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Tocodynamic evaluation of dystocia affected canines after administration of uterotonic drugs

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Abstract

Dystocia is defined as the inability to expel pups through the birth canal without assistance which constitutes a major problem in the female dog. Cardiotocomonitor is useful for monitoring uterine contractions in response to uterotonic drugs. Thirty female dogs were randomly divided into three groups and the dogs of group 1 were administered 5% Dextrose infusion at rate of 1 g/kg b.w. slow intra-venous and 10% Calcium gluconate (Calcium-Sandoz®, Novartis India) at rate of 0.2 ml/kg b.w. intra-venous. In group 2, in addition to the treatment given in group 1, Oxytocin at rate of 0.5-1 IU/kg b.w. (Evatocin®, Oxytocin 5 IU per ml) was infused twenty minutes after calcium administration. In addition to the treatment given in groups 1 and 2, the dogs of group 3 were administered a total dose of 20 mg Nitroglycerine (Sigma Aldrich®, Nitroglycerine 200 mg per ml). The comparison between the groups was done by employing statistical analysis techniques which were based on haemato-biochemical parameters and cardiotocomonitor readings. No significant ($p>0.05$) difference in pre-treatment hemato-biochemical estimations was observed in all the groups. The number of contractions were significantly ($p<0.05$) more in groups 3 and 2 than in group 1 and the duration of contractions were significantly ($p<0.05$) more in group 3 than in groups 1 and 2. The amplitude of uterine contractions was significantly ($p<0.05$) higher in group 3 than in groups 1 and 2.

Keywords: Cardiotocomonitor, dystocia, nitroglycerine, oxytocin, uterine inertia

Introduction

Dystocia is defined as difficult labour or the inability to expel pups through the birth canal without assistance which constitutes a major problem in the female dog and might lead to death of both mother and foetuses. In canines, dystocia has been often linked with higher percentage of neonatal mortality and stillbirth (Tønnessen, 2012) [1].

The most common form of dystocia in female dogs is primary uterine inertia which may be complete or partial (Prashantkumar, 2013) [2]. In complete primary uterine inertia, the uterine contractions do not initiate while in partial primary uterine inertia these end prematurely despite patent birth canal resulting in failure of normal delivery of foetus (Bergstrom *et al.* 2006) [3]. To overcome inertia and facilitate normal delivery uterine ecbolics are used. Oxytocin is the most traditional uterotonic drug used by most clinicians (Tamminen, 2020) [4]. Another potent chemical (Nitric oxide) plays a key role in regulating various reproductive processes like ovulation, implantation, pregnancy maintenance and cervical ripening (Maul *et al.* 2003) [5]. In this regard, nitroglycerine which emerged as a new drug plays an important role in cervical dilatation (Azawi *et al.* 2012) [6]. Another approach characterizing the frequency and amplitude of uterine contractions is tocodynamometry (Davidson, 1998) [7]. Cardiotocomonitor is useful for monitoring uterine contractions in response to uterotonic drugs. The monitoring system consists of tocodynamometer, a recorder and a modem. The uterine sensor detects changes in intrauterine and intra-amniotic pressures. A sensor is fixed over lightly clipped area of the caudo-lateral abdomen. Subsequent to each recording session, data is transferred from recorder to service by a modem (Gropetti *et al.* 2010) [8].

Limited studies (Prashantkumar, 2013) [2] in canines have shown that tocodynamometer was helpful in accurate and precise diagnosis of primary uterine inertia along with its relationship with infrequent uterine contractions. The authors further reported that amplitude of uterine contractions was less than 10 percent throughout the 30 minutes monitoring period during complete primary uterine inertia. However, studies on use of tocodynamometer to evaluate and quantify uterine contractions vis-à-vis uterotonic drugs and physiological parameters are still obscure in canines.

Objective of the present article was to evaluate uterine contractions using cardiocotomitor in dystocia affected canines after the administration of uterotonic drugs.

