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DETERMINATION OF GESTATIONAL TIME AND PREDICTION OF PARTURITION IN DOGS AND CATS: AN UPDATE

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Summary

Accurate prediction of delivery date in canine and feline allows a better management of parturition, reducing the loss of neonates. This review evaluates the most common methods adopted to accurately predict the day of delivery: determination of ovulation and hormonal assays, first appearance of embryonic/foetal structures using ultrasound or radiography, echographic measurement of extra-foetal and foetal structures, or evaluation of foetal flux and heart rate. Determination of ovulation and hormonal assays at the time of breeding and close to pregnancy term is widely used to predict parturition in dogs (Concannon et al. American Journal of Veterinary Research 44, 1983, 1819; Hayer et al. Journal of Reproduction and Fertility, Suppl. 47, 1993, 93; Hase et al. Journal of Veterinary Medical Science, 62, 2000, 243; Kutzler et al. Theriogenology, 60, 2003a, 1187). In cats, some studies have been carried out, but no hormonal parameters for accurate prediction of parturition have been described so far (Buff et al. Journal of Reproduction and Fertility, Suppl. 57, 2001, 187; De Haas van Dorsser et al. Biology of Reproduction, 74, 2006, 1090; DiGangi et al. Journal of the American Veterinary Medical Association, 237, 2010, 1267; Dehnhard et al. Theriogenology, 77, 2012, 1088). Many studies suggested that gestational timing can be obtained by observation using ultrasound or radiography of specific structures in relation to the time of appearance during gestation (Concannon and Rendano American Journal of Veterinary Research, 44, 1983, 1506; Rendano et al. Veterinary Radiology, 25, 1984, 132; Shille and Gontarek Journal of the American Veterinary Medical Association, 187, 1985, 1021; Davidson et al. Veterinary Radiology, 27, 1986, 109; England et al. Journal of Small Animal Practice, 31, 1990, 324; Yeager et al. American Journal of Veterinary Research, 53, 1992, 342; Zambelli et al. Theriogenology, 57, 2002a, 1981; Zambelli et al. Journal of Feline Medicine and Surgery, 4, 2002b, 95; Zambelli and Prati 2006; Lopate Theriogenology, 70, 2008, 397; Davidson and Baker Topics in Companion Animal Medicine, 24, 2009, 55). Ultrasonographic measurement of extra-foetal and foetal structures is a common and accurate

method for the prediction of parturition day during pregnancy, when specific formulae are used depending on the ultrasonographic parameter, the species and, in canines, the size of the bitch (Shille and Gontarek Journal of the American Veterinary Medical Association, 187, 1985, 1021; England et al. Journal of Small Animal Practice, 31, 1990, 324; Luvoni and Grioni Journal of Small Animal Practice, 41, 2000, 292; Luvoni and Beccaglia Reproduction in Domestic Animals, 41, 2006, 27; Lopate Theriogenology, 70, 2008, 397; Michel et al. Reproduction in Domestic Animals, 46, 2011, 926; Beccaglia and Luvoni Reproduction in Domestic Animals, 47, 194, 2012). Recent studies demonstrated that in dogs, the imminence of parturition could be predicted by evaluating foetal flux and foetal heart rate by ultrasound (Gil et al. Theriogenology, 82, 2014, 933; Giannico et al., Animal Reproduction Science, 154, 2015, 105). For an accurate prediction of parturition date, the combination of different methods is desirable.

Introduction

Loss of newborns at the time of parturition, due to an incorrect delivery management, can be considered both as a loss of pets and as a subject of potential importance, when coming from highly selected parents. Parturition is a critical event, and the possibility to accurately predict it allows a better planning of breeder and veterinarian activity, for assistance of the whelping female to reduce the peripartum losses of offspring. In the last decades, many studies have been published regarding the determination of gestational age and the prediction of delivery date in dogs and cats. Methods proposed can be divided into four main groups:

1. determination of ovulation and hormonal assays;
2. first appearance of embryonic/foetal structures using ultrasonographic or radiographic examination;
3. ultrasonographic measurement of extra-foetal or foetal structures;
4. ultrasonographic evaluation of foetal flux or heart rate.

Determination of ovulation and hormonal assays.

