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BLOQUEIO INFILTRATIVO INCISIONAL COM BUPIVACAÍNA EM CADELAS SUBMETIDAS À OVARIOHISTERECTOMIA POR CELIOTOMIA OU VIDEOASSISTIDA COM DOIS PORTAIS

DISSERTAÇÃO DE MESTRADO

Letícia Reginato Martins

Santa Maria, RS, Brasil
2017

BLOQUEIO INFILTRATIVO INCISIONAL COM BUPIVACAÍNA EM CADELAS SUBMETIDAS À OVARIOHISTERECTOMIA POR CELIOTOMIA OU VIDEOASSISTIDA COM DOIS PORTAIS

Letícia Reginato Martins

Dissertação apresentada ao Curso de Mestrado do Programa de Pós-Graduação em Medicina Veterinária, Área de Concentração em Cirurgia e Clínica Veterinária, da Universidade Federal de Santa Maria (UFSM, RS), como requisito parcial para obtenção do Grau de
Mestre em Medicina Veterinária

Orientador: Prof. André Vasconcelos Soares

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Universidade Federal de Santa Maria
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A Comissão Examinadora, abaixo assinada,
aprova a Dissertação de Mestrado

BLOQUEIO INFILTRATIVO INCISIONAL COM BUPIVACAÍNA EM CADELAS SUBMETIDAS A OVARIOHISTERECTOMIA POR CELIOTOMIA OU VIDEOASSISTIDA COM DOIS PORTAIS

elaborada por
Letícia Reginato Martins

como requisito parcial para obtenção do grau de
Mestre em Medicina Veterinária

COMISSÃO EXAMINADORA:

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Santa Maria, 14 de julho de 2017.

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“Educação, em boa síntese,

é luz que circula vitoriosa do sentimento ao raciocínio,

sustentando o equilíbrio entre o cérebro e o coração.

A ideia esclarece. O sentimento cria. A palavra edifica.”

(Emmanuel)

Dissertação de Mestrado

Programa de Pós-Graduação em Medicina Veterinária
Universidade Federal de Santa Maria, RS, Brasil

BLOQUEIO INFILTRATIVO INCISIONAL COM BUPIVACAÍNA EM CADELAS SUBMETIDAS À OVARIOHISTERECTOMIA POR CELIOTOMIA OU VIDEOASSISTIDA COM DOIS PORTAIS

AUTOR: LETÍCIA REGINATO MARTINS
ORIENTADOR: ANDRÉ VASCONCELOS SOARES
Data e Local da Defesa: Santa Maria, 14 de julho de 2017.

Este estudo objetivou avaliar o uso de anestesia local infiltrativa com bupivacaína a 0,5% na área da incisão cirúrgica como parte de uma abordagem analgésica multimodal em cães submetidos à ovariohisterectomia (OVH) por celiotomia ou vídeo-assistida por dois portais. Para isso foram selecionadas vinte e oito cadelas adultas (2,08±1,45 anos) hígidas, pesando 12,67±1,94kg. Os animais foram pré medicados com maleato de acepromazina (0,05mg.kg^{-1}, IM), anestesiados com propofol (4mg.kg^{-1}, IV), seguida de manutenção da anestesia geral com isoflurano vaporizado em oxigênio a 100%. A analgesia transoperatória foi promovida com fentanil em infusão contínua (20µg.kg^{-1} hora^{-1}), precedida de dose *bolus* (2,5µg.kg^{-1}, IV). Os animais foram alocados aleatoriamente em quatro grupos: grupo controle celiotomia (CC, n=7), grupo bloqueio celiotomia (BC, n=7), grupo controle vídeo-assistido (CV, n=7), e grupo bloqueio vídeo-assistido (BV, n=7). Nos grupos em que foi realizado bloqueio (BC e BV), a bupivacaína a 2mg.kg^{-1} foi administrada por via subcutânea na linha de incisão ou na entrada dos portais. Nos grupos controle, foi infiltrado 3 ml de solução salina nos mesmos locais. Foi administrado meloxicam (0.2mg.kg^{-1}) ao final da cirurgia e a c formulação comercial de metamizol sódico e hioscina N-butilbromida a cada 8 horas durante dois dias. Todos os animais tiveram a dor pós-operatória avaliada por três avaliadores experientes e cegos para o tratamento e cirurgia, usando as escalas de dor de Melbourne e visual analógica a cada hora nas primeiras 8 horas e às 12, 18, 24, 36 e 48 horas após a extubação. A glicemia e o cortisol sérico também foram avaliados. Não houve resgate analgésico em nenhum dos animais de grupos que receberam bloqueio anestésico (BC e BV). Em todos os animais do CC e um em CV receberam resgate analgésico até a segunda hora de pós-operatório. O bloqueio infiltrativo anestésico realizado com 2,0mg.kg^{-1} de bupivacaína foi eficiente na promoção do conforto pós-operatório quando utilizado em OVH por celiotomia e vídeoassistidas.

Palavras-chave: Analgesia. Bupivacaína. Videocirurgia. Ovariohisterectomia. Bloqueio incisional

ABSTRACT

Master's Dissertation
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USE OF BUPIVACAINE INFILTRATIVE LOCAL BLOCK IN BITCHES SUBMITTED TO OVARIOHYSTERECTOMY BY CELIOTOMY OR VIDEO-ASSISTED WITH TWO PORTALS

AUTHOR: LETÍCIA REGINATO MARTINS
ADVISER: ANDRÉ VASCONCELOS SOARES
Date and Place of Defense: Santa Maria, July 14th, 2017