Material and Methods

This study was conducted on 30 clinical cases presented to Multi Specialty Veterinary Hospital, Teaching Veterinary Clinical Complex, GADVASU, Ludhiana during 2019-20. The diagnosis regarding peri-parturient complications was made on the basis of clinical history, detailed clinical examination and diagnostic procedures. A thorough clinical history of each female dog was recorded which included age of animal, parity, duration of gestation, previous birth complications if any, signs of whelping observed, colour of vaginal discharge, approximate time of onset of parturition, number of puppies delivered and time of delivery of last pup. At the presentation of case, clinical signs such as polydipsia, polyuria, restlessness, nesting behaviour were noted down. Visually, the animal exhibited greenish or blackish vaginal discharges at the time of examination. The various diagnostic procedures were carried out in each female dog *viz.* gloved finger exploration of vagina to identify and rule out foetal malpresentation and/or narrow pelvis, ultrasound scanning (5 to 7.5 MHz probe) of abdomen to detect the viability of foetus and tocodynamometric investigations to determine the frequency and amplitude of uterine contractions.

All the female dogs exhibiting dystocia were randomly divided into three treatment groups *viz.* group 1, group 2 and group 3 with 10 animals in each group. The dogs of group 1 were administered 5% Dextrose infusion @ 1g/kg b.w. slow iv and 10% Calcium gluconate (Calcium-Sandoz®, Novartis India Limited) @ 0.2 ml/kg b.w. iv, but not exceeding a total dose of 10 ml. In group 2, in addition to the treatment given in group 1, Oxytocin at rate of 0.5-1 IU/kg b.w. (Evatocin®, Oxytocin solution 5 IU per ml; Vibha, 2012)^[9] was infused twenty minutes after the administration of calcium. The outcome of oxytocin *vis-à-vis* uterine contractions was monitored using cardiocotomitor. In addition to the treatment given in groups 1 and 2, the dogs of group 3 were administered a total dose of 20 mg Nitroglycerine (Sigma Aldrich®, Nitroglycerine 200 mg per ml; Azawi *et al.*, 2012)^[6].

Blood samples (5 ml) from each animal were collected from cephalic vein in a sterile 5 ml disposable syringe. Out of this 2.5 ml of blood was transferred in an EDTA tube for haematological analysis. The remaining 2.5 ml was dispensed into a serum collection tube for biochemical analysis. Both haematological and biochemical estimations were carried out in the ADRC laboratory of Department of Teaching Veterinary Clinical Complex of the university on the day of presentation of the animal (Pre-treatment).

The haematological parameters were estimated by Mythic 18 vet haematology which is validated for multi-species use. The haematological parameters determined in plasma samples of all female dogs included haemoglobin (Hb; g/dl), packed cell volume (PCV; %) and total leukocyte count (TLC; 1000/ μ l).

Various biochemical parameters determined before treatment protocol included liver function test (Aspartate aminotransferase; AST, U/L and Alanine aminotransferase; ALT, U/L), renal function tests (Blood urea nitrogen; BUN, mg/dl and creatinine, mg/ dl), total protein (g/dl), calcium (Ca), phosphorus (P), magnesium (Mg), sodium (Na) and potassium (K). All biochemical parameters were estimated

using VITROS 350 automatic analyser.

The frequency and amplitude of uterine contraction in each animal were monitored using a tocodynamometer (Philips medicine, Germany). The tocodynamometer consists of a uterine sensor and a recorder. The animal was placed on an examination table in the lateral recumbency. The uterine sensor was placed on the lateral abdomen and secured with abdominal bandages. The monitoring of uterus consisted of recording of various parameters *viz.* frequency, duration, amplitude and baseline shifts in uterine contraction for a minimum of 15 minutes. The female dogs which did not respond to medical treatment were subjected to caesarean section (C-Section) using ventral midline approach. The data generated was analysed using Statistical analysis system (SAS) software (Version 9.4). The results were expressed as Mean \pm SE. The data on haematological parameters, biochemical estimations, and tocodynamometer readings was analysed by one way analysis of variance (ANOVA) and Post hoc Tukey's comparison test. Significant differences were noticed when the P value was <0.05.