In dogs, parturition occurs 65 ± 1 days after LH peak and 63 ± 1 days after ovulation (Concannon, Whaley, Lein, & Wissler, 1983). However, both the detection of LH peak and the ultrasonographic identification of ovulation may be unpractical, because of the necessity of daily determinations (Hase, Hori, Kawakami, & Tsutsui, 2000; Hayer, Günzel-Apel, Lüerssen, & Hoppen, 1993). Nevertheless, LH peak and ovulation can be indirectly determined by progesterone rise. It has been demonstrated that serum progesterone ranges between 2 and 3 ng/ml during LH peak and between 4 and 10 ng/ml during ovulation (Kutzler, Mohammed, Lamb, & Meyers-Wallen, 2003a). Progesterone concentration decreases below 2 ng/ ml approximately 24 hr before parturition (Concannon, Butler, Hansel, Knight, & Hamilton, 1978), and it can be indirectly recognized by the drop in body temperature (Geiser, Burfeind, Heuwieser, & Arlt, 2014; Johnston, Root Kustritz, & Olson, 2001a). If compared with other domestic animals, in the physiology of reproduction, cats are characterized as inducer ovulatory because ovulation is induced by coitus and an unknown number of matings is necessary to induce the LH peak; there is not the pre-ovulatory luteinization of the follicular granulosa cells, thus progesterone rises only after the occurrence of ovulation. At term, progesterone concentration declines only after parturition. For these reasons, in cats, progesterone assay cannot be used neither during oestrus, nor close to parturition to predict the day of ovulations and delivery date, respectively (Johnston, Root Kustritz, & Olson, 2001b). Measurement of relaxin hormone concentration has been used for pregnancy diagnosis between 19 and 28 days after LH surge in dogs and between 20 and 35 days after mating in cats (Buff, Fontbonne, Lopez, Rauer, & Crevat, 2001; De Haas van Dorsser, Swanson, Lasano, & Steinetz, 2006; DiGangi, Griffin, Levy, Smith, & Baker, 2010). However, this does not allow an accurate gestational timing. In some wild felids, the determination of faecal prostaglandin metabolite (PGFM) has been proposed for pregnancy diagnosis between 35 and 41 days after mating. This metabolite increases in concentration starting from 30 to 41 days after mating, it reaches a peak (2.1 μg/g faeces and 7.8 μg/g faeces in sand cat and fishing cat, respectively) 3–5 days before parturition and, after it begins to decrease reaching basal level within few days after parturition (Dehnhard et al., 2012). However, the use of PGFM levels to predict delivery day might be unreliable because of normal variations during gestation. In the canine species, the identification of the onset of dioestrus, through daily vaginal cytology after mating, has been used to predict the parturition. This occurs approximately 57 ± 1 days after the transitional smear from a cytological pattern characterized by a high number of keratinized cells to a pattern with predominance of basal and parabasal cells and leucocytes (Concannon, 2000).

First appearance of embryonic/foetal structures using ultrasonographic or radiographic examination.

Gestational timing can be based on the evaluation of the first appearance of specific embryonic and foetal structures using ultrasonography or radiography (Concannon & Rendano, 1983; Davidson, Nyland, & Tsutsui, 1986; England, Allen, & Porter, 1990; Lopate, 2008; Rendano, Lein, & Concannon, 1984; Shille & Gontarek, 1985; Yeager, Mohammed, Meyers-Wallen, Vannerson, & Concannon, 1992).

In the canine species, the anechogenic gestational sac can be detected on day 18 after ovulation; the embryo, with heartbeat, is first detected as an oblong structure apposed to the uterine wall in the chorionic cavity on day 23. Between days 27 and 31 after ovulation, the embryo becomes bipolar in shape and limb buds can be detected. The deep portion of diencephalo-telencephalic vesicle (DPTV), an anechogenic area in the foetal head representing the thalamus and basal nuclei primordia, can be first visualized between day 29 and 33. The first detected abdominal viscera are the stomach and the urinary bladder on day 29–33 and 31–35, respectively. The skeleton is visualized as a hyperechoic structure on day

