Inadvertent injection of medetomidine in the *cerebromedullaris cisterna* of a dog during myelographic exam

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Versehentliche Medetomidin Injektion in die Cisterna cerebromedullaris während der myelographischen Untersuchung bei einem Hund

Ein Mischlingshund wurde zur Abklärung von akut auftretenden Nackenschmerzen für die diagnostische Myelographie anästhesiert. Aufgrund eines menschlichen Fehlers wurde anstelle des Kontrastmittels versehentlich 444 µg/kg Medetomidin in die *Cisterna cerebromedullaris* injiziert. Unmittelbar nach der Injektion wurden schwere Bradykardie, kein peripherer Puls, Atemstillstand und Verlust der Pupillar-, Palpebral- und Kornealreflexe beobachtet. Zwanzig Minuten nach der Medetomidin-Injektion entwickelte der Hund eine Hypothermie mit einer Ösophagustemperatur von 33 °C. Es wurde 1 mg/kg Atipamezol intramuskulär verabreicht, gefolgt von einer intravenösen Injektion von 0,5 mg/kg 20 min danach. Die kardiorespiratorischen Parameter und die Körpertemperatur wurden überwacht und eine unterstützende Therapie (Beatmung, Erwärmung und 5 µg/kg/min Dopamin iv) eingeleitet. Der klinische Zustand des Hundes verbesserte sich innerhalb einer Stunde und das Vorliegen von Spontanatmung, Korneal- und Schluckreflex erlaubten die Extubation. Fünf Tage später konnte der Hund klinisch gesund aus Spitalpflege entlassen werden.

Menschliches Versagen und Ablenkung führten zu einer lebensbedrohlichen Komplikation im vorliegenden Fall und hätten möglicherweise durch die Verwendung von Checklisten, klaren Abläufen und Verantwortlichkeiten des beteiligten Personals verhindert werden können. Die intrazisternale Injektion von Medetomidin verursachte eine kardiovaskuläre, respiratorische und thermoregulatorische Depression, die mittels parenteraler Verabreichung des Antagonisten und einer unterstützende Intensivbehandlung behoben werden konnte.

Schlüsselwörter: menschliches Versagen, intrazisternale Injektion, Medetomidin, perianästhetische Morbidität

Summary

A mixed breed dog was anesthetized for diagnostic myelography to investigate acute onset neck pain. Instead of contrast medium, 444 µg/kg medetomidine were inadvertently injected into the *cerebromedullaris cisterna* owing to a human error. Severe bradycardia, undetectable peripheral pulse, respiratory arrest and loss of pupillary, palpebral and corneal reflexes were observed immediately after injection. Profound hypothermia developed and esophageal temperature, measured 20 minutes after medetomidine injection, was 33 °C. Atipamezole at 1 mg/kg im was administered, followed by a second dose of 0,5 mg/kg iv 20 minutes thereafter. In the meantime, cardiorespiratory parameters and body temperature were monitored, and supportive care that included manually assisted pulmonary ventilation, active warming, and administration of 5 µg/kg/min dopamine was initiated. The dog's clinical condition improved within one hour from the beginning of supportive care, at which time ocular reflexes and swallowing returned, spontaneous ventilation was deemed as adequate and the trachea could be extubated. The dog was discharged in good clinical conditions five days later.

Human error and distraction led to a potentially life-threatening complication in the dog of this report and could have possibly been prevented with the use of checklists and with a clearer definition of roles and responsibilities of the personnel involved prior to commencing the clinical procedure. Profound cardiovascular, respiratory, and thermoregulatory depression caused by intracisternal injection of medetomidine responded to parenteral administration of its antagonist and supportive care.

Key words: human error, intracisternal injection, medetomidine, perianesthetic morbidity

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Introduction

The authors describe the accidental injection of a sedative agent, inadvertently mixed up with contrast medium, into the *cerebromedullaris cisterna* of a dog during myelography. This complication resulted from a human error and could have been prevented with the use of measures aimed at improving patient safety in the hospital.

Human errors, defined as a deviation from intention, expectation, or desirability, have been identified as the primary cause of 51–77% of anesthesia-related deaths in humans.[1–2] Human errors have been investigated extensively in human patients but very little in veterinary medicine; however, it is hypothesized that they could play a similar role with respect to peri-anesthetic morbidity and mortality.[3–5]

The development and refinement of safety measures aimed to minimize human errors, and therefore improve patient outcome, are raising increasing interest in veterinary medicine; this topic could be object of further future investigations.