Result and Discussion

Haematological parameters in dystocic dogs

The mean haemoglobin (Hb) was 11.0 \pm 1.1 g/dl in group 1, 10.8 \pm 0.7 g/dl in group 2 and 10.0 \pm 0.9 g/dl in group 3 (Table 1). A non-significant difference ($p>0.05$) in plasma Hb profiles was seen between three different groups. The mean packed cell volume (PCV) in groups 1, 2 and 3 was 35.3 \pm 1.7%, 32.4 \pm 1.5% and 32.9 \pm 1.8%, respectively and was similar ($p>0.05$) in all the three groups (Table 1). The total leukocyte count (TLC) varied from 7000 to 19275 cells/mm³ in all the dogs with a mean of 13740.3 \pm 307.6 cells/mm³, 13960.5 \pm 351.2 cells/mm³ and 14299.7 \pm 208.4 cells/mm³ in groups 1, 2 and 3, respectively and revealed no significant difference ($p>0.05$) in the three treatment groups (Table 1). Similar findings were reported in dogs suffering from dystocia as well as in normally whelped dogs (Emily *et al.*, 2006)^[10].

Table 1: Haematological parameters (Mean \pm SE) in dogs suffering from dystocia

Parameters	Treatment groups		
	Group 1 (n = 10)	Group 2 (n = 10)	Group 3 (n = 10)
Hemoglobin (g/dl)	11.0 \pm 1.1	10.8 \pm 0.7	10.0 \pm 0.9
PCV (%)	35.3 \pm 1.7	32.4 \pm 1.5	32.9 \pm 1.8
TLC (1000/ μ l)	13740.3 \pm 307.6	13960.5 \pm 351.2	14299.7 \pm 208.4

Serum biochemical analysis in dogs suffering from dystocia

The aspartate aminotransferase (AST) in 30 female dogs ranged between 7-58 U/L with a mean of 25.0 \pm 2.0 U/L in group 1, 30.0 \pm 2.6 U/L in group 2 and 23.0 \pm 2.2 U/L in group 3 (Table 2). The mean alanine aminotransferase (ALT) was within the physiological limits with 27.0 \pm 2.4 U/L, 24.0 \pm 2.1 U/L and 28.0 \pm 2.5 U/L in groups 1, 2 and 3, respectively (Table 2). There was no significant ($P>0.05$) difference in ALT and AST in the three groups. Limited studies (Kimura & Kotani, 2018)^[11] in canines have shown that levels of liver enzyme *viz.* ALT (10-55 U/L) remained within the normal range throughout the pregnancy.

The mean creatinine levels were 1.22 \pm 0.04 mg/dl in group 1, 1.16 \pm 0.09 mg/dl in group 2 and 0.68 \pm 0.04 mg/dl in group 3

and were within the normal range indicating no muscle wastage (Table 2). The blood urea nitrogen (BUN) concentrations were within the normal range (6-28 mg/dl) with mean of 15.0±1.7 mg/dl in group 1, 17.0±1.4 mg/dl in group 2 and 12.9±1.2 mg/dl in group 3. No significant difference ($p>0.05$) was noticed in creatinine and BUN profiles in all three groups. However, a slightly lower ($p>0.05$) levels in group 3 could merely be due to individual variation, if any, and short-time period of observations. Likewise, no difference in BUN levels were noticed in dystociac dogs (18.93 mg/dl) and spontaneously whelped dogs (17.52 mg/dl; Chethana, 2016) [12]. The total protein recorded in all the dogs ranged between 5-7.7 g/dl. The mean total protein levels were 6.1±0.7 g/dl, 6.6±0.5 g/dl and 5.9±0.4 g/dl in groups 1, 2 and 3, respectively (Table 2). There was no significant difference ($p>0.05$) between the three groups. The observed mean serum calcium levels were 10.0±0.7 mg/dl, 9.0±0.4 mg/dl and 9.3±0.6 mg/dl in groups 1, 2 and 3 with a range of 6.4 to 11.8 mg/dl (Table 2). In all the groups, the serum calcium levels were similar ($p>0.05$) and within the physiological range. In the current study, none of the female dogs suffering from dystocia showed hypocalcemia, signifying not being a cause of inertia. Previous studies (Bergstrom *et al.* 2006; Vibha 2012) [3, 9] demonstrated that serum calcium concentrations in female dogs with primary inertia (10.16 mg/dl) were similar to those having normal myometrial contractions (10.25 mg/dl). The mean serum phosphorus concentrations in groups 1, 2 and 3