29–33 after ovulation, and foetal movements are observed on day 32–34. On day 34–36, the abdomen and thorax are distinct; the lung is hyperechoic, compared with the liver, that appears hypo-echoic, compared with the rest of the abdomen on day 35–38. The kidneys are first visualized on day 41–43 (Beccaglia & Luvoni, 2004). The bowel is considered the last organ to be identified by ultrasonography in the canine foetus, around 57–63 days of gestation (Gil, Garcia, & Froes, 2015). Even if the visualization of the bowel and the identification of peristaltic contractions observed by ultrasound indicate the end of foetal organogenesis, authors agree that these features should not be used as the sole parameters indicating that the foetus is full term. Daily foetal monitoring combined with the evaluation of oscillations of foetal heart rate is considered a more reliable predictor of day of parturition (Gil et al., 2015). In felines, the first ultrasonographic pregnancy detection is as early as 10 days after mating (Davidson & Baker, 2009; Zambelli, Castagnetti, Belluzzi, & Bassi, 2002a; Zambelli, Caneppele, Bassi, & Paladini, 2002b; Zambelli and Prati 2006). The embryo may be visualized around 14 days of pregnancy, and on day 17, it appears with the characteristic C-form. The first identification of urinary bladder and stomach, kidney and bowel is, respectively, approximately 30, 39 and 40 days of gestation (Zambelli and Prati 2006). Determination of gestational age has been also attempted by radiographic examination, through the identification of the degrees of foetal mineralization and the first appearance of different foetal skeletal structures (Haney, Levy, Newell, Graham, & Gorman, 2003; Rendano, 1983; Rendano et al., 1984). The mineralization of structures occurs earlier in cats than in dogs (Haney et al., 2003; Lopate, 2008) in which the bone structures characterized by the narrowest period of mineralization are the humerus at 20 ± 1 day (range between 20 and 24 days) and femur at 21 ± 1 day (range between 19 and 23 days) prior to parturition (Boyd, 1971). Some other bones, like fibula, calcaneus and phalanges, mineralize only after birth. According to the literature, radiographs can provide a rough estimate of gestational age, but are not adequate to determine foetal maturity. A foetus may be completely mineralized as early as 58 days after the LH surge, but it would not survive if Caesarean section is performed at this stage (Concannon, 2000; Rendano, 1983; Rendano et al., 1984). Moreover, the application of a proper technique and an adequate patient restraint and preparation is of critical importance for a correct evaluation of the radiography. A single lateral radiograph of the abdomen is usually sufficient for pregnancy diagnosis and foetal counting, but a ventro-dorsal radiograph is more suitable to evaluate gestational age although with the aforementioned limitations (Concannon, 2000; Rendano, 1983; Rendano et al., 1984).

Ultrasonographic measurement of extra-foetal or foetal structures.

Ultrasonographic measurement of extra-foetal and foetal structures is a common and accurate method for the prediction of delivery date during pregnancy, even when the time of ovulation is unknown. During the first half of gestation (between 19 and 37 days after LH peak), measurements of gestational sac diameter (inner chorionic cavity, ICC or outer uterine diameter, OUD) or foetal crown-rump length (CRL) can easily be obtained. In the second half of pregnancy (after 37 days), foetal measurements of the biparietal diameter (BP) and body diameter (BD) can be used to predict the delivery date (England et al., 1990; Lopate, 2008; Luvoni & Beccaglia, 2006; Luvoni & Grioni, 2000; Michel, Spörri, Ohlerth, & Reichler, 2011; Shille & Gontarek, 1985). From days 35 to 58, the deep portion of the foetal diencephalon-telencephalic vesicle (DPTV) can be recognized as a symmetric anechoic area viewed on sagittal midline of the foetal head and its measurement could be useful to determine the gestational age (Beccaglia, Faustini, & Luvoni, 2008; Beccaglia & Luvoni, 2004). An accurate gestational timing in the first and second half of pregnancy is provided by ICC and BP parameters, respectively (Kutzler, Yeager, Mohammed, & Meyers-Wallen, 2003b; Lopate, 2008; Luvoni & Beccaglia, 2006; Michel et al., 2011). Specific formulae for ICC and BP are available for dogs of small (up to 10 kg) and medium size (11–25 kg) (Luvoni & Grioni, 2000). Some authors (Kutzler et al., 2003b) proposed the application in large size breeds of the equations elaborated for medium size dogs, using a correction factor (−2 days for bitches weighting > 40 kg) to increase the accuracy. The ICC and BP formulae for medium size dogs resulted in a good accuracy when applied to giant bitches (Socha, Janowski, & Bancerz-Kisiel, 2015). Prediction of delivery date by measurement of ICC and BP diameter is also possible in queens, and no differentiation based on body weight (i.e. small size breeds vs large size breeds) or phenotype (i.e. brachycephalic vs dolichocephalic) has been elaborated (Beccaglia & Luvoni, 2012). The maximum accuracy of the prediction is obtained when species-specific (canine or feline) and, in bitches, when size-related formulae (small and medium size) are used. The following equations are those previously published (Beccaglia & Luvoni, 2012; Beccaglia et al., 2008; Luvoni & Grioni, 2000) and daily used by the authors of the present review to obtain the days before parturition (DBP):

For bitches:

ICC in small size bitches: $\mathrm{DBP} = (\mathrm{mm} - 68.68)/1.53$;

ICC in medium size bitches: $\mathrm{DBP} = (\mathrm{mm} - 82.13)/1.8$;

BP in small size bitches: $\mathrm{DBP} = (\mathrm{mm} - 25.11)/0.61$;

BP in medium size bitches: $\mathrm{DBP} = (\mathrm{mm} - 29.18)/0.7$;

For queens:

ICC in queens: $\mathrm{DBP} = (\mathrm{mm} - 62.03)/1.1$;

BP in queens: $\mathrm{DBP} = (\mathrm{mm} - 23.39)/0.47$.

