioning for many hours, in addition to soft, irregular brownish lesions with a grayish focus, indicating areas of necrosis in the muscles adjacent to the femoral and sciatic nerves. Histopathological examination showed mild active inflammatory migration with perivascular organization, highlighting the presence of lymphocytes, plasmocytes, segmented heterophiles, and areas of hemorrhagic foci, in addition to acute myositis and hemorrhagic traces. The pairs of nerves evaluated showed edematous areas, but no inflammatory infiltrate, a histopathological finding that is considered to be nonspecific (Figure 1).

DISCUSSION

The femoral and sciatic nerves are responsible for sensory and motor innervation of the pelvic limb in birds, and their anesthetic block is very useful in surgeries on these limbs. The use of local anesthetics in birds is common practice due to their ease of use, the absence of environmental pollution, and specific equipment is not required [8]. Regarding the chicken in the case reported here, the technique described for dogs and adapted for birds of prey [3] was used to block the femoral and sciatic nerves.

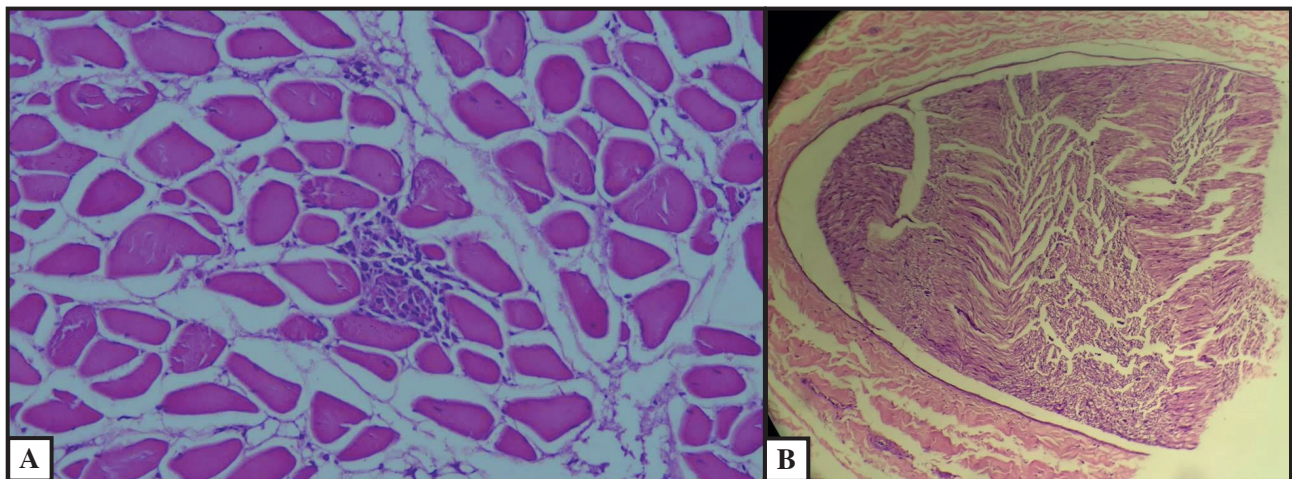


Figure 1. A- Acute myositis characterized by the presence of a discrete inflammatory infiltrate in non-necrotic muscle fibers [10x]. B- Nerve fiber showing an edematous area, unaffected by inflammatory infiltrate [20x] from the co-infected animal. The left arrow indicates macrophage aggregation and the right arrow indicates neutrophilic inflammation.

The adverse effects and local toxicity induced by these drugs in birds are not yet well defined, such that dose and concentration are the primary factors used to avoid side effects. The dose used in the case described was that recommended for birds, 4 mg/kg of 2% lidocaine and 2 mg/kg of 0.5% bupivacaine [6].

Local anesthetics have been used in these species, with unfortunate consequences, including convulsions and cardiac arrest due to overdoses [6]. In the case described, no systemic changes were observed, only local changes in the limb where the drugs were administered.

Cases of neurotoxicity and local myotoxicity have been described due to activation of caspases, mainly caused by bupivacaine, such that it is considered the local anesthetic that presents the highest cytotoxicity to neural cells [10]. The microscopy of case described here showed acute myositis, hemorrhagic traces and fibrinoid foci in the interstitial region. Inflammatory migration with perivascular organization was observed, with the presence of lymphocytes and plasma cells, indicating low cellularity vasculitis. There are reports that a dose of 0.5% bupivacaine alone, applied to the gracilis muscle of rats, was sufficient to cause the destruction of muscle fibers, 15 min after application [11].

The myotoxicity reported is proportional to the concentration of the anesthetic injected and is related to the deregulation of the intracellular calcium concentration and/or changes in mitochondrial bioenergetics [6]. Again, in a study conducted on pigs, bupivacaine appears to be more toxic than other local

agents because it caused irreversible musculoskeletal damage characterized by calcified myonecrosis [13].

