

Current Treatment Aspects of Bovine Reproductive Disorders

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ABSTRACT

Economy of the dairy farming mainly depends on first service conception rate and 12-months calving interval to get a calf each year which is advantageous for high milk yield per cow with the good economic return. Reproductive disorders are the major threats antagonizing fertility as well as productivity of dairy cattle. Antimicrobial therapy, phytotherapy (herbal remedy), homeopathy and immunotherapy are currently used for the alleviation of these disorders. But due to more negative impacts of antibiotics; phytotherapy, homeopathy and immunotherapy have been given more attention as a treatment approach in recent years because they are cost effective, have minimal side effects and milk residues which are important from public health point of view.

Keywords: RFM, Metritis, Endometritis, Pyometra, Anoestrus, Dystocia, Prolapse

Reproduction is a luxurious process first to be negatively affected and last to show positive response under optimum conditions depending on general well-being of the animal. Yet, it is an essential characteristic exhibited by all living organisms in order to replicate them. Situations where survival of animal is critical, reproductive events are put on hold necessitating the complete well-being of the animal. In this modern era due to an ambitious vision in the interest of maximizing production, man has manipulated animal's reproductive cycle unconsciously thus, aggravating lactational, nutritional and managemental stress to the animal. Subsequently, this has led to hormonal imbalances and increased likelihood of periparturient disorders such as RFM. Retention of fetal membrane (RFM) has been positively associated with the occurrence of endometritis, metritis, ketosis, mastitis, milk fever and

lameness predisposing to cystic ovarian disease in dairy animals. Negative consequences such as delayed uterine involution, prolonged post partum estrus interval, conception failure and increased services per conception, increased days' open and inter-calving interval adversely impact the fertility and substantially aid to economic losses. In view of the above constraints in the dairy production systems, an attempt has been made to compile mainly four therapeutic approaches including recent advances in these areas for the alleviation of bovine reproductive disorders and enhancement of general well-being, fertility and productivity of animals.

Antimicrobial therapy (Antibiotics)

Bacterial contamination of uterus occur after every calving and most cow eliminate these contamination during involution of uterus,

but, depending upon species of pathogens that are present, their degree of colonization and ability of cow to mount an immune response results in infection ranging from severe life threatening metritis to mild, non-persistent or chronic endometritis and subsequently to pyometra. Abortion, induced calving, dystocia and delayed parturition conditions predispose to retention of fetal membranes and RFM has been identified as of major importance in the aetiology of these post-partum complications. *E. coli*, *A. pyogenes*, *M. haemolytica*, *Pseudomonas spp.*, *Streptococcus spp.*, *Staphylococcus spp.*, *Clostridium spp.*, *Fusobacterium spp.* and *Prevotella spp.* are bacterial isolates associated with uterine infections reduce fertility of animals by reducing the chances of conception. Manual removal of RFM should be strictly prohibited as it increases the likelihood of metritis and endometritis conditions. Antimicrobial therapy as such not implied for RFM alone but, it is indicated to reduce the risk of further complications. Judicial use of antibiotics based on pathogen isolation and in vitro susceptibility testing is best approach, but this is not always feasible at field conditions.

In puerperal metritis condition, intrauterine antibiotics are of little use, so treatment should be parenteral. Some favour *bactericidal* antibiotics to control systemic infection and pyaemia in which broad spectrum penicillins and cephalosporins are the most efficacious choices. Ceftiofur is the drug of choice that achieve concentrations in uterine tissue and fluid greater than minimum inhibitory concentration (MIC) for most of the common metritis pathogens. Others prefer *bacteriostatic* antibiotics as they limit the endotoxic damage during killing of pathogens. OTC at higher doses can be given intravenously but, it does not reach MIC level in uterine tissue. A wide range of antibiotics has been used in the treatments of endometritis in the past. While parenteral treatment is preferred for metritis, intrauterine antibiotic instillation should be reserved for the treatment of endometritis. Several antibiotics

such as Nitrofurazone, Aminoglycosides, Sulphonamides and Penicillins are inappropriate for intrauterine application. Antibiotics that have been formulated for intrauterine use include OTC and Cephapirin. As intrauterine OTC does not penetrate uterine wall well enough and is not particularly effective against *A. pyogenes*, therefore, Cephapirin IU become the drug of choice for endometritis and pyometra treatment. However, Ciprofloxacin hydrochloride 125 mg + Tinidazole 150 mg/5ml (Cflox-Tz IU) and Levofloxacin 100mg + Ornidazole 200mg+ Vitamin E 25mg/5ml (Lenovo AP IU) are most commonly used in clinical as well as subclinical endometritis .