Although ICC and BP are both highly accurate for the prediction of delivery date, the accuracy can be affected by some elements: • gestational period in which the examination is performed. The estimation of gestational age in dogs is more precise during early pregnancy (before 35 days of gestation), than afterwards (England et al., 1990; Kim, Travis, & Meyers-Wallen, 2007; Kutzler et al., 2003b). In our previous study, we demonstrated that at week 5 of gestation in dogs and in cats, both ICC and BP are equally accurate at ±2 days (ICC: 85.9%; BP: 95.2%) (Beccaglia & Luvoni, 2012). The BP measurement maintains a high accuracy ±1 day (78.9%) up to week 6 of pregnancy; afterwards, a gradual decrease in accuracy is observed, but a good accuracy ±2 days (85.3%) is still maintained until week 8. Close to term (week 9) the accuracy ±1 day and ±2 days of the prediction obtained with BP measurement decreases to 50.9% and 69.8%, respectively (Beccaglia & Luvoni, 2012).

• *litter size*. In dogs, the accuracy obtained by ICC measurement is not affected by the number of embryonic vesicles. For the BP, a higher accuracy is obtained in normal litter size (2–6 pups and 5–9 pups in small and medium size dogs, respectively) than in small and large litters (Beccaglia & Luvoni, 2006). Recently, Gatel, Rault, Chalvet-Monfray, Saunders, and Buff (2015) proposed a formula for predicting delivery day in cats based on measurement of foetal femur length or biparietal diameter, taking into consideration also litter size, maternal body weight and maternal age. The study demonstrated that these parameters might affect the gestational length: larger litters, longer femurs and older queens are associated with shorter duration of pregnancy. In addition, the queen's weight before mating affects time to parturition, with heavier queens having longer gestation (Gatel et al., 2015).

• *breed variations*. Some breed variations in gestational length have been suggested, with German Shepherd (Okkens, Hekerman, De Vogel, & Van Haaften, 1993; Okkens et al., 2001) and Hound dogs (Eilts, Davidson, Thompson, Paccamonti, & Kappel, 2005) characterized by short pregnancies, and West Highland White Terriers showing long gestation lengths (Okkens et al., 1993, 2001). In Drever bitches, when litter size exceeds the average for the breed (pups per litter 6.81 ± 2.11), each additional puppy reduces gestation length by 0.25 day, and 0.25 day should be added to the due date for each puppy below breed average (Bobic Gavrilovic, Andersson, & Linde Forsberg, 2007).

Some authors proposed the elaboration of breed-specific formulae to further increase the accuracy of the prediction of the day of parturition (Groppetti, Vegetti, Bronzo, & Pecile, 2015).

Although in cats the overall mean gestation length is 65.1 days with 90.2% of values occurring between 63 and 67 days, some breeds like Oriental Shorthair and Siamese might show longer gestation (about 66 days), than others breeds like Korat (63 days) (Sparkes et al., 2006). Differently, Musters, de Gier, Kooistra, and Okkens (2011), using data from a questionnaire sent to breeders, observed that length of gestation is not influenced by breed group and parity, whereas it is increased in small litters.

Ultrasonographic evaluation of heart rate or foetal flux.

In human medicine, it is known that a variation in foetal heart rate (FHR) is connected to antepartum uterine contraction (Nageotte, 2015). In the canine species, it has been reported that FHR should be greater than 220 beats per minute (bpm), with FHR between 180 and 220 bpm indicate moderate foetal distress and values less than 180 bpm indicate severe foetal distress (Zone & Wanke, 2001). Recently, Gil, Garcia, Giannico, & Froes, 2014 observed that a variation of foetal heart rate occurs close to parturition. Although the precise moment of FHR variation could not be easily ascertained, an increment of FHR approximately 72 hr before parturition and an involvement of all foetuses within 6–1 hr antepartum, with a drop in FHR from 200–220 to 160–180 bpm, have been detected. However, because of the high number of Caesarean operations performed in this study and the lack of a tocodynamometric evaluation of the uterus, further observations are required for defining the close relationship between the parturition stage and the FHR trends. In dogs, the evaluation of foetal fluxes close to delivery and the analysis of their modifications to predict the imminent parturition were the aims of a recent study (Giannico, Gil, Garcia, & Froes, 2015). It has been proved that when umbilical artery resistivity index (RI) is less than 0.7 in all foetuses, the delivery will occur within 12 hr. As foetal distress could affect this value, the FHR variations should be measured at the same time.

Conclusions

Predicting parturition day has important practical applications, and for this purpose, a variety of methods can be used. Among these, indirect determinations of ovulation time at breeding in dogs and ultrasonographic measurements of extra-foetal and foetal structures in dogs and cats allow an accurate prediction of delivery, and the combination of different methods further increases its accuracy.

Author contributions

All authors contributed to collect and analyze the data. MB draft the paper. All authors have approved the final version.

Conflict of interest

None of the authors of this article has a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of the study.

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