This study aimed to investigate the use of local infiltrative anesthesia with 0.5% bupivacaine in surgical incision site as part of a multimodal analgesic approach in dogs submitted to ovariohysterectomy (OVH) by celiotomy or video-assisted by two-port. Twenty-eight adult (2.08 ± 1.45 years) and healthy bitches, weighing 12.67 ± 1.94 kg, with aptitude confirmed by clinical and laboratory tests were selected. Dogs were pre-medicated with acepromazine (0.05mg.kg^{-1}, IM), induced and maintained in general anesthesia with propofol (4mg.kg^{-1}, IV) and isoflurane vaporized in 100% oxygen, respectively. Intraoperative analgesia was promoted with fentanyl in continuous infusion (20µg.kg^{-1}.hour^{-1}), preceded by a loading dose (2,5µg.kg^{-1}, IV). Dogs were divided into four groups: control group celiotomy (CC, n = 7), blocking group celiotomy (BC, n = 7), control video-assisted group (CV) and blocking video-assisted group (BV). In the blocked groups (BC and BV), bupivacaine (2mg.kg^{-1}) was administered subcutaneously in the incision line or port entry sites. Control groups received 3 ml of saline solution at the same sites. Meloxicam (0.2mg.kg^{-1}) administered at the end of the surgery with the combination of metamizole sodium and Hyoscine N-butyl bromide every 8 hours for 2 days. Postoperative pain was evaluated by three evaluators blinded to surgery and treatment established, using Melbourne Pain Scale and visual analogue scale. Pain was assessed hourly in the first 8 hours and, then, at 12, 18, 24, 36 and 48 hours post-extubation. Glycemia and serum cortisol were evaluated too. Rescue analgesia was administered to one animal in CV after one hour postoperative, while seven dogs in CC received additional analgesia in the first two hours postoperative and was not required by any of the animals that received anesthetic block (BC and BV). Statistical analysis suggested that the anesthetic infiltrative blockade performed with 2,0mg.kg^{-1} bupivacaine was efficient in promoting postoperative comfort when used in both celiotomy and video-assisted OVH..

Palavras-chave: Analgesia. Bupivacaine. Video Surgery. Ovariohysterectomy. Incisional block

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INTRODUÇÃO

A ovariohisterectomia (OVH) é um procedimento cirúrgico amplamente utilizado na medicina veterinária, além de ser considerado um efetivo método de contracepção em animais domésticos (MUSAL; TUNA, 2005). Este procedimento objetiva tratar ou prevenir diversas afecções no sistema reprodutivo (SCHIOCHET et al., 2007), incrementando a qualidade de vida dos animais domésticos, ao passo que é ferramenta de auxílio no tratamento de afecções sistêmicas. (HOWE, 2006; PÖPPL; ARAÚJO, 2010).

Procedimentos minimamente invasivos estão revolucionando a abordagem cirúrgica em pequenos animais, entre eles, destaca-se a OVH videoassistida. Malm et al., (2004) destacam que, embora não sejam substitutos aos procedimentos convencionais, estas possibilidades cirúrgicas estão sendo incorporadas. Além disso, evidencia-se uma constante evolução e refinamento das técnicas de videocirurgia aplicadas a pequenos animais (MAYHEL, 2011).

A incorporação dessas técnicas alcançaram aceitação entre os profissionais devido a possibilidade de realização de procedimentos diagnósticos e terapêuticos associada a diversos fatores como: pequenas incisões, menor trauma tecidual, menos desconforto e dor pós-operatória, menor período de hospitalização e recuperação pós-operatória, menores custos e melhores resultados estéticos, quando comparadas a técnicas convencionais. (BRUN, 2015; CULP; MAYHEW; BROWN, 2009; DEVITT; COX; HAILEY, 2005a; HANCOCK et al., 2005).

Técnicas videocirúrgicas tem se mostrado vantajosas na grande maioria dos fatores considerados na comparação com grandes incisões cirúrgicas. No entanto, o custo dos equipamentos e a maior curva de aprendizado para operar os mesmos apresentam-se como contrapontos importantes (DAVIDSON; MOLL; PAYTON, 2004).

Por muitos anos a dor em pequenos animais foi negligenciada por acreditar-se que os mesmos não eram capazes de senti-la ou se seria expressada de maneira diferente dos humanos. Uma melhor compreensão sobre a dor em animais é relatada devido à anos de pesquisa e aprendizagem, podendo então, ser afirmado que, como os animais de companhia dispõem de caminhos neurais e neurotransmissores de dor semelhantes aos nossos, é altamente presumível que também a vivenciem dor de forma equivalente (HELLYER et al., 2007).

O conceito de dor é descrito de maneira complexa. De acordo com Morton et al. (2005), em animais, ela pode ser definida como uma experiência sensorial e emocional negativa, capaz de produzir ações motoras protetoras, resultando em uma aversão condicionada, a qual modifica os traços de comportamento específicos para a espécie, incluindo o comportamento social.

O manejo da dor em pacientes incapazes de autorrelato é desafiador, pois o diagnóstico e o tratamento adequado e efetivo tornam-se subjetivos. Dessa maneira, o reconhecimento da dor tem um papel fundamental e a utilização de métodos como ferramentas de avaliação é crucial para identificação e acompanhamento da eficácia do tratamento analgésico. Neste contexto, a utilização de escalas unidimensionais ou multidimensionais se faz cada vez mais útil, ainda que não exista um método que supra todas as necessidades (HELLYER et al., 2007; HOLTON et al., 1996). A abordagem com múltiplos aspectos para a avaliação da dor é geralmente aceita como a melhor alternativa, oferecendo melhores resultados (HELLYER et al., 2007; MATICIC et al., 2010). Por este motivo, entende-se que a avaliação de dor em pequenos animais forneça melhores resultados quando associadas diferentes abordagens, aumentando a sensibilidade, evitando ponderação indevida de qualquer medida subjetiva ou objetiva única (MATHEWS, 2000).

