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Intraperitoneal lidocaine hydrochloride for prevention of intraperitoneal adhesions following laparoscopic genitourinary tract surgery in ewes

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ABSTRACT: Adhesion formation involving the genitourinary tract is common following laparoscopic procedures. To evaluate the effectiveness of intraperitoneal lidocaine hydrochloride 1% solution for the prevention of abdominal adhesions, twenty four Santa Ines ewes submitted to laparoscopic ovum pick-up, uterine puncture and local rinsing, were randomly distributed into two groups of 12 animals, according to rinsing solution: normal saline (SG) or 1% lidocaine hydrochloride solution (LG). Laparoscopy for manipulation of the reproductive tract (uterine puncture trauma model and ovum pick-up) was applied. A standard laparoscopic approach using three ports in triangulation was employed. The uterus and ovaries were rinsed at the end of the procedure (using either saline or lidocaine hydrochloride) for removal of blood clots from the ovaries and uterine horn surfaces. Inflammation was assessed postoperatively by plasma fibrinogen, and all animals underwent a second laparoscopic procedure 21 days after surgery for macroscopic assessment of adhesion formation. Four cases of adhesion were observed in each group. The plasma fibrinogen did not differ between groups and among different time points, indicating an absence of systemic inflammation following laparoscopic procedures. There were no significant differences between treatments. Both normal saline and 1% lidocaine hydrochloride were similarly effective in the prevention of adhesion formation.

Keywords: reproduction; endosurgery; ovary; uterus; laparoscopic; sheep

List of abbreviations

ET = embryo transfer, **LOPU** = laparoscopic ovum pick-up**, LAI** = laparoscopic artificial insemination**, LG** = lidocaine group, **SG** = normal saline (0.9% NaCl) group

Endosurgery is a minimally invasive procedure that greatly improves the success of reproduction biotechnologies, such as artificial insemination, embryo transfer and ovum pick-up in small ruminants (Teixeira et al. 2013; Cordeiro et al. 2014).

Adhesion formation involving the genitourinary tract is common following procedures such as laparoscopic artificial insemination (LAI), embryo transfer (ET) and laparoscopic ovum pick-up (LOPU). Formation of adhesions may affect convalescence and future production and reproduction of the animals with high genetic potential (Teixeira et al. 2011; Ward and Panitch 2011). Adhesions occur due to peritoneal inflammation following surgical manipulation or infection, leading to an imbalance between fibrin deposition and degradation. Fibrinous exudate may be reabsorbed by the animal without adhesion formation or reorganize follow-

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ing migration of fibroblasts, becoming permanent fibrosis (Arung et al. 2011; Ward and Panitch 2011).

Laparoscopic procedures of the genitourinary tract in small ruminants result in decreased trauma. Thus, local rinsing using normal saline is usually effective for preventing adhesion formation following LOPU (Teixeira et al. 2011; Teixeira et al. 2013). Lidocaine rinsing solution revealed promising results in rats with respect to the prevention of intraperitoneal adhesion formation, possibly due to modulation of oxidative stress, in an experimental peritonitis model (Brocco et al. 2008; Yuzbasioglu et al. 2008).

Therefore, the purpose of this study was to compare local rinsing with normal saline or a 1% lidocaine hydrochloride solution for the prevention of intraperitoneal adhesion formation in ewes which had undergone laparoscopic ovum pick-up and uterine puncture.

MATERIAL AND METHODS

Animals and treatment. Twenty four Santa Ines adult multiparous ewes, 3.1 ± 1.1 years old, weighing 35.1 ± 6.2 kg and exhibiting a mean body score of 3 (range 1–5), were used. The animals received a balanced diet twice a day and *ad libitum* water and mineral salt.

The animals were distributed randomly and assigned to one of two treatments following laparoscopic ovum pick-up and uterine puncture: rinsing the ovary and uterus with normal saline (SG, $n = 12$) or with a 1%lidocaine hydrochloride solution (LG, $n = 12$).

Anaesthesia and laparoscopic procedures. Following a 36-hour food and water fast, the animals were anaesthetised. Premedication consisted of 0.5 mg/kg of chlorpromazine (Clorpromazina®, Uniao Quimica, Sao Paulo, Brazil) and 4 mg/kg tramadol (Cloridrato de Tramadol®, Hipolabor, Sabara, Brazil), in combination, intramuscularly. After 10 min, general anaesthesia was induced using a combination of 5 mg/kg of ketamine (Dopalen® Sespo, Paulinia, Brazil) and 0.2 mg/kg midazolam (Dormire®, Cristalia, Itapira, Brazil), intravenously. Following orotracheal intubation, anaesthesia was maintained using the combination of ketamine (10 mg/kg/h) and midazolam (0.2 mg/kg/h) in constant rate infusion, administered in normal saline, and delivered at 10 mg/kg/h.

After patient positioning and aseptic preparation of the abdomen, a three port laparoscopic access was established, as well as CO_2 pneumoperitoneum, as reported previously (Teixeira et al. 2013).

