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Recent Approaches in The Treatment of Retained Fetal Membranes in Cows

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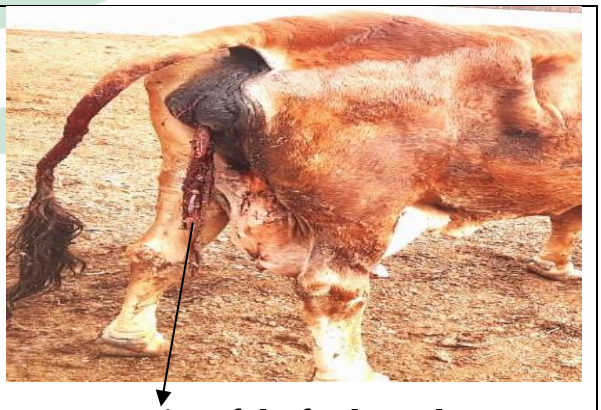
Introduction

The fetal membrane or placenta is a vital organ for the pre-natal transport of nutrients and oxygen from the dam to the fetus, and it is expelled within 6 to 8 hours after calving in cows. If the placenta is kept for more than 8 to 12 hours, it is considered pathological and is known as retention of the fetal membrane (RFM). RFM is a prevalent postpartum disorder in cattle, primarily caused by the failure of fetal membrane expulsion and dehiscence, even after 12 to 24 hours of parturition. Additionally, the failure of cotyledon and maternal caruncle separation was caused by excessive or insufficient collagen degradation (Sharpe et al., 1989), which is linked to a failure of collagen dissolution within the placenta (Eiler and Hopkins, 1992). The incidence is about 4 to 11% in the total herd which leads to which leads to reduced milk yield, endometritis and poor fertility and mortality resulting from RFM is reported to be 1 to 4%. Temporary impairment of appetite and reduction in milk yield occurs in 55 to 65% of affected cows (Hanafi *et al.*, 2011).



Retention of the fetal membrane

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A variety of methods have been used in the treatment of RFM, which includes manual removal and / or administration of oxytocin, PGF2α, antibiotics, immune modulators etc., although the efficacy of these treatments are questionable (Eiler, 1997).

a. **Manual Removal:** Manual removal of RFM is not advised, because the postpartum uterine wall is thin and fragile which is susceptible for frequent uterine infection.
b. **Antiseptics:** The use of antiseptics including chlorhexidine and diluted iodine preparations should be administered with caution, especially some of the iodine preparations are extremely irritating; oxy tetracycline has been the most popular agent recommended for intrauterine infusion in cows, however, this agent is poorly absorbed in the deeper layers of the uterus (Sheldon and Noakes, 1998).
c. **Intrauterine boluses:** The RFM cows treated with uterine boluses containing nitrofurazone (0.12gm) and urea (12.32 gm) resulted in no significant improvement in treatment efficacy compared to control cows (Dowlen *et al.,* 1983). Narasimhan (1987) opined that the dairy cows treated with intrauterine proteolytic boluses comprising of nitrofurazone and urea was found to be effective as 100 per cent. Similar reports were made by Dutta and Dugwekar (1988) that the proteolytic boluses used for the treatment of RFM was found to be effective in controlling uterine infections in cows and buffaloes with RFM.
d. **Antibiotics:** The penicillin was not effective until days 10-15 postpartum due to the presence of penicillinase producers; aminoglycosides were ineffective, as they were not active in anaerobic environment; sulphonamides were not recommended because, they were inactive in the presence of cellular debris; however, intrauterine application of oxytetracycline on alternate days till the foetal membranes were 7 expelled, resulted in improved fertility equivalent to that of non RFM cows (Bretzlaff, 1988).
e. **Intra uterine boluses with antibiotics:** The RFM dairy cows treated with steclin and furea bolus were found to be effective than antrima bolus. Had achieved 83.3, 50 and 50 per cent efficacies in RFM dairy cows treated with Inj. Oxytetracycline with 10 mg/ kg b.wt., and Nitrofurazone 60 mg / bolus; Inj. Streptopenicillin 2.5 gm with 10 ml of distilled water through intrauterine route; Nitrofurazone 30 ml liquid (2 per cent) through intrauterine route, respectively for 3 days (Narladkar *et al.* ,1992). The intrauterine boluses containing povidone iodine, metronidazole, nitrofurazone and urea

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were more effective than nitrofurazone and urea (Sheetal *et al.*, 2014). The treatment with either sulpha drugs and furea or with terramycin had similar effect in normal calving, while in RFM cases, terramycin was better than sulfa plus furea when used locally in dairy cows (Sainims *et al.*, 1989). The herbal intrauterine bolus was effective in the treatment of clinical cases of retained placenta in bovine (Markandeya *et al.*, 2014).