O desenvolvimento de grande parte das escalas utilizadas foram adaptadas de sistemas desenvolvidos para utilização em seres humanos (HOLTON et al., 1996). A escala visual analógica (EVA) (ANEXO A) é um sistema de pontuação unidimensional ilustrada como uma linha reta horizontal de 100mm, onde em cada extremidade da linha é descrita a intensidade de dor (nenhuma dor à dor máxima). Enquanto na medicina humana, a escala é preenchida pelo paciente enfermo, na medicina veterinária o avaliador identifica e interpreta visualmente os comportamentos de dor (GAYNOR; MUIR, 2009; HOLTON et al., 1996). A escala de Melbourne (MPS) (ANEXO B) trata-se de uma escala multidimensional, sendo composta por um somatório de pontos baseado em respostas comportamentais e fisiológicas específicas, incluindo descritores múltiplos em seis categorias (FIRTH; HALDANE, 1999).

Segundo Firth e Heldane (1999), é importante que o avaliador tenha conhecimento prévio do comportamento do animal para contextualização dos parâmetros avaliados. Devido a isso, entende-se por fundamental a análise dos parâmetros basais do paciente no momento em que o mesmo chega ao ambiente hospitalar, principalmente quando este passará por algum procedimento cirúrgico.

Procedimentos dolorosos que tendem a causar estresse do animal, alteram a secreção de hormônios hipofisários, em especial ao hormônio adrenocorticotrófico (ACTH), responsável pelo estimulo à secreção de corticosteroides (SACKMAN, 1991). Utiliza-se a variação da concentração de cortisol plasmático como indicador de dor induzida e relacionada à estresse em cães em período pósoperatório. Em cães, considera-se como um bom indicador e observase um declínio em valores absolutos após procedimentos laparoscópicos quando comparados com cirurgias convencionais, podendo indicar um menor grau ou uma resolução mais rápida do estresse cirúrgico (HANSEN; HARDIE; CARROLL, 1997; KO et al., 2000; ZANELLA et al., 2009).

É de consenso atual que a analgesia deve ser feita de maneira eficiente a fim de prevenir ou aliviar a dor. Eticamente, classifica-se como inaceitável a submissão do paciente a dor como forma de diagnóstico veterinário ou para restrição a locomoção dos animais, como realizado durante muitos anos (HELLYER et al., 2007).

A dor pós-operatória aguda ainda se mostra como um problema médico relevante. Os pacientes submetidos à cirurgia comumente apresentam dor pós-operatória clinicamente significativa (BRENNAN, 2011). De acordo com Carpenter, et al. (2004), a dor pós-operatória associada a OVH é caracterizada como uma dor leve a moderada e, embora ainda haja resistência de muitos veterinários, o uso de analgésicos mais fortes para controlá-la aumentou substancialmente em um período recente (HEWSON; DOHOO; LEMKE, 2006). O uso isolado de opioides e antiinflamatórios não esteroidais (AINES) pode não proporcionar alívio eficiente da dor. Além disso, esses analgésicos podem causar efeitos adversos substanciais como sedação, disforia, depressão respiratória, no caso dos opioides, além de úlceras gastrintestinais, dano renal e hepático nos AINES (HELLYER et al., 2007; LAMONT; MATHEWS, 2007).

O conceito de analgesia multimodal surgiu juntamente com a evolução dos protocolos analgésicos, os quais tem por objetivo melhorar a analgesia ao passo que reduz a incidência de efeitos adversos associados aos opioides. Esta modalidade pode ser definida como a utilização de fármacos analgésicos com diferentes mecanismos de ação, objetivando analgesia suficiente devido aos efeitos aditivos ou sinérgicos entre as diferentes classes de analgésicos, reduzindo ou evitando estímulos nociceptivos a níveis de receptores por meio de diferentes formas de estimulação nervosa. Skinner (2004), comprovou eficácia em humanos na aplicação de protocolos analgésicos multimodais, reduzindo a morbidade e mortalidade pós-operatória, aumentando a qualidade de vida e satisfação dos pacientes. A associação de uma anestesia local, combinada com uma analgesia sistêmica é um exemplo simples e efetivo de aplicação do protocolo multimodal (BUVANENDRAN; KROIN, 2009; LASCELLES et al., 2008a; MARTINS et al., 2010; SLINGSBY; MURRELL; TAYLOR, 2010).

A maneira mais eficiente de impedir ou reduzir impulsos nociceptivos durante e após a cirurgia acontece por meio da infiltração de anestésico local durante o transoperatório, o qual atua na interrupção da transmissão neural dos nervos ou tratos sensoriais aferentes. Obtém-se efeito semelhante se a infiltração é realizada antes do procedimento cirúrgico, diminuindo a quantidade de anestésicos gerais e opióides a serem utilizados (CUVILLON et al., 2009).

A bupivacaína é um anestésico local amplamente utilizado na rotina do médico veterinário devido ao seu longo período de ação. Quando utilizada a 0,5% resulta em um bloqueio sensorial e motor adequado para procedimentos cirúrgicos em animais de companhia. Sua formulação consiste em uma mistura 50:50 de dois enantiômeros [(S (-) e R (+)], ambos com potência e duração de ação semelhantes (FOSTER; MARKHAM, 2000; TORSKE; DYSON, 2000).

O presente estudo objetivou investigar a qualidade e eficácia do uso de bupivacaína em bloqueio local na área da incisão cirúrgica e sua atuação como parte de uma abordagem multimodal no controle da dor em cães submetidos a OVH por técnica videoassistida ou convencional por celiotomia.

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USO DE BUPVACAÍNA EM BLOQUEIO INFILTRATIVO EM CADELAS SUBMETIDAS A OVARIO-HISTERECTOMIA POR CELIOTOMIA OU VIDEOASSISTIDA COM DOIS PORTAIS

Use of bupivacaine infiltrative local block in bitches submitted to ovariohysterectomy by celiotomy or video-assisted with two portals

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(**) = Material removed by editor for blinding

Abstract

Objective To investigate the use of incisional infiltration of 0.5% bupivacaine as part of a multimodal analgesic approach in dogs undergoing ovariohysterectomy by celiotomy or video-assisted.