Phytotherapy (Herbal remedy)

It is the use of plant or plant part extracts in order to maintain health and to prevent or cure disease. Nowadays, world is more inclining towards plant based therapeutic approach over chemotherapy as it has no harmful side effects and is cost-effective. Another aspect is that it increases immunity and enhances the body's natural healing process to combat disease conditions. There are various indigenous preparations such as Prajana HS (Indian Herbs, Natural Remedies), Janova (Dabur, Ayurved), Fertivet (Ar Ex Labs), Sajani (Sarabhai), Heat-Up (Century) and Heatraj (Rajan) commercially formulated to induce ovarian activity in anoestrus animals. Polyherbal drug preparations such as Exapar (Dabur Ayurved), HimROP (Himalaya), Uterotone (Cattle Remedies), AV/UTL/17 (Ayurved), AV/RMI/45 (Ayurved; as intrauterine infusion) have been used by field veterinarians to facilitate expulsion of fetal membranes, secretion of lochial discharge, and involution of uterus for the resumption of normal cyclic activity in farm animals. Mixture of Turmeric-50 gm, shatavari-50gm, ginger-50gm, tejpatta-10 leaves, black pepper-10gm, jaggery-200gm and 2 lit. Water first boiled then cooled is prescribed orally *b.i.d* for 3 days to prevent RFM and subsequent uterine infections at our Referral Veterinary Polyclinic. Various plants and plant

part extracts used in different reproductive disorders are listed in Table 1.

HOMEOPATHY

Homeopathic remedies are derived from all natural sources, animal or biological, mineral or plant based on principle of 'let likes be cured by likes' and their preparation is not only a simple dilution rather it is attenuation which is dependent on the technique known

as potentiation (Macleod, 1981). Remedy is prepared by first dilution of crude product and then, succussion. More the remedy is diluted and succussed, more the curative properties of the drug are retained, while all poisonous or unpleasant side-effects are lost. The dilutions prepared in this way are referred as potencies, and are used in either of three ways: (1) decimal system mainly used in Germany, and expressed by the letters x and D which indicate one part of crude product is mixed with nine parts of water

Table 1

Plant or plant part extracts	Reproductive disorder	Route of administration	Reference
Fenugreek (<i>Trigonella foenum-graecum</i>) powder	Anoestrus	Oral	(Mishra <i>et al.</i> 2002)
2-3 kg chopped unripe papaya (<i>Carica papaya</i>) fruits	Anoestrus	Oral (once a day for 4-5 days)	(Nayak, 1995)
Cucumber leaves	Anoestrus	Oral	(Chander and Mukherjee, 1994)
<i>Aegele marmelos</i> (bael leaves) and <i>Murraya koenigii</i> (Curry leaf)	Anoestrus	Oral	(Dutt <i>et al.</i> 2011)
<i>Leptadenia reticulata</i> , <i>Asparagus racemosus</i> , <i>Couroupita guianensis</i>	Anoestrus	Oral	(Koradia, 1995)
Leaves of jute plant (about 2-2.5 kg), Bamboo tree, Mann tree (approx. 15-20 kg)	Anoestrus	Oral	(Gupta, 1993)
Mixture of black pepper (10 grains) and vanghuchi (20-25)	Anoestrus	Twice a day at the interval of 6-8 hours for 1-2 days orally	
Leaves of silk cotton tree powdered together with fermented boiled rice water	Anoestrus	500 ml, three times a day for 3 consecutive days orally	(Rajan and Sethuraman, 1997)
Pods of dudheli (<i>Pergularia daemia</i>)	Anoestrus	Oral	(Parmar, 1998)
3-4 seeds or fruits of bhilama (<i>Semecarpus anacardium</i>)	Anoestrus	Orally for 3-4 day	(Bechardas, 1992)
Bamboo leaves and bark boiled with paddy husk	RFM	Oral	(Verma, 1998)
<i>Ficus benghalensis</i> (banyan leaves)	RFM	Oral	(Vale, 1994)
Burned ash (Leaves and twigs of ber) along with water	RFM	Oral	(Baraiya, 1994)
250 g of leaves of jingara	RFM	Oral	(Rabari, 1994)
Cotton shells and roots of cotton plant	RFM	Oral	(Darbar, 1993)
<i>Legernaria vulgaris</i> (ruraikai)	RFM	Oral	(Balasundaram, 1998)
Tassles of 20-25 maize cobs boiled in water	RFM	Oral	(Baraiya, 1994)
1 litre of sugarcane leaf juice	RFM	Oral	(Ninama, 1999)

