Short Communication

EFFICACY OF MISOPROSTOL TREATMENT ON EXPULSION OF DEAD FOETUSES RETAINED IN-UTERO

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ABSTRACT

A great challenge in canine obstetrics is averting a caesarean section particularly in a partially delivered litter with one or two non viable foetuses remaining in utero. Response to routine medical management with calcium and oxytocin in many of these delayed cases will be deficient. The efficiency and safety of misoprostol (PGE_1) for augmentation and completion of whelping in such dystocic dogs were studied. Nine of the ten dogs (90%) responded to misoprostol administration, of which eight dogs experienced unassisted expulsion of foetuses and in one dog the foetus was removed using whelping forceps. Induction of foetal expulsion with misoprostol reduced the rate of caesarean section in dogs with partial uterine retention of dead foetuses.

Key words: *Dog, Dystocia, Misoprostol, Dead foetus*

Prolonged labour in dogs frequently does not respond to medical management with oxytocin and terminate with caesarean sections. Also, when the uterus becomes refractory to oxytocin therapy, repeated doses does not result in uterine contractions. However, in dogs with one or two non viable retained foetuses in the normal course of whelping or that had partially responded to medical management with calcium and oxytocin; an alternative therapy to avoid caesarean in non obstructed dystocia becomes essential.Misoprostol, a prostaglandin E_1(PGE_1) analogue is characterized by strong uterine contracting effects and is currently used in dogs for termination of unwanted pregnancy in conjunction with progesterone receptor antagonists (Amritha,2004; Agaoglu *et al*.,2011). The clinical efficiency and safety of misoprostol (PGE_1) for augmentation and completion of whelping with uterine retention of one or two non-viable foetuses not responding to medical management with dextrose, calcium and oxytocin were studied.

Ten dogs of different breeds in their advanced pregnancy, which had commenced with the whelping process presented to the University Veterinary Hospital, Kokkalai, KVASU and confirmed with uterine retention of one or two foetuses by radiography (Fig.1) were utilized for the study. The intra uterine foetuses were confirmed non-viable by trans-abdominal ultrasonography(Fig.2). Eight dogs had a single retained dead foetus while two dogs had two non–viable retained foetuses. These dogs were medically managed with Inj. Dextrose @ 1gm /kg. b.wt,Inj. Calcium sandoz @ 0.2 ml/ kg. b.wt and Inj. Oxytocin @ 5 units in 100 ml normal saline as slow intra venous drip. However, neither was there any progression withlabour completion, nor was there any contractions noticeable. These dogs that didn't respond to this medical management were given Tab. Misoprostol @ 200 µg for dogs less than 20 kg b.wt and @ 400 µg for dogs more than 20 kg b.wt. orally. Dogs which didn't expel the dead foetus within six hours of first misoprostol administration were given another dose of misoprostol six hour following the first and the response was studied. An oral dosing of antibiotic was initiated in these dogs on the day of admission.

The data on the efficacy of misoprostol administration on expulsion of dead foetuses are presented in Table1.Nine of the ten dogs (90%) responded to misoprostol administration,of which eight dogs experiencedunassisted expulsion of foetuses (Fig.3)in eight dogs (80%),while in one dog (10%), the foetus was retained in the anterior vagina and was removed using whelping forceps. In a German Shepherd dog with single pup syndrome (10%), the foetus was retained deep in the uterus and was removed following caesarean section. Thus, out of the 12 dead foetuses retained in utero, 10 foetuses were expelled and one was removed by forceps delivery while another one was removed following caesarean section (Table).No side effects were noticed except transient pyrexia in a few dogs.

Augmentation of whelping is the practice of stimulating the uterus to increase the frequency, duration and intensity of contractions subsequent to the commencement of spontaneous labour. It has regularly been used to treat delayed labour when uterine contractions are considered to be inadequately strong or improperly synchronized. Whelping augmentation has conventionally been performed with the use of oxytocin alone or in combination with calcium. The procedure aims

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to shorten the whelping process in order to avoid problems relating to unwarranted prolongation which may compromise foetal wellbeing, and to avert caesarean section which can be unfavourable for the dam (Davidson, 2001).

Oxytocin has been used therapeutically to relieve non-obstructive dystocia in bitches.It has been demonstrated that intramuscular doses of 5 IU or more are associated with uterine tetany and that intramuscular doses as low as 0.25 IU of oxytocin may stimulate effective contractions (Davidson, 2001).Moreover, repeated doses do not result in uterine contractions as the uterus becomes refractory to oxytocin therapy (Johnston *et al*., 2001). Oxytocin is effective in early stages to overcome partial inertia, the uterus tends to lose its sensitivity towards the end of the prolonged parturition and its effect is relatively lower to deliver the final pup in large litter (Arthur, 1975).