Study design Prospective clinical trial.

Animals A total of 28 female dogs, aged (mean ± standard deviation) 2.08 ± 1.45 years and weighing 12.67 ± 1.94 kg.

Methods Dogs were administered acepromazine (0.05 mg kg^{-1}) intramuscularly, anesthesia was induced with propofol (4.0 mg kg^{-1}) intravenously (IV) and maintained with isoflurane in oxygen. Fentanyl was administered IV intraoperatively (loading dose of 2.5 μg kg^{-1} followed by a continuous infusion of 20 μg kg^{-1} $hour^{-1}$). Animals were divided into four groups: control celiotomy group (CC), bupivacaine celiotomy group (BC), control video-assisted group (CV) and bupivacaine video-assisted group (BV). Bupivacaine (2.0 mg kg^{-1}) used in BC and BV was administered subcutaneously to dogs in BC and BV 15 minutes before skin incision. Saline (3ml) was infiltrated to dogs in the control groups. Visual Analogue Scale and Melbourne Pain Scale were used for pain evaluation. Glycemia and serum cortisol were also evaluated.

Results 28 dogs completed the study. BC, CV and BV showed similar pain scores. Analgesic rescue was required by all dogs in CC and 1 in CV in the first two hours postoperative. None of the animals in BC and BV were administered supplemental analgesia. Any evidence of better analgesic effect of blockade associated with video-assisted surgery over celiotomy OVH could be traced.

Conclusions and clinical relevance It can be stated that 2.0 mg.kg^{-1} of 0.5% bupivacaine administered in the infiltrative blockade at the incision line, meloxicam (0.2 mg kg^{-1}) administered at the end of the surgery with the combination of metamizole sodium and Hyoscine N-butyl bromide, constitutes a suitable multimodal postoperative protocol for OVH performed by both celiotomy and the video-assisted technique.

Keywords analgesia, bupivacaine, videosurgery, ovariohysterectomy, block incision line

Introduction

Advances in Ovariohysterectomy (OVH) techniques have been observed over the years (Malm et al.,2004). Minimally invasive approaches revolutionized surgery and have been used to replace conventional procedures. Besides incorporating innovative modalities for diagnostic and therapeutic surgical procedures, other benefits are observed: access through small incisions, less tissue trauma, less discomfort and postoperative pain, shorter time of hospitalization, faster post-surgical recovery, lower costs and better aesthetic results (Brun 2015; Culp et al. 2009; Devitt et al. 2005; Hancock et al. 2005).

Among the techniques of ovariohysterectomy in dogs, the video-assisted technique has gained popularity in veterinary medicine, since it maintains the characteristics of minimally invasive surgery despite performing complex procedures outside the abdominal cavity. It involves an intra and extracavitary phase. This component, which differs from the other laparoscopic techniques, significantly reduces its complexity, making it more versatile for routine use. (Devitt et al., 2005 Brun, 2015)

According to Morton et al. (2005), pain in animals is defined as a negative sensory and emotional experience that produces protective motor actions, resulting in a conditioned aversion, and modifies behavioural traits specific to the species. As animal patients are unable to self-report, pain management is defiant, on this account, the ability to treat and diagnose it effectively becomes subjective. Thus, methods of pain assessment are crucial for identifying and monitoring the efficacy of analgesic treatment. A multiple-aspect approach to pain assessment is generally accepted as the option that provides better results (Firth & Haldane 1999; Hellyer et al. 2007).

According to Firth and Heldane (1999), it is important that the evaluator has previous knowledge of the behaviour of the animal to contextualize the evaluated parameters. Therefore, it is important to analyse the baseline parameters of the animal patient at its arrival to the hospital environment, especially when undergoing a surgical procedure.

Multimodal pain management designates the use of analgesic drugs with different mechanisms of action, with the objective of reducing or avoiding nociceptive stimuli at receptor levels through different forms of nerve stimulation. Skinner (2004) demonstrated the efficacy of multimodal analgesic protocols in reducing postoperative morbidity and mortality pain-related, increasing quality of life and patient satisfaction. The association of locoregional anaesthesia combined with systemic analgesia is a simple way of applying the multimodal protocol. Local anaesthetics act on the interruption of neural transmission of afferent sensory nerves or sensory tracts (Slingsby et al. 2010; Lascelles et al. 2008; Martins et al. 2010). The infiltration of local anaesthetic before the surgical procedure has been demonstrated to decrease the number of general anaesthetics and opioids to be used in surgeries performed by celiotomy (Cuvillon et al. 2009), being an efficient manner to prevent or reduce nociceptive impulses or pain during and after surgery.

The aim of this study was to investigate the use of infiltrative blockade with bupivacaine in the surgical incision line or port entry sites and the effectiveness of this drug as part of a multimodal approach in postoperative pain control in dogs submitted to OVH by video-assisted or conventional technique by celiotomy.

Material and methods

After approval by the Ethics Committee on Animal Use (CEUA) of the **, under protocol number 021/2014, there were selected twenty-eight bitches to be ovariohysterectomized. The inclusion criteria included age of 2-4 years, 10-15 kg of body weight (BW), American Society of Anesthesiologists (ASA) physical status of I and owner signed consent about the study participation.

The aptitude to participate in the study was confirmed by thorough clinical and laboratory examination, including platelet counts, haematological and biochemical tests (albumin, alkaline phosphatase (FA), alanine aminotransferase (ALT), creatinine and urea). Serum glucose and cortisol were also evaluated. Animals were hospitalized 24 hours prior surgical procedure to provide the animals an appropriate adaptation to the evaluation site and evaluators.