f. **PGF2α, and oxytocin:** PGF2α, and oxytocin has long been advocated to expel the placenta, but does not reduce the incidence of RFM. Thus, the intramuscular injection of PGF2α, does not appear to be uterotonic in the postpartum cow (Eiler and Hopkins, 1984), if the placenta is not detached from the caruncle, the oxytocin will not hasten its passage (Borsberry and Dobson, 1989). Administration of oxytocin and PGF2α via umbilical artery soon after parturition or dystocia was tried with the hypothesis of hastening the shedding of fetal membranes. The results are not conclusive. Further studies regarding treatment of hormones along with enzymes which helps to cause dehiscence of placenta is highly essential.

Immunomodulators:

Significance of immunosuppression in retention of fetal membranes is not fully understood till date (Peter and Bosu, 1987). The common belief that altered neutrophil and macrophage functioning might be one of the reason responsible for retention of fetal membranes. Any interruption in normal hormonal changes that used to occur within the uterine environment stops epithelial cell protease release and further immunosuppression might compromise leukocytic protease activity LPS has been seen to act as a strong signal for endometrial epithelial cells and leukocytes to support the Secretion of a number of inflammatory mediators and immunoregulatory cytokines. Nadja *et al.* (2007) have reported that there is no adverse effect on intrauterine infusion of E coli LPS in mares, thereby supporting its use in expulsion of RFM cases. Intra uterine infusion of recombinant human interleukin 8 (rhIL-8) in cattle and mare pulls out/ attracts polymorphonucleocytes into uterus within 6 hours of infusion (Zerbe *et al.*, 2003). So, any one of these conditions can cause RFM by compromising protease activity. The use of immunomodulators reduces the uterine inflammation and infection, but not used routinely in the treatment of RFM (Amin *et al.*, 2013).

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Collagenase:

Several researchers have suggested that the collagenase administration through Umbilical artery is the effective treatment for RFM in dairy cows (Guerinet et al., 2004). Intra-placental injection of collagenase through umbilical cord arteries may also help to detach retained placenta in women, mare and cows. Bacterial collagenase from Clostridium histolyticum was used as it could degrade several types of collagens (Azawi, 2013). Collagenase is effective in digesting human, equine and bovine placental collagens (Fecteau *et al.,* 1998). The advantages of collagenase over other proteolytic enzymes are its substrate specificity, high enzyme activity at body pH and temperature and its ability to cause blood clotting (Eiler and Hopkins, 1993). However, such collagenase treatment is costly and more difficult to administer through umbilical cord (Beagley *et al.,* 2010).

Ozone treatment:

ozone is a strong disinfectant and also possess activity against pathogenic fungi and their spores (Travagli *et al.,* 2009). Ohtsuka et al. (2006) has reported that ozone activates lymphocytes or monocytes, thereby supports secretion of cytokines such as (IFN) α, β, γ, tumour necrosis factor (TNF-α), interleukins (IL) 1, 2, 4, 6, 8 and 10, granulopoiesis (GM-CSF) and transforming growth factor β (TGF β) from these cell types. Ozone causes tissue regeneration, favours granulation and epithelialization and also improves the local uterine metabolism. Administration of 30 ml of ozone flush spray intrauterine alone or coupled with 4500 mg of cephalexin intramuscularly on days 1, 11, 21 and 32 post-calving is more effective when compared to the antibiotics administered parenterally or the hormone treatment options for retained placenta. The ozone therapy has already been used with good results on urovagina, it can be considered as an effective treatment for retained placenta to reduce clinical endometritis during puerperium (Gopi Krishnan *et al.,* 2017).

Conclusion:

Prepartum hormonal and biochemical changes set the stage for the complicated processes of placental detachment and expulsion following parturition. It is possible to choose treatment plans and avoid RFM in cows by having a thorough grasp of the physiology of placental retention. Numerous popular treatments for RFM have not been proven to work, and some may even be harmful to procreation in the future. While there is currently insufficient data to support their usage, treatments such as manual removal, local antibiotics, and

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prostaglandins are employed. Collagenase may be useful in obtaining a quicker release, although it is often prohibitively expensive. Supplementing with vitamin E and selenium may be a useful preventative strategy, according to recent research. The goal of new treatments should be to address certain causes of RFM. In order to prevent RFM in cattle, it is advised that cows be kept comfortable, that stress related to parturition be minimized, and that nutritional management be closely monitored, especially during the transition phase.

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