In this context, an alternative therapy that can stimulate uterine contractions without the mediation of oxytocin receptors becomes essential to avoid a caesarean, particularly with one or two dead foetuses in utero. A beneficial effect of combination therapies in termination of pregnancies has been proved in human beings (Agaoglu *et al*., 2001) and also in dogs attributable to the uterotonic effects of misorprostol (Cadepond *et al*., 1997). Raheema *et al.* (2018) recorded a high number of live born puppies, a decreased medical and surgical assistance for completing the whelping process in canine high risk pregnancies using an induction of whelping protocol with mifepristone orally and anterior vaginal administration of misoprostol.

Misoprostol causes relaxation of the cervix and stimulation of uterine contractions after selective binding to EP-2/EP-3 receptors (Weeks and Faundes, 2007). The uterine contracting action of misoprostol have been tested in dogs and cats with pyometra as well as in termination of unwanted pregnancies for which it appears to be effective in causing evacuation of uterine content, although it does not have any luteolytic properties. Misoprostol is gradually replacing $PGF_2\alpha$ compounds in dogs and cats as it is available as tablets and therefore can be prescribed and administered at home by the owner, and also it has no side effects (Agaoglu *et al*., 2011)

The outcome of the study suggests the successful use of misoprostol for labour augmentation without any undesirable side effects in dogs with uterine retention of one or two dead foetuses of a partially whelped litter / delivery not responding to management with oxytocin, without any undesirable side effects.The study also recommends the repeated use of misoprostol twice at six hour interval in non effective cases with a single dose. However, an antibiotic coverage should be provided in such dogs chosen to expel following misoprostol medication.

The study revealed the merits of inducing expulsion of dead foetusesusing misoprostol in canine pregnancies which had not responded to oxytocin treatment.The protocol can effectively avoidemergency caesarean section, without any deleterious effects on the dam.

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Table : Efficacy of misoprostol treatment on expulsion of dead foetuses retained in-utero

No: of dogs	Dead foetus in utero	Dogs that responded to treatment	Dogs that required a single dose	Dogs that required a second dose	Dogs that required assisted vaginal delivery	No:of foetuses expelled without assistance	Interval (mean ±SE) from 1st dose to foetal expulsion (min)	Interval (mean ±SE) from 2nd dose to foetal expulsion (min)	Overall (mean ±SE) duration from 1st dose of misoprostol to expulsion of puppies (min)
10	12	9	6	2	1	10	145 ± 50.24 (90 to 240)	105 ±15.00 (90 to 120)	225 ± 54.96 (90 to 480)

Table 1: Clinical findings of dystocia in buffaloes

Particulars (n)	Category	Incidence	Significance
Types of Dystocia (n=152)	Fetal	9.87% (15/152)	χ^2 =97.92, d.f.=1 P=0.001
	Maternal	90.13% (137/152)	
Cause of Fetal Dystocia (n=15)	Mummification	33.33% (5/15)	χ^2 =1.6, d.f.=2 P=0.449
	Maceration	20.00% (3/15)	
	Fetal mal-disposition	46.67% (7/15)	
Cause of maternal dystocia (n=137)	Incomplete Cervical Dilation	16.06% (22/137)	χ^2 =63.13, d.f.=1 P=0.001
	Uterine torsion	83.94% (115/137)	
Side of the uterine torsion (n=115)	Right	80.87% (93/115)	χ^2 =43.83, d.f.=1 P=0.001
	Left	19.13% (22/115)	
Location of the uterine torsion(n=115)	Post-cervical	73.04% (84/115)	χ^2 =24.43, d.f.=1 P=0.001
	Pre-cervical	26.96% (31/115)	
Degree of uterine torsion(n=115)	90-180	11.30% (13/115)	χ^2=56.99, d.f.=3 P=0.001
	180-270	30.44% (35/115)	
	270-360	21.74% (25/115)	
	>360	36.52% (42/115)	
Parity(n=152)	1	38.16% (58/152)	χ^2 =23, d.f.=3 P=0.001
	2	19.74% (30/152)	
	3	29.60% (45/152)	
	4	12.50% (19/152)	
	Primiparous	38.16% (58/152)	χ^2 =8.53, d.f.=1 P=0.003