The reproductive tract was manipulated using laparoscopic atraumatic Babcock forceps. The ovaries were grasped and the follicles were aspirated using a transabdominal needle (18 G). For simulation of uterine manipulation as required for embryo recovery and artificial insemination, the right uterine horn was grasped and three punctures were performed using the same needle used for OPU.

At the end of the procedure, equal volumes (0.6 ml/kg) of either normal saline or 1% lidocaine solutions were used to assist removal of blood clots from the surface of the ovaries and uterus to prevent adhesion formation. The trocars were withdrawn and the wounds were closed routinely using nylon 2-0 and an ointment was used for wound care (Unguento Plus®, Pearson, Brazil). Anaesthetic recovery was monitored until the animals were able to stand and walk without any aid. For pain control, tramadol (2 mg/kg, intramuscularly, BID, for three days), as well as penicillin-streptomycin association (Penfort PPU®, Ourofino, Cravinhos, Brazil) were administered in a single dose, according to the manufacturer's recommendations.

Postoperative assessment. Systemic inflammation was assessed by sampling plasma fibrinogen and performing a haemogram before surgery, immediately after the operation, and 2, 4, 6, 8, 10, 12, 14 and 16 days after surgery. The animals underwent a second laparoscopic procedure on the 21st postoperative day for macroscopic assessment of adhesion formation. Adhesions were scored according to presence, number, dimensions and organs involved.

Data analysis. All data were analysed using a Kolmogorov normality test and are presented as the mean ± standard deviation. Plasma fibrinogen was assessed using the ANOVA one-way for multiple comparisons and Tukey post-hoc test. The presence of adhesions was compared between groups using the Chi-squared test. Differences were considered significant if $P < 0.05$. The software R™ was used for all statistical analysis.

RESULTS

There were no adhesions on the right uterine horn in the LG, and in SG, one ewe developed an adhe-

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sion between the uterine horn and the respective ovary (8.3%), which could hinder new manipulations and ovum sampling. There were four instances of mild adhesions on the ovaries in the ewes of LG (33.3%) and in three of SG (25.0%). In both cases, there was a single adhesion, which involved the mesovarium, broad ligament and oviduct. Thus, there was no difference between groups.

The levels of plasma fibrinogen remained within the normal range (100 to 500 mg/dl) for all sheep post-operatively.

DISCUSSION

The absence of significant uterine and ovarian adhesions in both groups and the presence of only single mild adhesions highlight the invasive nature of laparoscopic reproductive tract manipulation. Strict adherence to meticulous surgical technique can ensure that adhesion formation occurrence remains below what is expected for ovine species (Teixeira et al. 2011).

Due to their close relationship to other peritoneal surfaces, the ovaries are the most common site of intraperitoneal adhesion formation associated with endoscopic procedures (Pittaway et al. 1985). Another study reported the occurrence of intraperitoneal adhesions on the reproductive tract of 15% of goats following ovum pick-up, even though the organs were rinsed with heparin solution following surgery (Cordeiro et al. 2014). Unilateral and bilateral ovarian adhesions were reported in ewes following 10 sessions of laparoscopic OPU, which were performed at seven-day intervals (Stangl et al. 1999).

Both normal saline and 1%lidocaine hydrochloride solution were effective in preventing intraperitoneal postoperative adhesion formation. Although adhesions formed over the ovaries, those were considered easy to dissect and irrelevant for repeated OPU. The use of other anti-adhesion therapies, such as a heparin-based one (Baldassarre and Karatzas 2004; Cordeiro et al. 2014) or carboxymethylcellulose solutions (Ewoldt et al. 2004) have been recommended; however, even these solutions were not fully efficient in preventing adhesions.

High plasma fibrinogen levels indicate a systemic inflammatory response in ruminants (Meyer et al. 1995). In this study, no significant variations were found in plasma fibrinogen levels when compared to the normal range for the ovine species (Jain 1993), corroborating similar findings in another trial involving ewes undergoing laparoscopic procedures (Mariano et al. 2014).

In a rat septic peritonitis model, lidocaine hydrochloride solution was an effective prophylaxis against adhesion, probably due to blocking the development of oxidative stress (Brocco et al. 2008, Yuzbasioglu et al. 2008; Arung et al. 2011; Ward and Panitch 2011). In another study, lidocaine was effective for the treatment of peritonitis, while NaCl 0.9% minimally affected adhesion formation (Gallos et al. 2004). In the present study, both normal saline and lidocaine rinsing solutions were equally effective in adhesion prevention. It is important to note that laparoscopic manipulation of the reproductive tract resulted in less surgical trauma, thus naturally leading to decreased adhesion formation. Therefore, the lidocaine-based rinsing solutions should be investigated in severe reproductive tract trauma models in order to determine their real potential for the prophylaxis of postoperative intraperitoneal adhesion formation.

Both normal saline and 1%lidocaine hydrochloride rinsing solutions can be employed to avoid adhesion formation in ewes undergoing endoscopic reproductive procedures.

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