Food and water were withdrawn 12 and 6 hours before surgery, respectively. Dogs were premedicated with an intramuscular (IM) injection of acepromazine maleate (0.05 mg kg^{-1}, Apromazin 2 mg ml^{-1}, Syntec, Brazil). After 15 minutes, the right cephalic vein was catheterized with a 22G catheter using an aseptic technique and abdominal hair was clipped. General anaesthesia was induced using intravenous (IV) propofol at 4.0 mg kg^{-1} (Propovan® 10mg mL^{-1}, Cristália Prod. Quím. Farm. Ltda., Brazil) and maintained with isoflurane (Isoflurano, Instituto BioChimico Ind. Farm. Ltda. Brazil) vaporized in 100% oxygen, with an adequate concentration to maintain the animals in anaesthetic plane by partial gas rebreathing system. The intraoperative analgesia was promoted by the continuous intravenous infusion of fentanyl citrate (20 μg kg^{-1} $hour^{-1}$, Fentanest® 0,05 mg ml^{-1}, Cristália Prod. Quím. Farm. Ltda., Brazil) by peristaltic infusion pump, preceded by a 2.5 μg kg^{-1} IV bolus dose of the same drug. Sodium ampicillin (20 mg kg^{-1}, IV, Ampicilina Sódica 200 mg ml^{-1}, Teuto Brasileiro S/A, Brazil) was administered as antimicrobial chemoprophylaxis.

During all over the surgery heart rate, respiratory frequency (*f*), systolic, diastolic and mean blood pressures by a non-invasive device, partial O_2 saturation (SpO_2), end-tidal CO_2 ($EtCO_2$) were monitored by a multiparameter monitor (PM 9000, Mindray) and registered at 5 minutes interval.

Dogs were randomly allocated into two large groups according to the type of ovariohysterectomy surgery to be submitted: OVH by celiotomy or video-assisted. Then, each group was subdivided into two smaller groups according to the proposed analgesic procedure: with or without incision line block. Namely, the four groups were: control celiotomy group (CC: n=7), blocking celiotomy group (BC: n=7), control video-assisted group (CV: n = 7) and blocking video-assisted group (BV: n = 7).

After stabilization of the anaesthetic plane, the experimental protocol was applied: dogs from control groups received 3 mL of saline solution (Sodium Chloride 0,9%, Halex Istar Ind. Farm., Brazil) subcutaneously in the incision line. The standard volume of 3 mL, administered in both control groups, was based on previous data from a preliminary study performed by the same research group under similar conditions. The blocking groups were administered bupivacaine hydrochloride at 0.5% (2 mg kg^{-1}, Neocaína® 5 mg ml^{-1}, Cristália Prod. Quím. Farm. Ltda., Brazil) in the incision line. In the video-assisted group, half of the total volume of bupivacaine or saline solution was injected in each of the two-port entry lines. A dermatographic pen was used to mark the site of injection.

Conventional celiotomy technique was performed in the groups CC and BC, while the two-port technique described by Brun (2015) was performed in CV and BV. Meloxicam (0.2 mg kg^{-1}) was administered at the end of the surgery (0.2 mg kg^{-1}, Maxicam 2%, Ourofino, Brazil). Postoperative analgesia was composed of a commercial formulation containing metamizole sodium (25 mg kg^{-1}) and hyoscine N-butylbromide (0.2 mg kg^{-1}, Buscofin Composto, metamizole sodium 500 mg ml^{-1} and hyoscine N-butylbromide 4.0 mg ml^{-1}, União Química Farmacêutica Nacional S/A, Brazil) administered IV immediately after the end of surgery. Subsequent doses were given subcutaneously every eight hours for 48 hours.

The postoperative pain measurement was performed by three experienced evaluators blinded to the anaesthetic protocol and surgery technique using two scales: the visual analogue scale (VAS) and the Melbourne Pain Scale (MPS). Animals were evaluated hourly in the first eight hours (T1 to T8) and, then, at 12 (T12), 18 (T18), 24 (T24), 36 (T36) and 48 hours (T48) postoperative.

The guidelines described by Mich and Hellyer (2009) for VAS and by Firth and Heldane (1999) for Melbourne scale were followed strictly. Scores above 5 cm or 6 points in VAS or MPS, respectively, were used as the threshold for the administration of anaesthetic rescue which consisted of tramadol (4 mg kg^{-1}, IM, Tramadon® 50 mg ml^{-1}, Cristália Prod. Quím. Farm. Ltda., Brazil). The threshold score in MPS used in this study is in accordance with a study by Pohl et al. (2011) who identified that the moderate pain score on VAS scale (5 cm) is compared in equivalence to 5.88 in Melbourne Pain Scale due a high correlation. All animals that received anaesthetic rescue were retested every hour after administration of the supplemental analgesia until reaching scores below threshold point in both scales and were removed from the statistical analysis. The abdomen of the dogs was covered with bandages to prevent the evaluators to identify the groups. The bandages were changed according to the need, by a non-participatory team in the analgesic evaluation.

In parallel with pain assessment, blood samples were collected to measure serum cortisol and glucose levels by quimioluminescence technique and blood glucometer (G-Tech free 1, G-Tech, Brazil) at the following times: T0-basal (before the surgical procedure) T1, T6, T12, T24 and T48.

During the experiment, animals were hospitalized in individual cages, receiving commercial food and water *ad libitum* for 48 hours postoperatively and then subsequently discharged from the hospital with postoperative care prescription.

Statistical analysis

All variables analysed followed a non-normal distribution. Kruskal-Wallis test was used to access the distribution origin of the variables studied. As mean ranks were statistically different among groups by this test (p-value 0.000005), *post hoc* Dunn test was used to perform multiple comparisons two-by-two in order to determine which treatment was significantly different. The difference of mean scores according to time of evaluation for each group was assessed by t-test after utilizing bootstrap to build confidence intervals. Kruskal-Wallis at 5% of significance was also used to compare serum glucose and cortisol levels among groups in the different assessment periods of time. Correlation between the pain scores acquired by VAS and MPS were obtained by the Pearson Coefficient Correlation. Statistical tests were performed using SPSS 18.0 (IBM Corp., USA).