Case report

A 6-year-old, female mixed breed dog weighing 4,5 kg was referred to the Teaching Hospital of the Faculty of Veterinary Medicine of the University of Perugia (Italy) for diagnostic investigation of neck pain. Medical history included recent onset stiffness in the neck and back and reluctance to walk. Blood results were unremarkable. Neurological examination revealed pain upon flexion/extension of the neck, but normal spinal nerve reflexes, proprioception, and cranial nerve function. The dog was scheduled for diagnostic myelography following injection of contrast medium into the *cerebromedullaris cisterna* under general anesthesia.

At preanesthetic exam, heart rate (HR) was 100 beats/minute and respiratory rate (RR) rate 9 breaths/minute; chest auscultation was unremarkable. Rectal temperature was 39 °C. After premedication with butorphanol (0,3 mg/kg im, Dolorex; MSD Animal Health, Milan, Italy) and midazolam (0,4 mg/kg im, Midazolam IBI; Giovanni Lorenzini, Aprilia, Italy), general anesthesia was induced with thiopental (8 mg/kg iv, Pentothal Sodium; Hospira, Liscate, Italy), and maintained with isoflurane (Vetflurane; Virbac, Milan, Italy) in oxygen, following tracheal intubation. Clinical monitoring during anesthesia consisted of femoral pulse assessments by palpation every 5 minutes, continuous heart auscultation with an esophageal stethoscope and visual assessment of breathing function.

After aseptic preparation of the cervical area, a 22-gauge, 5-cm spinal needle (Becton Dickinson; San Agustin de Guadalix, Madrid, Spain) was inserted between the base of the skull and the first cervical vertebra, into the *cerebromedullaris cisterna*. Correct needle placement was confirmed by observation of cerebrospinal fluid flowing from the needle hub. At the time of contrast injection, a vial containing medetomidine (Domitor®; Pfizer, Rome, Italy) that had been accidentally put in the tray with the contrast medium was inadvertently presented by the technician to the neurologist. Without checking the vial, the neurologist drew up 2 ml of medetomidine instead of contrast medium and injected it into the *cerebromedullaris cisterna*. Immediate onset apnoea, centralization of the eye globe, mydriasis, loss of photopupillary, palpebral and corneal reflexes, and sudden decrease in HR (from 100 to 25 beats/minute) were observed; femoral pulse could no longer be detected with palpation. Isoflurane was immediately discontinued, and atipamezole (1 mg/kg im, Atipam; Dechra, Turin, Italy) was administered, calculated based on the amount of medetomidine given (444 µg/kg). The dog was then transferred to a room where instrumental monitoring and assistance were available, connected to an anesthetic machine (Dräger SA1; Draeger, Milan, Italy) used to deliver 100% oxygen through a non-rebreathing system and instrumented with a multiparametric monitor (GT9003E; Guoteng Science & Technology Development, Zhuhai, China). Monitoring consisted of electrocardiography, non-invasive arterial blood pressure (ABP) measurement via oscillometry (cuff size: 2), pulse oximetry, capnography and continuous esophageal temperature measurement. Heart frequency markedly improved five minutes after atipamezole administration (from 25 to 82 beats/minute). Manual ventilation was performed at 15 breaths/min to maintain the end-tidal carbon dioxide tension ($EtCO_2$) at 35–45 mmHg for 15 minutes, after which the dog started to breathe spontaneously. During spontaneous breathing, hypocapnia occurred ($EtCO_2$ range: 24 –29 mmHg), with RR ranging from 12 to 14 breaths/minute. However, owing to persistent absence of palpable femoral pulse and ocular reflexes, and inability to obtain pulse oximetry, temperature and ABP readings, 20 min after the first dose atipamezole was repeated as a bolus at 0,5 mg/kg iv. One minute later, a pulse waveform detected by pulse oximetry was displayed on the monitor screen. At this time, peripheral arterial oxygen saturation (SpO_2) was 95% and pulse frequency and HR were the same (128 beats/min); APB reading (SAP/DAP) was 118/72 mmHg, with a mean arterial pressure (MAP) of 82 mmHg. A first esophageal temperature reading revealed profound hy-

