Theriogenology 107 (2018) 211–218

Contents lists available at ScienceDirect

Theriogenology

journal homepage: www.theriojournal.com

The precision of predicting the time of onset of parturition in the bitch using the level of progesterone in plasma during the preparturient period

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ARTICLE INFO

Article history:
Received 13 August 2017
Received in revised form
12 November 2017
Accepted 13 November 2017
Available online 14 November 2017

Keywords:
Progesterone
Parturition
Bitch

ABSTRACT

Precise prediction of the time of onset of parturition in the bitch is of clinical importance. Many parturition management cases in clinical practice are presented in the last two weeks of pregnancy without a reliable estimate of the parturition date. The aim of this study was to assess the value of a single progesterone level in the blood plasma from a preparturient bitch to predict the time of onset of parturition. The temporal relationship between the decrease in the plasma progesterone levels and the time of cervical dilatation (TCD)—which correlates to the onset of stage 1 of parturition—was evaluated in 25 bitches in the preparturient period. Among bitches destined to reach TCD within 12 h there is a 2% probability of having a plasma progesterone level of 15.8 nmoL/L or above and a 6% probability of having a level of 8.7 nmoL/L or above. Conversely, if the level is below 8.7 nmoL/L there is a 99% probability of reaching TCD within 48 h and if the level is below 3.18 nmoL/L there is a 100% probability of reaching TCD within 24 h. These results allow the veterinary obstetrician to make prompt decisions in the management of parturition.

1. Introduction

Predicting the time of onset of spontaneous parturition in the bitch in late gestation is clinically important. The time spent observing parturition may be drastically shortened if one can accurately predict a particular interval wherein the bitch is either very likely or very unlikely to enter spontaneous parturition.

The onset of parturition (the first stage of parturition) is characterized by the dilatation of the cervix which also signals readiness for caesarean section (CS) [1]. Because the behavioral signs associated with early stage 1 of parturition may be variable [2], cervical dilatation offers a reliable and objective indicator of onset of the first stage of parturition. Following the first stage are the second and third stages, during which the fetuses and the placentas are delivered.

The majority of bitches presented in late gestation for parturition management are ones for which only mating dates are available. Mating dates are of no help in predicting parturition dates [3–6]. In late pregnancy it was concluded that the biparietal diameter was most accurate in predicting gestational age and that the crown rump length may be difficult to measure because of fetal flexion and fetal lengths that exceed the size of the ultrasound image [7–9]. A study involving English bulldogs suggested that caesarean sections (CSs) can be scheduled safely when the fetal biparietal diameter has reached a value of 29.5 mm or above [10]. Further studies are required to establish whether it is routinely safe to time CS based on methods involving gestational age estimation in dogs by ultrasonographic assessment of fetal biometric measurements.

Progesterone appears thermogenic in the dog [11] but the effect may be variable [12–17] and some bitches may not demonstrate a detectable preparturient decrease in rectal temperature even when monitored three times daily [18]. It may therefore be concluded that the preparturient temperature decrease can give important clues but that it is not accurate or reliable enough to use as sole predictor of the time of parturition or indicating fetal maturity and safety for intervention by CS.

The level of progesterone in blood plasma or serum (PL) decreases prior to parturition [19–21]. The usefulness of PL in

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https://doi.org/10.1016/j.theriogenology.2017.11.018
0093-691X/

predicting the TCD requires further investigation.

It is safe to perform a CS once the cervix has dilated [1]. The time of onset of spontaneous cervical dilatation (TCD), corresponds to the time of onset of the first stage of spontaneous parturition and therefore it would be helpful if there were a method to predict TCD in bitches that are in the preparturient period.

The aim of this study was to assess the value of a single PL from a preparturient bitch to predict TCD.

2. Materials and methods

The protocol was approved by the Animal Ethics Committee of the Faculty of Veterinary Science, University of Pretoria, (Onderstepoort, South Africa) (protocol number V010/14).

2.1. Bitches

The experimental animals were all English bulldog and Boerboel bitches presented to a private veterinary clinic for routine estrus observation, artificial insemination and elective CS. The decision to plan an elective CS was based on breed in the case of English bulldogs and on the history of previous dystocia, puppy losses and CS in Boerboels. All bitches weighed more than 20 kg. All owners declined an attempt to allow the bitches to undergo spontaneous unassisted parturition. The current study included 28 bitches (12 English bulldog and 16 Boerboel). All bitches used in the current study were well habituated, used to travelling, showing and residing at the obstetric clinic for purposes of artificial insemination and management of parturition. Bitches that were combative or resisted the minimal restraint required to collect blood were not included in the study. All experimental animals were housed and fed commercial dry pellets twice daily with ad-lib water.