Results

A total of 28 dogs were selected and completed the study. One dog was excluded due to pyometritis. There was not difference among groups concerning age, weight or duration of anaesthesia and surgery (34±8.24 and 22.10±5.02 minutes respectively).

Regarding postoperative pain scores, it was observed difference between measurements obtained by VAS (visual analogue scale) and Melbourne Pain Scale (MPS), not being able to demonstrate a strong correlation between these methods (table 1), except in case surgery was performed by celiotomy under bupivacaine block. The Analgesic rescue was based on the achievement of scores above 6 points in Melbourne Pain Scale.

Rescue analgesia was administered to one animal in CV after one hour postoperative, while seven dogs in CC received additional analgesia in the first two hours postoperative. Animals in CC were excluded from subsequent pain evaluations. None of the animals from groups receiving anaesthetic blockade (BC and BV) were administered supplemental analgesia. BC, CV and BV groups showed similar pain scores.

According to Dunn Test, the anaesthetic infiltrative blockade performed with 2 mg kg^{-1} of bupivacaine was efficient in promoting postoperative comfort when used in both celiotomy and video-assisted surgeries. By this test, the comparison of BC and BV when assessed by VAS or Melbourne Pain Scale resulted in p-values of 0.3021 and 0.1518, respectively. Thus, no evidence of better analgesic effect of the anaesthetic blockade associated with video-assisted surgery over celiotomy OVH with blockade could be traced. Statistical difference was found when comparing BC and CV both by VAS and MPS (p=0.0002 and p=0.0129, respectively). According to this test, CC was also significantly different from BC (p=0.043) and CV (p=0) by VAS and only from CV (p=0.0379) in MPS evaluation.

The t-test performed two-by-two with confidence intervals built by a bootstrap demonstrated significant difference among treatments in each time point (table 2). The scales presented different results for each time point. At T1, CC, BC and BV presented statistically high pain scores than CV when evaluated by VAS scale. In Melbourne Pain Scale, CC obtained the higher score comparing to the other groups, which implicated in rescue analgesia, while BV showed the statistically smaller score. Two hours postoperatively, CV presented the significant smaller pain score among all groups in VAS measurement and similar to BC and BV in MPS. CC obtained the statistically higher pain scores in both scales. At T3, there was not difference among the means presented by CC, BC and BV in VAS and CC, CV and BC in MPS. At this time point, CV and BV showed the significant smaller pain scores in both scales.

CV maintained the statistically smaller score among groups when evaluated by VAS from T4 until the end of the observations at T48. In VAS assessment, from T4 to T48, VB showed the higher pain scores. BC presented similar score to CC at T4 and, then, similar to BV until 48 hours postoperative.

For Melbourne Pain Scale assessment, there was not difference among groups at T4, T5 to T8 and T18. Different from the evaluation by VAS, CV presented the statistically higher scores in comparison with the other groups along T6, T12, T24, T36 and T48 evaluations using Melbourne Pain Scale. At T6, T12 and T24 BC showed the smaller scores. BV presented statistically similar pain scores to BC at T12 and T24, presenting the significant smaller score in relation to CV and BC at T36 and T48.

However, although there was a statistical difference among treatments at some specific time points of pain assessment, this difference was not significant when considering 48 hours of observation which is demonstrated by the overlapping of confidence intervals of treatments assessed by VAS or Melbourne Pain Scale. The only exception is for VB when analysed by VAS which confidence interval was outside the others confidence interval range.

Serum glucose and cortisol levels were assessed at 0, 1, 6, 12 and 24 hours (T0, T1, T6, T12 and T24) after surgery. To compare groups (BC, CV and BV) in the different periods of time, Kruskal-Wallis test was used. CC group was excluded from statistics since serum glucose and cortisol from this group was sampled only at T0 and T1.

In relation to glucose, although sample mean values were punctually different, there was no statistical difference at any time point (Table 3). In relation to cortisol, there was not statistical difference among cortisol values measured at T1, T6, T12, T24 and T48, although in T1 p-value for Kruskal-Wallis test was 0,05.

Discussion

In the present study, the anaesthetic protocol administered before and during the anaesthetic and surgical period, besides the administration of metamizole sodium with hyoscine N-butylbromide as postoperative analgesia did not provide adequate analgesia for the animals submitted to OVH by celiotomy without the use of incisional block (CC). This fact is evidenced by the analgesic rescues received by 100% of the animals from this group (n=7) until the third postoperative hour (T3). The dogs submitted to the local incisional blockade with bupivacaine (BC and BV), regardless the surgical technique applied, experienced less pain (lower scores on Melbourne and VAS scale) when compared to CC.

In the first hour of postoperative evaluation, which is considered by Desborough (2000) as a critical period in anaesthetic and surgical recovery, animals from BV group presented lower pain scores by the Melbourne scale, also confirmed by serum cortisol levels near baseline, which indicates the effectiveness of the blockade until this moment, a fact expected because it is a potent local anaesthetic drug (Cuvillon et al. 2009). Besides that, this group had the lowest scores on this scale most of the time. The BC group, which also received infiltrative anaesthetic block, obtained similar scores from the sixth postoperative hour, corroborating the efficiency of the pre-incisional anaesthetic block for both celiotomy and video-assisted surgeries.

The short analgesia period given by the administration of fentanyl and the absence of residual effect (Lamont & Mathews 2007) might explain the ineffective analgesia in the CC group in the first hours of evaluation, due to this drug period of action. This is associated with the fact that celiotomy surgeries promote pain of moderate intensity (Carpenter et al. 2004) justifying the need for rescue analgesia in the third hour of evaluation in this group. On the other hand, bupivacaine has onset of effect of approximately 16 ± 9 minutes after the administration and duration of up to 4 hours (Cuvillon et al. 2009), explaining the lower scores reached by the BC group compared to CC group.