pothermia (33 °C). Five minutes later, a Cushing reflex was suspected based on increase in ABP (systolic arterial pressure/diastolic arterial pressure (SAP/DAP): 142/90 mmHg; MAP:109 mmHg) and concomitant decrease in HR from 120 to 69 beats/minute, and treated with mannitol (1 g/kg iv over 40 min). During mannitol infusion, frequent changes in ABP (SAP range: 78–142 mmHg; MAP range: 48–109 mmHg; DAP range: 57–92 mmHg) and HR (range: 59–81 beats/minute), together with I and II atrio-ventricular blocks, were observed; capnography revealed hypocapnia ($EtCO_2$ range: 24–29 mmHg) and esophageal temperature further decreased to 32,7 °C. At this point, arterial blood gas analysis (i-STAT; Abbott, Assago, Italy) confirmed mild respiratory alkalosis (pH: 7,43; arterial partial pressure of carbon dioxide: 33,9 mmHg, arterial partial pressure of oxygen: 568 mmHg, HCO_3-: 23,7 mmol/l).

One hour after the beginning of supportive care, photopupillary, corneal and palpebral reflexes returned, followed by increased muscular tone and swallowing; at this point, the trachea was extubated and oxygen supplemented via flow-by (2 l/min). Active warming was provided via an electric heating pad (Safety; Bovisio Masciago, Italy) and HR and ABP were continuously monitored. Rectal temperature was 33,7 °C after extubation. Hypotension (SAP/DAP: 78/48 mmHg; MAP: 44 mmHg) was detected during extubation, and treated with a dopamine infusion (5 µg/kg/min iv, Reviva; AstraZeneca, Basiglio, Italy), which effectively improved ABP (SAP/DAP: 87/67 mmHg; MAP: 78 mmHg) within 10 min and was discontinued after one hour owing to the development of hypertension and bradycardia. The latter persisted for approximately 3 hours after discontinuation of dopamine infusion (SAP range: 136–162 mmHg; DAP range: 108–145 mmHg; MAP range: 100–130 mmHg; HR ranges: 41–63 beats/min); thereafter, ABP and HR values returned to normal ranges for the species.

Four hours after extubation, the dog was able to maintain sternal recumbency and was responsive to vocal call and stimulation. At this time, rectal temperature was 39 °C and no abnormalities were detected during neurologic exam. Two days later, blood biochemistry and hematology results were unremarkable and the dog was anesthetized for myelography and surgical removal of a neoformation, subsequently identified as connective inflammatory tissue and C3–C4 bone metaplasia. Anesthesia was uneventful and the dog was discharged from the hospital in good clinical condition 3 days after surgery.

Discussion

Inadvertent administration of the wrong substance caused the complication described in this report. It is hypothesized that an entanglement of unfortunate circumstances resulted in failure to communicate and caused confusion with respect to roles and responsibilities. The medetomidine vial should not have been in the tray for the material needed for myelography. In addition, the two vials (contrast medium and medetomidine) were similar in size and shape, which presumably generated confusion. Moreover, the clinician relied on correct preparation and did not double check the label of the provided vial. Therefore, a chaotic working environment, a factor that is known to predisposes for human error,[1–3] led to inaccurate medication administration during the procedure.

The authors hypothesize that the complication hereby described could have been prevented with the use of a clinical checklist. In human medicine, safety checklists are increasingly being suggested as a tool to improve protocol adherence, quality of care and patient safety. Most checklists include a section dedicated to medications, equipment and material to be used, with a box for the initials of the person who performed the check, features that would have been very useful to prevent the complication described in this report. As an example, the «five rights of safe» focuses on medication administration (right patient, right medication, right dose, right route, right time).[6] Some studies showed benefits of routine use of procedural guidelines and checklists in decreasing the incidence of complications in human patients.[4,5] Recently, checklists specific for veterinary use have been developed and evaluated to improve patient perioperative safety, as well as to implement wellness in companion animal primary care.[7,8]

Another measure to improve clinical safety could have been avoiding performing procedures that carry a risk for complication in a poorly equipped room, where no means for performing monitoring and assisted ventilation were available.