were 4.9±0.6 mg/dl, 4.4±0.8 mg/dl and 4.2±0.5 mg/dl, respectively (Table 2). The mean serum phosphorus concentrations exhibited no significant difference ($p>0.05$) in all the groups. Similar to present study, no difference in concentrations of phosphorus was reported in dystocia affected dogs and normally whelped dogs (Bergstrom *et al.*, 2006) [3]. In the present study, the serum magnesium concentrations ranged between 1.50 to 2.90 mg/dl in all the dogs with a mean of 2.4±0.4 mg/dl, 2.7±0.3 mg/dl and 2.1±0.6 mg/dl in groups 1, 2 and 3, respectively (Table 2). There was no significant ($p>0.05$) difference in the mean serum magnesium concentrations of all animals between the different groups. The findings of the present study are in accordance with Prashanthkumar (2013) [12] who demonstrated nearly similar range of magnesium (1.82-2.28 mg/dl) with an average concentration of 2.04±0.17 mg/dl. The mean serum sodium levels were 143.0±3.3 mEq/L, 146.0±2.7 mEq/L and 149.0±3.0 mEq/L in groups 1, 2 and 3, respectively with a range of 138 to 157 mEq/L in all the animals (Table 2). The mean serum potassium profiles were 4.1±0.2 mEq/L in group 1, 3.6±0.4 mEq/L in group 2 and 3.7±0.5 mEq/L in group 3 (Table 2). No significant variation ($p>0.05$) was observed in the mean serum sodium and potassium concentrations in female dogs in the three groups. Previous studies in canines have shown that the electrolyte variables (Na, K) were not influenced by the type of parturition (Simoes *et al.*, 2016) [13].

Table 2: Biochemical parameters (Mean±SE) in dogs suffering from dystocia

Biochemical parameters	Treatment groups		
	Group 1 (n = 10)	Group 2 (n = 10)	Group 3 (n = 10)
AST (U/L)	25.0±2.0	30.0±2.6	23.0±2.2
ALT (U/L)	27.0±2.4	24.0±2.1	28.0±2.5
BUN (mg/dl)	15.0±1.7	17.0±1.4	12.9±1.2
Creatinine (mg/dl)	1.22±0.04	1.16±0.09	0.68±0.04
Total protein (g/dl)	6.1±0.7	6.6±0.5	5.9±0.4
Calcium (mg/dl)	10.0±0.7	9.0±0.4	9.3±0.6
Phosphorus (mg/dl)	4.9±0.6	4.4±0.8	4.2±0.5
Magnesium (mg/dl)	2.4±0.4	2.7±0.3	2.1±0.6
Sodium (mEq/L)	143.0±3.3	146.0±2.7	149.0±3.0
Potassium (mEq/L)	4.1±0.2	3.6±0.4	3.7±0.5

Cardiotocomonitor studies in dystocia affected female dogs

Tocodynamometer is a device which helps in diagnosing difficulties owing to whelping through objective monitoring of uterine activity using specialised uterine pressure sensors (Davidson, 2001) [14]. The tocodynamometric investigations carried out in 30 female dogs revealed that the monitoring time ranged from 15 to 30 minutes. The mean number of contractions recorded in groups 1, 2 and 3 was 1.4±0.7, 3.2±0.6 and 3.5±1.0 with a range of 0-6 contractions, 0-7 contractions and 0-8 contractions, respectively. The mean duration of contraction was 1.6±0.4 minute (1-3 minutes) in group 1, 2.2±0.3 minute (1-5 minutes) in group 2 and 3.0±0.3 minute (1-5 minutes) in group 3 (Table 3). The number of contractions were significantly ($p<0.05$) more in groups 3 and 2 than in group 1. Although non-significant ($p>0.05$), the number of contractions were more in group 3 as compared to that in group 2. The duration of contractions were significantly ($p<0.05$) more in group 3 than in groups 1 and 2. A similar trend though non-significant ($sp>0.05$) was seen in