2 kg pearl millet (<i>Pennisetum americanum</i>) grain, 100g of methi (<i>Trigonella foenum-graecum</i>) seeds, 50 g of asalio (<i>Lepidium sativum</i>), 25 g of suva (<i>Anethum graveolens</i>) and 500 g of jiggery boiled in water for one hour and cooled	RFM	Oral	(Vaghasiya, 2001)
Root of jepti (500 g)	RFM	Oral	
<i>Abrus precatorius</i> , <i>Abutilon indicum</i> , <i>Anethum suva</i> , <i>Ficus glomerata</i>	RFM	Oral	(Singh and Khan, 1999)
Root bark of <i>Caesalpinia bonducella</i> (kanarej)	RFM	Oral	(Ali Sagar <i>et al.</i> 2003)
Raspberry leaves, garlic, Thyme (<i>Thymus sepillum</i>), starwort (Helonias root)	RFM	Oral	
Chick pea flour mixed with butter milk (rabri)	RFM	Oral	
Extracts obtained from boiling <i>Leptadenia pyrotechnica</i> root, <i>Abrus precatorius</i> , chopped bamboo leaves with black pepper, coriander, ajwain, sonth and methi	RFM	Oral	
Liquid extract of ergot (8 ml), quinine sulphate (5 g), magnesium sulphate (200 g), pulv. Gentians (16 g) and molasses	RFM	Oral (electuary)	
Roots of Chicory and Prosea, tender culms of <i>Phragmites maxima</i> , fruits of <i>Foeniculum vulgare</i> , and solidified sugarcane juice crushed and boiled	RFM	Oral	(Ali, 1999)
Whole plant of <i>Ludwigia octovalvis</i> crushed to make a fine paste; Fresh leaves of <i>Saccharum spontaneum</i>	RFM	Oral	(Ali, 1999)
Gum of <i>Acacia nilotica</i> subsp. Indica; Leaf paste of <i>Basella alba</i> ; whole plant of <i>Boerhavia diffusa</i> , <i>Oxalis corniculata</i> and <i>Centella asiatica</i>	RFM	Oral	(Kumar and Kumar, 2013)
Oil from seeds of <i>Brassica napus</i> ; Dried flower of <i>Corchorus capsularis</i> ; Leaf of <i>Mimosa pudica</i> and <i>Musa paradisiaca</i> ; whiskey of <i>Saccharum officinarum</i>	RFM	Oral	(Kumar and Kumar, 2013)
White radish-1or2 / Lady's finger-1.5 kg (salt and jaggery for taste)	RFM	Oral	Punniamurthy and Balakrishnan, NDDB
<i>Aristolochia indica</i> (Exapar)	Uterine Infection	Oral	(Ali Sager <i>et al.</i> 2003)
Approx. 100g of <i>Convolvulus microphyllus</i> (roots) powdered and mixed with 300 ml of water boiled, filtered and then cooled	Uterine Infection	Orally once a day for 3 days	(Parmar, 1999)
<i>Cheonopodium album</i> (boiled grain), <i>Girardinia diversifolia</i> (dried leaves), and <i>Hedychium spicatum</i> (seeds)	Dystocia	Oral	(Kumar <i>et al.</i> 1999)
20-25 leaves paste of <i>Argyria nervosa</i> with 25 ml of rice beer	Dystocia	Oral	(Pal, 1980)
Decoction of <i>Daedalacanthus roseus</i> roots with 50 ml country liquor	Dystocia	Oral	(Pal, 1980)
Stem bark of <i>Bombax ceiba</i> (crushed)	Dystocia	Slime; applied on vaginal ostium	(Bhattari, 1994)