Medetomidine is a potent α2-adrenoreceptor agonist commonly used as sedative agent in animals. Owing to its lipophilicity, it is rapidly absorbed after both intravenous and intramuscular injections.[9] Lumbosacral neuraxial administration of medetomidine, at doses 100 times lower than that received by the dog of this report, has also been described in animals to provide spinal analgesia mediated by the α2 adrenoreceptors located in the *substantia gelatinosa* of the dorsal horn of the spinal cord.[10–13] Delivery of α2-adrenoreceptor agonists into the *cisterna cerebellomedullaris*, however, has been reported in dogs only in the experimental setting, and at doses considerably lower then in the dog of this report.[14] Sabbe et al. described the effects of intracisternal medetomidine at 1 µg/kg, namely decreases in both HR and temperature.[14] Somnolence, antinociception

and remarkable respiratory depression were not produced, suggesting that the cardiac effects may have resulted from systemic absorption of medetomidine, rather than from its direct application in close proximity to the *medulla oblongata* and brain.[14]

Medetomidine has profound effects on cardiovascular function, mediated by both central and peripheral adrenoreceptors.[9,15] In dogs, such hemodynamic effects have been described as a biphasic blood pressure response characterized first by stimulation of the peripheral α adrenoreceptors, which results in peripheral vasoconstriction and increased ABP.[9,15] Secondary to the initial hypertension and consequent increase in vagal tone, sinus bradyarrhythmias and atrioventricular blocks can also occur. Following the initial phase, as a result of its crossing of the blood brain barrier and stimulation of the central α adrenoreceptors, medetomidine causes a decrease in sympathetic outflow with consequent central bradycardia and hypotension.[15] The cardiovascular changes that occurred in the dog of this report were biphasic, characterized by initial hypertension and bradycardia followed by hypotension, and could be interpreted as pharmacological effects of medetomidine; however, considering that atipamezole was administered immediately after the accident, a contribution of the latter to the initial hypertension cannot be excluded.

Profound initial vasoconstriction of peripheral arterial vessels could also explain the inability to detect a peripheral pulse for the first 25 minutes after inadvertent medetomidine administration. In support of this hypothesis, α2-adrenoreceptor agonists are known to affect pulse oximetry accuracy owing to powerful arterial vasoconstriction.[16]

Besides the pharmacological effects of medetomidine, bradycardia and hypertension could have occurred in the dog of this report also as a result of intrathecal volume overload during injection, which could have triggered a Cushing's reflex.[17] The Cushing's reflex is caused by increased intracranial pressure (ICP). The observed hypertension occurs to maintain brain perfusion through an increased sympathetic outflow. Increased ICP leads to respiratory depression, and the hypertension to bradycardia through the baroreceptor reflex.[16–20] Previously published literature suggests that volumes of injectate as high as that administered in this dog (0,44 ml/kg) may be sufficient to trigger a Cushing's response.[21] Moreover, subarachnoid administration of as little as 0.3 ml/kg of contrast medium resulted in increased ICP sufficient to reduce cerebral perfusion in dogs.[22] Furthermore, whilst intravenous medetomidine may cause miosis by acting on both pre- and postjunctional peripheral α2 receptors in the eye, the sudden onset mydriasis that occurred shortly after intracisternal injection could be interpreted as an early sign of decreased cerebral blood flow secondary to increased ICP.[19,20]

Another observed clinical sign was profound hypothermia, that persisted despite active warming for many hours from injection. Hypothermia is a common side effect of medetomidine, as a result of both central inhibition of the thermoregulatory center and peripheral vasoconstriction.[23]

Making clinical decisions regarding antagonization of medetomidine was challenging. Published recommended doses for atipamezole, which range from four- to sixfold the medetomidine dose, are intended for antagonization following intravenous or intramuscular sedation.[24] Atipamezole overdose is not without risks, and may result in neurological, cardiovascular, and gastrointestinal side effects.[24] The dog of this report received a total atipamezole dose of 1666 µg/kg, which corresponds to approximately fourfold the administered dose of medetomidine and falls therefore within recommended dose ranges. Although the manufacturer recommends intramuscular route for administration of atipamezole, in the dog of this report it was decided for an off-label intravenous use, to cope with the emergency situation. Additionally, it was believed that the vasoconstriction potentially occurring after systemic absorption of such high dose of medetomidine could have jeopardized atipamezole uptake from the muscles.

In conclusion, human error was at the origin of the life-threatening complication that occurred in the dog of this report. Inadvertent intracisternal injection of medetomidine resulted in profound cardiovascular, respiratory, and thermoregulatory depression that responded to administration of atipamezole and supportive care.

