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Calcium, parathyroid hormone, oxytocin and pH profiles in the whelping bitch

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Abstract

Despite the high prevalence of primary uterine inertia in whelping bitches, the underlying pathogenesis remains unclear. The objectives were to i) determine serum concentrations of total calcium, ionized calcium (iCa), parathyroid hormone (PTH), and blood pH in normally whelping bitches throughout the peri-parturient period; and ii) investigate relationships among iCa, PTH, and acid-base status, and the role that they and oxytocin may have in the underlying pathogenesis of canine uterine inertia. Bitches were randomly selected from a population of German Shepherd Dog bitches with a history of uncomplicated parturition (Group 1; $n = 10$), and from a population of Labrador bitches with a clinical history of an increased incidence of uterine inertia and stillbirths (Group 2; $n = 20$). Jugular blood samples were collected daily from -4 d to the onset of whelping (t = 0 h), and then every 4 h until the last pup was born. Overall, bitches from Group 2 had higher mean ± SEM serum concentrations of PTH (4.72 ± 2.45 pmol/L, $P < 0.001$), lower iCa (1.31 ± 0.08 pmol/L, $P < 0.05$), and higher venous pH (7.41 ± 0.03, $P < 0.005$) than bitches from Group 1 (2.9 ± 1.44 pmol/L, 1.38 ± 0.06 mmol/L, and 7.33 ± 0.02, respectively) during the periparturient period. However, there was no significant difference between Groups 1 and 2 for serum oxytocin concentrations during the periparturient period (45.5 ± 40 and 65.5 ± 82 pg/mL). We inferred that low iCa resulting from a rising pH and decreasing PTH during the periparturient period may have contributed to decreased uterine contractility and increased risk of stillbirths. Therefore, manipulating the cationic/anionic difference in diets of pregnant bitches, similar to the bovine model for hypocalcamia, may reduce the incidence of stillbirths in the bitch.

Keywords: Canine parturition; Whelping; Uterine inertia; Ionized calcium; Dog

1. Introduction

Primary uterine inertia is a well recognized clinical complication in the parturient bitch, which is often resolved with slow intravenous administration of calcium gluconate [1–3], despite total serum calcium often being within the 'normal reference range' for non pregnant dogs (clinical observations and [4]). Resolution of dystocia caused by primary uterine inertia with the administration of calcium indicates its potential role in this disease. Oxytocin, alone or in association with calcium, has also been widely used in the treatment of suspected uterine inertia [2,3], despite equivocal evidence regarding its role in uterine inertia [5,6].

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Indeed, oxytocin is difficult to measure and a 'normal' reference range has not been established for whelping bitches. However, resolution of some primary uterine inertia associated with dystocia with oxytocin indicates also its potential role in the pathogenesis of primary uterine inertia.

Unfortunately, the pathogenesis of either 'complete' or 'partial' uterine inertia in the bitch has not been studied in detail [1,2,4,7]. If hypocalcaemia is involved, there are, to the authors' knowledge, no reports on the relationship between blood calcium and parathyroid hormone (PTH) concentrations, the effect that acid-base status has on these end points during the peripartum period in the bitch, and their effects on the incidence of uterine inertia.

During the peripartal period, the bitch has an increased demand for calcium resulting from skeletal ossification of the fetuses, initiation of lactation, and increased activity of myometrial muscle. Forceful uterine contractions required for the expulsion of pups during whelping is dependent on the influx of free, ionized calcium into the myometrial cells [2,8]. However, free calcium availability may be restricted during this period of high demand due to transient inappetence, which many bitches experience on the day of whelping [2], or it may be further exacerbated by an acute respiratory alkalosis caused by panting, anxiety, fear, and pain (Henderson-Hasselbach Equation [9]) occurring in many bitches during whelping [10]. Increased protein binding of serum calcium [11] associated with a reduction in the amount and delay in the secretion of PTH in response to demand [12] may then occur, resulting in subsequent hypocalcaemia. This may then result in uterine inertia with delayed delivery, intrapartal hypoxia, and eventually birth of ''stillborn'' pups [1,13]. A pre-existing parathyroid gland atrophy has also been implicated in the underlying pathogenesis of eclampsia [3,14], and may be a contributing factor in the development of primary uterine inertia.

Two reports have documented the plasma concentrations of calcium and PTH in pregnant and lactating bitches [15,16]. However, in one study, only two bitches were used, only total non-ionized calcium was measured, and concentrations were only determined only once weekly during pregnancy and lactation [16]. The second study measured total and ionized serum calcium concentrations on the day prior to and the day of parturition, but not throughout whelping [15]. Furthermore, the latter authors did not investigate the relationship of calcium and PTH during whelping, nor their relationship with dystocia.

To better understand the pathogenesis of primary uterine inertia and thus eventually implement prevention and management strategies to reduce the incidence of this disease, determination of reference ranges for calcium (total and ionised), PTH, and oxytocin concentrations in bitches during the peri-parturient period is required.

The objectives of this study were to: i) determine the serum concentrations of total calcium, ionized calcium (iCa), parathyroid hormone (PTH), and oxytocin in 10 normally whelping bitches during the periparturient period; ii) investigate the relationship between blood calcium (iCa), PTH, and acid-base status (blood pH); and iii) investigate the potential role of oxytocin during the days around whelping in a subset of bitches randomly selected from a much larger population of breeding bitches, either with a clinical history of uncomplicated parturition (Control; Group 1), or with a clinical history of an increased incidence of uterine inertia and stillbirths (Group 2).

2. Materials and methods

2.1. Animals

2.1.1. Historical colony data

Group 1: Bitches in Group 1 ($n = 10$) were randomly selected from a research colony of German Shepherd Dog (GSD) bitches, aged from 2 to 7 yr, which were housed at The College of Veterinary Medicine, Cornell University, Ithaca, NY, USA. This colony had a history of low stillbirth prevalence (<1% over 5 yr).

Group 2: Bitches in Group 2 ($n = 20$) were randomly selected from a colony of Labrador bitches, aged from 2 to 7 yr, located at ''The Guiding Eyes'', NY, USA. This colony had a clinical history of a high prevalence of stillborn pups due to primary uterine inertia (7%) over a 2 yr period. Other causes of stillbirths were ruled out, based on clinical examinations of both bitches and stillborn pups. Furthermore, necropsy and histopathology were performed on each stillborn pup to detect underlying infectious (e.g., bacterial, viral, protozoal) causes.

The historical stillbirth rates differed between the two colonies ($P < 0.05$). Confidentiality agreements prevent us from publishing raw historical stillbirth data.

2.1.2. Experimental animals

Procedures described herein were approved by the Institutional Animal Care and Use Committee at Cornell University.

Bitches from both Groups 1 and 2 were fed a balanced, pelleted commercial diet (Purina Pro Plan