2.2. Collection of specimens and data

During pro-estrus and estrus, vaginal speculum examinations and vaginal smears were made once daily to establish the first day of cytological diestrum (D0), using the criteria set out by Holst and Phemister (1974). An ultrasound examination was performed between D26 (26 d after the onset of D0) and D35 to confirm pregnancy and identify bitches carrying a singleton. In the preparturient period, starting at D54, each bitch was admitted for parturition management and if a small litter was suspected, a radiograph was taken to confirm litter size and exclude singleton pregnancies from the study. On the day of admission, a central venous catheter (18 gauge, 20 cm in length, Catalogue Number 04218, Arrow International, Pennsylvania, USA) was instilled in their jugular vein and heparinized blood was collected every 6 h at 6:00, 12:00, 18:00 and 24:00, with the last collection at TCD. Immediately before each blood collection, a Perspex tubular speculum (22 mm outer diameter, 17 mm inner diameter, length 280 mm) was passed into the vagina to determine whether the cervix had dilated. A cold light source was used to illuminate the speculum. In cases where mucus in the anterior vagina obscured viewing the cervix, the mucus was suctioned using a Perspex bovine insemination pipette and a 20 ml syringe. In 16 bitches that showed signs of first-stage labor a vaginal speculum examination was performed less than 5 h after the last scheduled examination and revealed that cervical dilatation had begun. In these 16 bitches, the blood sample at TCD was collected more than 1 h before the next scheduled time. Once at TCD, a bitch was considered ready for immediate CS. TCD identified the day and time of onset of spontaneous parturition.

The blood was immediately transferred to a 10-ml green-stoppered heparinized glass vial (BD Vacutainer® (170 IU lithium heparin), BD Plymouth, UK) and was centrifuged within 30 min after collection, following which it was transferred to 1.8 ml cryo vials (Catalogue number 750273, PlastPro Scientific, Edenvale South Africa), labelled and frozen at −20 °C until analyzed.

The levels of progesterone and cortisol were determined in each plasma sample, using the Coat-A-Count® radioimmunoassay (Siemens Health Care Diagnostics Inc. Los Angeles, CA 90045 USA) for each hormone. This assay has been validated for dog plasma [22] and used to determine the progesterone level (PL or PLs for progesterone levels) in the serum or plasma of bitches for decades [23–28] and for cortisol assays [29–31].

All determinations of PL and cortisol were done in duplicate (two replicates simultaneously done in the same assay). The intra-assay coefficient of variation was determined for the PLs of the two replicates of each sample. The levels of cortisol of 19 plasma samples were each determined in two assays and the mean level of each sample in each assay used to determine the interassay coefficient of variation.

Six plasma samples from peri-estrous bitches—two of which had PLs between 2 nmoL/L and 4 nmoL/L, two had PLs between 13 nmoL/L and 14 nmoL/L and two had PLs between 22 nmoL/L and 23 nmoL/L—were each analyzed in six or seven different assays and the interassay coefficient of variation calculated.

2.3. Data analysis

Data of bitches carrying more than one fetus and on which a CS was performed once cervical dilatation was first noticed were used for analysis.

2.3.1. General investigation of the pattern of change, and variability of progesterone levels during the preparturient period

A set of line graphs were compiled showing the PL at each of the six-hourly measurements prior to TCD in each bitch and the pattern of change in individual bitches and the variability among bitches visually appraised.

We used a mixed-effect regression with progesterone level as response variable, time before cervical dilation and breed as covariates and bitch as random effect. The interaction between the covariates was also included in the model. This analysis was done on 272 progesterone levels, excluding the 25 at the time of onset of cervical dilatation in each bitch, because these 25 were only measured after vaginal speculum examination had confirmed the onset of cervical dilatation.

2.3.2. Selecting the progesterone level that would best predict the time to cervical dilatation

2.3.2.1. Identifying possible cross points. A scatterplot of PL against time was generated, where time represents the time until cervical dilatation was first noted (TCD), which was denoted time zero. Progesterone level was plotted on the y-axis, with PL increasing with height on the axis. Time was plotted on the x-axis, with Time zero on its right extreme and the time most distantly preceding Time zero on its left. Vertical lines on the graph are referred to as time lines and horizontal lines as PL lines. The point where a time line and a PL line cross we termed a cross point. All PLs from each of the 25 bitches were plotted on the scatterplot.

Ignoring the PLs at Time zero—by which time the cervix had started to dilate—the scatterplot (Fig. 2) was visually inspected and subjectively appraised for a pattern of change of PL over time. Given the downward trend in PL as time zero approached, a search for possible cross points was done.

Either of two criteria defined useful cross points. The first was that the top right quadrant (the zone above or on the PL line through the cross point and to the right of or on the time line through it) should have as few as possible of the PLs on the