Injection accidentelle de médétomidine dans la Cisterna cerebromedullaris chez un chien lors d'un examen myélographique

Un chien croisé a été anesthésié pour une myélographie diagnostique afin d'étudier une douleur aiguë au niveau du cou. Au lieu du produit de contraste, 444 µg/kg de médétomidine ont été injectés par inadvertance dans la citerne cérébello-médullaire en raison d'une erreur humaine. Une bradycardie sévère, un pouls périphérique indétectable, un arrêt respiratoire et une perte des réflexes pupillaire, palpébral et cornéen ont été observés immédiatement après l'injection. Une hypothermie profonde s'est développée et la température œsophagienne, mesurée 20 minutes après l'injection de médétomidine, était de 33 °C. De l'atipamézole à 1 mg/kg im a été administré, suivi d'une seconde dose de 0,5 mg / kg iv 20 minutes après. Dans l'intervalle, les paramètres cardiorespiratoires et la température corporelle ont été surveillés et des soins de soutien comprenant une ventilation assistée manuellement, un réchauffement actif et l'administration de 5 µg/kg/min de dopamine ont été initiés. L'état clinique du chien s'est amélioré dans l'heure qui a suivi le début des soins, moment où les réflexes oculaires et la déglutition sont réapparus, la ventilation spontanée a été jugée adéquate et où on a pu procéder à l'extubation. Le chien est sorti dans de bonnes conditions cliniques cinq jours plus tard.

Une erreur humaine et de la distraction ont conduit à une complication potentiellement mortelle chez le chien décrit dans ce rapport et auraient pu être évitées grâce à l'utilisation de listes de contrôle et avec une définition plus claire des rôles et des responsabilités du personnel impliqué avant le début de la procédure clinique. Une profonde dépression cardiovasculaire, respiratoire et de la thermorégulation causée par l'injection intracisternale de médétomidine a répondu à l'administration parentérale de son antagoniste et à des soins de soutien.

Mots clés: erreur humaine ; injection intracisternale ; médétomidine ; morbidité péri -anesthésique

Iniezione accidentale di medetomidina nella cisterna magna di un cane durante un esame mielografico

Un cane meticcio è stato sottoposto ad anestesia per mielografia diagnostica per insorgenza di dolore cervicale acuto. A causa di un mero errore umano, 444 µg/kg medetomidina sono stati inoculati nella *cisterna cerebromedullaris* invece del mezzo di contrasto. Subito dopo l'inoculo sono comparsi grave bradicardia, assenza di polso periferico, arresto respiratorio e perdita dei riflessi pupillare, palpebrale e corneale. È insorta una grave ipotermia e la temperatura trans-esofagea rilevata 20 min dopo la somministrazione intracisterna di medetomidina era di soli 33 °C. Una dose di atipamezolo è stata somministrata IM, seguita dopo 20 min da una seconda dose IV. Nel frattempo, è stato predisposto un monitoraggio strumentale per rilevare i parametri cardiorespiratori e la temperatura corporea, ed istituita una terapia di supporto con ventilazione polmonare manuale, riscaldamento attivo e somministrazione di un vasopressore (dopamina). Le condizioni cliniche del cane sono migliorate entro un'ora dall'inizio della terapia di supporto, momento in cui sono tornati i riflessi oculari e di deglutizione cui è seguita l'estubazione. Il cane è stato dimesso in buone condizioni cliniche dopo cinque giorni.

L'errore umano e la distrazione sono stati all'origine di una complicazione potenzialmente pericolosa per la vita del cane di questo report e avrebbero potuto essere prevenuti usando liste di controllo e una più chiara definizione dei ruoli e delle responsabilità del personale coinvolto nella procedura prima dell'inizio. La profonda depressione cardiovascolare, respiratoria e di termoregolazione insorte dopo inoculo intracisterna di medetomidina sono state trattate con somministrazione parenterale del suo antagonista e con terapia di supporto.

Parole chiave: Errore umano, complicazioni durante mielografia, iniezione intracisternale, medetomidina

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S. Nannarone, C. Adami

References

[1] Reason J. The nature of human error. In: Reason J, ed. Human Error. Cambridge University Press, Cambridge, 1991: 1–19.

[2] Senders JW, Moray NP. Some queries and some definitions. In: Senders JW, Moray NP, eds. Human error. Cause, prediction, and reduction. CRC Press Taylor & Frances Group, Fl: Boca Raton, 1991: 25–26.

[3] Haller G, Laroche T, Clergue F. Morbidity in anesthesia: today and tomorrow. Best Pract. Res. Clin. Anesthesiol. 2011: 25: 123–132.

[4] Boyd J, Wu G, Stelfox H. The impact of checklists on inpatient safety outcomes: a systematic review of randomized controlled trials. J. Hosp. Med. 2017 : 12: 675–682.

[5] Ko HCH, Turner TJ, Finnigan MA. Systematic review of safety checklists for use by medical care teams in acute hospital settings – limited evidence of effectiveness. BMC Health. Serv. Res. 2011: 11: 211.