Although this is a rare reaction, the exposure of peripheral nerves to local anesthetics can cause direct damage, leading to the inhibition of rapid axon transport, rupture of the blood-nerve barrier, decreased nerve blood flow with associated ischemia and disorganized cell membrane integrity [5]. Microscopic examination showed the nerves had edematous areas, but were not affected by inflammatory cells, indicating minimal damage to the nerves evaluated.

Administration of drugs was performed with the aid of a neurolocalizer after identifying the anatomical landmarks and muscle contraction responses produced in reaction to the electrical stimulation. The use of this equipment is important as it promotes greater safety and efficiency compared with the palpation method [9]. The use of this method rules out possible technical errors during the application of anesthetics.

Only one among 32 birds used in the experiment, showed local hypersensitivity following the association of lidocaine and bupivacaine in anesthetic blocks of the femoral and sciatic nerves. This fact suggests a reaction specific to this chicken; however, further studies regarding the local adverse effects of these anesthetics in birds should be conducted, to make the practice of peripheral nerve block safer.

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Ethical approval. This research was approved by the Animal Ethics Committee (CEUA) of the Centro Universitário Católica do Tocantins (UniCatólica), under protocol no. 002/2019.

Declaration of interest. The authors report no conflicts of Interest. The authors alone are responsible for the content and Writing of paper.

REFERENCES

- 1 **Benoit P.W. & Belt W.D. 1970.** Destruction and regeneration of skeletal muscle after treatment with a local anaesthetic, bupivacaine (Marcaine®). *Journal of Anatomy*. 107(3): 547-556.
- 2 **Castro P.F., Fantoni D.T. & Matera J.M. 2013.** Estudo retrospectivo de afecções cirúrgicas em aves. *Pesquisa Veterinária Brasileira*. 33(5): 662-668.
- 3 **d'Ovidio D., Rota S., Noviello E., Briganti A. & Adami C. 2014.** Nerve stimulator-guided sciatic-femoral block in pet rabbits (*Oryctolagus cuniculus*) undergoing hind limb surgery: a case series. *Journal of Exotic Pet Medicine*. 23(1): 91-95.
- 4 **Gaynor J.S. 1999.** Is postoperative pain management important in dogs and cats? *Veterinary Medicine*. 94(3): 254-257.
- 5 **Kalichman M.W. 1993.** Physiologic mechanisms by which local anesthetics may cause injury to nerve and spinal cord. *Regional Anesthesia*. 18(6): 448-452.
- 6 **Ludders J.W. 2017.** Anestesia e Analgesia Comparada de Aves. In: Tranquilli W.J., Thurmon J.C. & Grimm K.A. (Eds). *Lumb and Jones' Veterinary Anesthesia and Analgesia*. 5.ed. São Paulo: Roca, pp.2339-2385.
- 7 **Mahler S.P. & Adogwa A.O. 2008.** Anatomical and experimental studies of brachial plexus, sciatic, and femoral nerve-location using peripheral nerve stimulation in the dog. *Veterinary Anaesthesia and Analgesia*. 35(1): 80-89.
- 8 **Massone F. 2003.** Anestesia local. In: *Anestesiologia Veterinária - Farmacologia e Técnicas*. 4.ed. Rio de Janeiro: Guanabara Koogan, pp.31-45.
- 9 **Nascimento F.M., Nunes T.L., Souza T.B.S., Andrade M.A.C. & Barbosa V.F. 2019.** Brachial Plexus Block with Use of a Neurostimulator in a Striped owl (*Asio clamator*) Undergoing Wing Amputation. *Acta Scientiae Veterinariae*. 47(Suppl 1): 361.
- 10 **Perez-Castro R., Patel S., Garavito-Aguilar Z.V., Rosenberg A., Recio-Pinto E., Zhang J., Blanck T.J.J. & Xu F. 2009.** Cytotoxicity of local anesthetics in human neuronal cells. *Anesthesia and analgesia*. 108(3): 997-1007.
- 11 **Soresini G.C.G., Pimpão C.T. & Vilani R.G.D.C. 2013.** Brachial plexus block in birds. *Revista Acadêmica: Ciências Agrárias e Ambientais*. 11(1): 17-26.
- 12 **Werther K.** Semiologia de Animais Silvestres. In: Feitosa F.L.F. (Ed). *Semiologia Veterinária*. São Paulo: Roca, pp.733-740.
- 13 **Zink W., Bohl J.R.E., Hacke N., Sinner B., Martin E. & Graf B.M. 2005.** The long term myotoxic effects of bupivacaine and ropivacaine after continuous peripheral nerve blocks. *Anesthesia and analgesia*. 101(2): 548-554.