It is suggested that the effect of bupivacaine started before the first incision and lasted over the first four to five hours postoperatively. Moreover, the metamizole and hyoscine N-butylbromide association was sufficient to maintain a low nociceptive threshold once the pain receptors could be already downregulated by the bupivacaine action (Lanitis et al. 2015). This result disagrees with Campagnol et al. (2012) who reported that there was not difference in the administration of bupivacaine instilled intraperitoneally or at the incision line in bitches submitted to OVH by celiotomy. For these authors, after the first postoperative hour, both pain scores and the number of analgesic rescues administered were similar for all groups. Local anaesthetic block prior OVH surgery was also tested by Mckune et al. (2014), who reported a non-significant difference between the block and non-block groups. This result was attributed to the non-use of systemic analgesia in association with local blockade during the surgical procedure. The expected action of local anaesthetics is to block nerve conduction by preventing the nociceptive signal to reach the central nervous system and therefore the hypothalamic-pituitary-adrenal (HPA) axis. The activation of this axis explains the changes caused by stress, which includes the postoperative increase of plasma levels of cortisol and glucose (Devitt et al. 2005).

The glucose concentration of all groups in this study increased considerably in the first hour after surgery, decreasing gradually until the twelfth hour when it returned to baseline values. Since there was not difference between the groups at any time point of assessment and the increased glucose levels were accompanied by a concomitant rise in cortisol levels, it is possible to infer that the association of anaesthetic blockade with continuous infusion of fentanyl did not block the HPA axis, although it might have desensitized the pain receptors. This result agrees with Romano et al. (2016), suggesting that, in clinical doses, fentanyl administration is not able to control adrenal and glycemic responses to surgical stimulation since the HPA axis may still be activated.

In relation to cortisol, there was no statistical difference among groups at different times. However, there was an increase in the first postoperative evaluation time point (T1), corroborating with Desborough (2000), who reported that the magnitude of the metabolic response may be attributed to the perception of pain and intensity of the surgical trauma, with cortisol concentrations increasing in a sustained manner during the beginning of the surgery until the maximum of 4 to 6 hours. This increase was more strongly evidenced in CC, while in the other groups, which received an anaesthetic block or underwent a low magnitude trauma procedure, the increase was less expressive, demonstrating that pain may be the cause of cortisol increase.

The results of the variables of animals from the control video-assisted group (CV) were similar to those of the blockade groups (BC and BV). This similarity is attributed to the less invasiveness of the video-assisted surgical procedures, which promote less somatic stimulation since both the surgical incision as the tissue damage of the skin and musculature are significantly smaller when compared to the celiotomy. This data corroborates with comparative studies between conventional and video-assisted OVHs using two-port, concluding that video-surgery promotes lesser pain and surgical stress (Case et al. 2015; Dalmolin et al. 2016).

Metamizole is widely used for acute postoperative pain treatment of moderate to severe intensities. Pohl et al. (2014) reported that the use of metamizole combined with hyoscine N-butylbromide as an analgesic protocol provided adequate analgesia for dogs submitted to videolaparoscopic OVH but not for those undergoing celiotomy. The present study obtained similar results. Although there was an increase in the pain scores of all the groups in the first postoperative hour, the threshold score requirement for analgesic rescue was not reached by any group, except by CC.

According to the literature, the latency period of intravenous metamizole is about 30 minutes (Nikolova et al. 2013). In this study, it was inferred that the onset of effect of this drug occurred within this period in all groups. However, a residual anaesthetic and tranquilizer effect in the first postoperative hour may have interfered in the evaluation of pain, increasing the scores by the behavioural factor. The CC scores were attributed to the non-administration of anaesthetic blockade and to the more invasive procedure in the animals of this group. Probably, the isolated therapy with metamizole is inefficient for controlling pain given this intensity of nociceptive stimuli.

Conclusion

The present study concludes that 2 mg kg^{-1} of 0.5% bupivacaine administered in infiltrative blockade at the incision line combined with the postoperative administration of metamizole and hyoscine N-butylbromide, constitutes a suitable multimodal postoperative protocol for OVH performed by both celiotomy and the video-assisted techniques.

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Table 1. Correlation between pain scores obtained by VAS and MPS.

Comparison between scales	**r**	CI
BC_{VAS} vs. BC_{MPS}	0.7417	[0.32, 0.91]
CV_{VAS} vs. CV_{MPS}	0.2684	[-.33, 0.71]
BV_{VAS} vs. BV_{MPS}	-0.148	[-0.64, 0.43]

The presented values refer to Pearson coefficient two-by-two. Values are sample correlation and intervals to 95% of confidence. CI: confidence interval; BC_{VAS}: Blocking celiotomy group evaluated by Visual Analogue Scale; BC_{MPS}: Blocking celiotomy group evaluated by Melbourne Pain Scale; CV_{VAS}: Control video-assisted group evaluated by Visual Analogue Scale; CV_{MPS}: Control video-assisted group evaluated by Melbourne Pain Scale; BV_{VAS}: Blocking video-assisted group evaluated by Visual Analogue Scale; BV_{MPS}: Blocking video-assisted group evaluated by Melbourne Pain Scale.

Table 2. Mean pain scores of the four groups on the visual analogue scale (VAS) or the Melbourne Pain Scale (MPS) of dogs submitted to ovariohysterectomy by celiotomy or video-assisted surgery in different time points of evaluation.