[6] Hughes RG, Blegen MA. Medication Administration Safety: Hughes RG, Patient safety and quality: an evidence-based handbook for nurses. Rockville MD: Agency for Healthcare Research and Quality, 2008.

[7] Menoud G, Axiak Flammer S, Spadavecchia C, Raillard M. Development and implementation of a perianesthetic safety checklist in a veterinary University Small Animal Teaching Hospital. Front. Vet. Sci. 2018: 5: 60.

[8] Nappier MT, Corrigan VK, Bartl-Wilson LA, Freeman M, Werre S, Tempel E. Evaluating checklist use in companion animal wellness visits in a veterinary teaching hospital: a preliminary study. Front. Vet. Sci. 2017: 4: 87.

[9] Kuusela E, Raekallio M, Antilla M, Falck I, Mölsä S, Vainio O. Clinical effects and pharmacokinetics of medetomidine and its enantiomers in dogs. J. Vet. Pharmacol. Ther. 2000: 23: 15–20.

[10] Klimscha W, Tong C, Eisenach JC. Intrathecal alpha 2 adrenergic agonists stimulate acetylcholine and norepinephrine release from the spinal cord dorsal horn in sheep. An in vivo microdialysis study. Anesthesiology 1997: 87: 110–116.

[11] Steagall PV, Millette V, Mantovani FB, Millette V, Mantovani FB, Gilbert P, Luna SP, Duke-Novakovski T. Antinociceptive effects of epidural buprenorphine or medetomidine, or the combination, in conscious cats. J. Vet. Pharmacol. Ther. 2009: 32: 477–484.

[12] Watanabe R, Fujita Y. Efficiency of medetomidine for epidural analgesia: Effects on isoflurane requirement and mean systemic arterial blood pressure in dogs. Can. Vet. J. 2017: 58: 742–746.

[13] Vesal, N, Cribb, PH, Frketic, M. Postoperative analgesic and cardiopulmonary effects in dogs of oxymorphone administered epidurally and intramuscularly and medetomidine administered epidurally: a comparative clinical study. Vet. Surg. 1996: 25: 361–369.

[14] Sabbe MB, Penning JP, Ozaki GT, Yaksh TL. Spinal and systemic action of the α2-receptor agonist dexmedetomidine in dogs. Anesthesiology 1994: 80: 1057–1072.

[15] Pypendop B, Verstegen J. Haemodynamic effects of medetomidine in the dog: a dose titration study. Vet. Surg. 1998: 27: 612–622.

[16] Kamat V. Pulse oximetry. Indian J. Anaesth. 2002: 46: 261–268

[17] Cushing H. Concerning a definite regulatory mechanism of the vaso-motor centre which controls blood pressure during cerebral compression. Johns Hopkins Hosp. Bull. 1901: 12: 290–292.

[18] Heymans C. The control of heart rate consequent to changes in the cephalic blood pressure and in the intracranial pressure. Am. J. Physiol. 1928: 85: 498–505.

[19] Kalmar AF, Van Aken J, Caemaert J, Mortier EP, Struys MMRF. Value of Cushing reflex as warning sign for brain ischaemia during neuroendoscopy. Br. J. Anaesth. 2005: 94: 791–799.

[20] Kalmar AF, De Ley G, Van Den Broecke C, Van Aken J, Struys MMRF, Praet MM, Mortieret EP. Influence of an increased intracranial pressure on cerebral and systemic haemodynamics during endoscopic neurosurgery: an animal model. Br. J. Anaesth. 2009: 102: 361–368.

[21] Arany-Tóth A, Csébi P, Jensen HS. Cisternal pressure measurement in dogs during myelography. Preliminary study. Magyar Allatorvosok Lapja 2008: 130: 698–703.

[22] Arany-Tóth A, Csébi P, Reiczigel J, Sére V, Némethet T. Subarachnoid pressures and cardiorespiratory parameters during cisternal myelography in isoflurane anesthetized dogs. Veterinary Anaesth. Anal. 2013: 40: 390–398.

[23] Cullen LK. Medetomidine sedation in dogs and cats: a review of its pharmacology, antagonism and dose. Br. Vet. J. 1996: 152: 519–535.

[24] Viiha-Vahe T. The clinical effectiveness of atipamezole as a medetomidine antagonist in the dog. J. Vet. Pharmacol. Ther. 1990: 13: 198–205.

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