group 2 when compared to group 1. In the current study, animals in group 3 were given nitroglycerine along with oxytocin for induction of whelping. Administration of nitroglycerine followed by induction with oxytocin augmented the frequency and duration of contractions and led to safer and faster outcome (Azawi *et al.*, 2012) [6]. Similarly, the number of uterine contractions and duration of each contraction in a study varied between 2-4 and 2-5 per minute, respectively assessed by cardiotocomonitor (Jayakumar, 2015) [15]. In the present study, female dogs showing primary complete uterine inertia (n=8 in group 1, n=5 in group 2 and n=4 in group 3) revealed no abdominal contractile activity. The mean amplitude was 17.8±4.5 mm Hg in group 1, 27.5±2.8 mm Hg in group 2 and 36.7±3.9 mm Hg in group 3. The amplitude was significantly ($p<0.05$) higher in group 3 than in group 2 and 1 (Table 3). In animals with complete uterine inertia, the strength of uterine contractions was less than 10 mm Hg, throughout monitoring session suggesting it to be the primary cause of dystocia. Previous studies (Prashanthkumar, 2013²; Jayakumar, 2015)¹⁵ also determined

that the amplitude of uterine contractions was <10 mm Hg in all cases of primary uterine inertia. To relieve the dystocia and initiate uterine contractions especially in cases of uterine inertia associated with infrequent low-amplitude uterine contractions dextrose, calcium, oxytocin and nitroglycerine either alone or in combination were used. Numerous studies (Vibha, 2012; Chethana, 2016) [9, 12] have demonstrated the use of ecbolics for the treatment of uterine inertia. Following administration of ecbolics, the response of uterus was monitored using tocodynamometer. During the expulsion phase, there was 30 mm Hg rise in the contraction strength. In the present study, prior to start of treatment, the uterine contractions were at baseline level (18-20 mm Hg), which became more regular and steep (25-30 mm Hg) following medical therapy. In spite of administration of ecbolics, about n=17 dogs did not respond to medical treatment and showed no advancement in the contractility pattern as revealed by tocodynamometric evaluation in the current study. This could be due to the desensitization and down regulation of oxytocin receptors in uterus (Plested and Bernal, 2001) [16]. After ensuring correct presentation, posture and position of foetuses per-vaginally in all the animals, two (20%) dogs in group 1, five (50%) in group 2 and six (60%) in group 3 successfully responded to the treatment regime with complete expulsion of the foetuses. Remaining animals (eight in group 1, five in group 2 and four in group 3) were subjected to caesarean section and recovered successfully thereafter.

Table 3: Tocodynamometric (Mean±SE) evaluation in dogs suffering from dystocia

Parameters	Treatment groups		
	Group 1 (n = 10)	Group 2 (n = 10)	Group 3 (n = 10)
Monitoring time (minutes)	27.9±1.3	28.0±2.1	29.5±1.7
Number of contractions	1.4±0.7 ^a	3.2±0.6 ^b	3.5±1.0 ^b
Duration of contractions (Per min.)	1.6±0.4 ^a	2.2±0.3 ^a	3.0±0.3 ^b
Change of amplitude (mm Hg)	17.8±4.5 ^a	27.5±2.8 ^b	36.7±3.9 ^c

Value marked with superscript indicate significant difference along the row at (P<0.05) level of significance

Conclusions

The number of dogs that successfully responded to the treatment protocol were marginally more following administration of nitroglycerine along with oxytocin which may partially be due to small number of animals, nitroglycerine could be used as an alternative for cervical dilatation and subsequent whelping in dogs. However, in the present study, side-effects like vomiting, urticaria and seizures pertaining to this regimen was noticed in few dogs (n=4) of group 3. Moreover, high cost treatment per animal using nitroglycerine could also deter the use of this drug especially amongst economically underprivileged owners. Thus, more studies are clearly required to validate and understand the regulatory role of nitroglycerine with special reference to cost factor prior to its routine use in relieving dystocia in combination with other ecbolics. Nevertheless, application of cardiotocomonitor on all the animals suffering from dystocia should be made mandatory.

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