	VAS				MPS			
	CG		BG		CG		BG	
Time (h)	CC	CV	BC	BV	CC	CV	BC	BV
1	3.03[a]	1.85[b]	3.20[a]	2.52[ab]	7.33[a]*	3.85[b]	3.78[b]	1.62[c]
2	2.82[a]	1.48[c]	2.32[ab]	2.11[b]	5.38[a]*	2.09[b]	2.28[b]	1.13[b]
3	2.38[a]	1.34[b]	1.96[a]	2.12[a]	2.71[a]	2.19[a]	2.44[a]	1.32[b]
4	1.88[b]	1.21[c]	1.76[b]	2.51[a]	1.86	1.76	1.50	1.72
5		0.80[b]	1.71[a]	1.89[a]		1.39	2.00	1.58
6		0.77[b]	1.75[ab]	1.89[a]		1.83[a]	1.11[b]	1.38[a]
7		0.87[b]	1.73[a]	1.98[a]		1.83	2.17	1.60
8		0.48[b]	1.63[a]	1.85[a]		1.78	1.50	0.87
12		0.62[b]	1.69[a]	1.99[a]		2.78[a]	1.56[b]	2.29[b]
18		0.52[b]	1.51[a]	1.40[a]		1.67	1.44	2.11
24		0.35[b]	1.25[a]	1.20[a]		2.78[a]	1.11[b]	2.16[b]
36		0.42[b]	1.14[a]	1.15[a]		2.05[ab]	2.28[a]	1.39[b]
48		0.31[b]	0.97[a]	0.90[a]		2.94[a]	1.67[b]	1.49[c]
Means		1.74	1.91	0.85		1.81	2.23	1.59
Confidence		[1.3; 2.1]	[1.5; 2.3]	[0.5; 1.1]		[1.5; 2.1]	[1.8; 2.6]	[1.3; 1.9]

[a,b,c] Different letters in the same line demonstrate significantly statistical difference in t-test at 5% level of significance.

* Administration of rescue analgesia.

CG: Control groups; BG: Blocking groups. CC: Control Celiotomy group; CV: Control video-assisted group; BC: Blocking celiotomy group; BV: Blocking video-assisted group.

Table 3. Means of serum glucose and cortisol of the four groups of bitches submitted to conventional and video-assisted ovariohysterectomy.

	Glucose					Cortisol				
	CG		BG			CG		BG		
Time (h)	CC	CV	BC	BV	p-value	CC	VC	BC	BV	p-value
0	88.29	85.86	89.67	115.63		3.93	2.74	4.71	4.60	
1	157.14	127.71	125.16	129.28	0.44	12.64	5.5	7.94	5.81	0.05
6		104.33	108.83	116	0.34		2.38	3.64	2.66	0.29
12		95.33	98.16	101.14	0.47		2	2.11	2.29	0.91
24		89.83	102.5	99.28	0.18		1.83	1.81	2.01	0.88
48		91.33	104.5	99.14	0.08		2.86	1.98	2.78	0.68

Values are expressed as median (range) and analysed by Kruskal-Wallis test at 5% of significance.

CG: Control groups; BG: Blocking Groups. CC: Control Celiotomy group; CV: Control video-assisted group; BC: Blocking celiotomy group; BV: Blocking video-assisted group.

CONSIDERAÇÕES FINAIS

Com esse trabalho podemos afirmar que bupivacaína a 0,5% na dose de $2mg.kg^{-1}$, administrada para bloqueio na linha de incisão ou na estrada dos portais, juntamente com a associação de dipirona e N-butilescopolamina IV constitui um protocolo de analgesia multimodal pós operatória adequada para as técnicas de OVH por celiotomia ou videoassistida.

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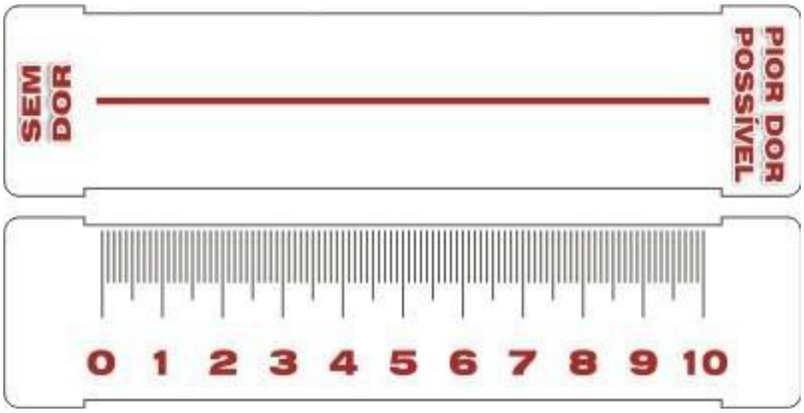
ANEXOS

Anexo A - Escala Visual Analógica (EVA). Linha reta horizontal de 100mm de comprimento, que descreve a intensidade dolorosa, variando entre nenhuma dor e pior dor possível, em cada uma das extremidades



Anexo B - Escala da Universidade de Melbourne, adaptada por Firth & Haldane (1999)

Observação	Score	Características
FC	1	> 20% valor basal
	2	> 50% valor basal
	3	> 100% valor basal
F	1	> 20% valor basal
	2	> 50% valor basal
	3	> 100% valor basal
PAS	1	> 20% valor basal
	2	> 50% valor basal
	3	> 100% valor basal
Temperatura retal	1	Acima do valor basal
Salivação	2	
Pupilas dilatadas	2	
Resposta à palpação	0	Normal
	2	Reage/ Protege a ferida no momento do toque
	3	Reage/ Protege a ferida antes do toque
Atividade	0	Dormindo
	0	Semiconsciente
	1	Acordado
	0	Alimenta-se
	2	Agitado
	3	Mudanças contínuas de posição, mutilação
Status mental	0	Dócil
	1	Amigável
	2	Cauteloso
	3	Alerta
Postura	2	Protege a área afetada
	0	Decúbito lateral
	1	Decúbito esternal
	1	Sentado ou em pé, cabeça elevada
	2	Em pé, cabeça baixa
	1	Movimenta-se
	2	Postura anormal
Vocalização	0	Não vocaliza
	1	Vocaliza quando tocado
	2	Vocalização intermitente
	3	Vocalização contínua