Inflorescences and fruits of <i>A. indicum</i> and <i>Piper nigrum</i> crushed and made into a fine paste	Dystocia	Applied on vaginal ostium	(Ali, 1999)
Acial portion of cactus (250-300 g) crushed and mixed in 200 g buttermilk	Cervico Vaginal Prolapse	Oral	(Vankar, 1994)
Flour of Singhara (water chestnut)	Cervico Vaginal Prolapse	Oral	(Singh <i>et al.</i> 2002)
Fruit juice of <i>Citrus medica</i> mixed with powdered fruits of <i>Cuminum cyminum</i>	Cervico Vaginal Prolapse	Oral	(Ali, 1999)
Paste of whole plant of <i>Gomphrena serrata</i>	Cervico Vaginal Prolapse	Oral	(Ali, 1999)
Leaf paste of <i>Trichodesma indica</i>	Cervico Vaginal Prolapse	Oral and topical on the back of cows	(Ali, 1999)
<i>Quercus infectoria</i> (Majuphal) + <i>Symplocos racemosa</i> (Lodh)+ <i>Acacia arabica</i> (babool) + Alum	Pre and post-partum prolapse	Oral and topical on prolapsed mass	
Boiled and cooled mix. of Aloe-vera gel + water + turmeric, then, <i>Mimosa pudica</i> leave paste	Cervico Vaginal Prolapse	Topical on prolapsed mass, 3-4 times a day	Punniamurthy and Balakrishnan, NDDB
<i>Lawsonia inermis</i> (leaves); <i>Musa paradisiaca</i> (leaf extract); <i>Cordial</i> sp (leaves); <i>Convolvul microphyllus</i> (roots); <i>Cicer arietinum</i> (germinated Bengal gram); <i>Pedaliium murex</i> (fruits)	Repeat breeder	Oral	(Das <i>et al.</i> 2002)
<i>Epimedium sagittatum</i> (Horny goat weed) and <i>Tribulus terrestris</i> (Gokshura)	Impotence and erectile dysfunction (ED), Poor semen quality	Oral	(Rost, 2009)
<i>Tinospora cordifolia</i>	Poor semen quality and libido	Oral	(Jayaganthan <i>et al.</i> 2013)
Mixture of <i>Eurycoma longifolia</i> , <i>Tribulus terrestris</i> and <i>Leuzea carthamoides</i>	Poor semen quality and libido	Oral	(Frydrychova <i>et al.</i> 2011)
Wild asparagus root (Tian Men Dong); Sarsaparilla herb; Muira Puama; Bitter Melon (Ku Gua) and <i>Curculigo orchioides</i> (Xian Mao); Ginko Biloba; Cardamom; Cordyceps (Dong Chong Xia Cao)	Impotence and erectile dysfunction (ED), Poor libido	Oral	

Source: Herbal Treatment in Animal Reproduction by Perumal *et al.* (2013).

or alcohol (2) centesimal system favoured more in Britain and U.S.A., expressed by the letter c which indicate 1 part is mixed with 99 parts of water or alcohol to form a “1c” medicine. Potencies of 30c or lower and 200c or higher are considered as low-potency medicines and high-potency medicines, respectively (Macleod, 1981). Acute conditions are treated by higher potency, while chronic conditions by lower potencies of the drug. Homeopaths mostly prefer the potencies from the centesimal system

(3) LM system or potency which indicates 1 part is diluted to a factor of 50,000, rather than 10 or 100. C and X potencies drug most often come in the form of medicated sugar pellets, whereas LM medicines in liquid form which is diluted and given frequently, often daily.

Homoeopathic remedies referred as ‘veterinary doses’ for use in cattle are sugar-granule based, which are directly emptied on animal’s tongue. It has got advantage over conventional drugs in being absorbed through the tongue or palate.

Post-partum complication such as puerperal metritis can be treated by *Aconitum Napellus 6c*. Dose: six doses at 30 minutes interval; *Echinacea 3x*. Dose: four doses at 2 hours interval; *Sabina 6c*. Dose: four doses at 2 hours interval; *Secale 30c*. Dose: *t.i.d.* for 4 days; *Lachesis*. Dose: *t.i.d.* for 4 days. *Hydrastis 30c*, *Caulophyllum 30c*, *Sepia 200c*, *Calcarea Phosphorica 30c*, *Pulsatilla 30c*, *Platina 6c* and *Apis 30c* are also used for the treatment of endometritis and pyometra.

Homeocyst Protocol was advocated for the treatment of cystic ovarian disease in dairy cattle (Castilhos *et al.*, 2003). It included *Apis Mellifica 6c* with *Oopherinum 6x* for the treatment of dairy cows with right ovarian cysts, and *Thuja occidentalis 6c* with *Oopherinum 6x* when the animals had cysts in the left ovary or both ovaries. In such protocol, *Thuja occidentalis 6c* had effect on the left ovary mainly and *Apis Mellifica 6c* on the right ovary. Moreover, *Oopherinum 6x*, prepared from the extract of healthy bovine or ovine ovaries, was used based on the principle that a diseased organ is sensitive to its healthy counterpart (Castilhos *et al.*, 2003). Drugs like *Murex Purpurea 30c* and *Colocynthis 6c* were effective when nymphomania was associated with ovarian cysts. Palladium 6c was also indicated when right ovary alone was affected (Castilhos *et al.*, 2003).

Drugs like *Sepia 200c*, *Folliculinum 6c* and *Aletris Farinosa 30c* are indicated in uterine atony condition which has tendency to prolapse whereas *Iodum 30c* is indicated for true anoestrus condition. *Viburnum Opulis 30c* (weekly for 3 weeks) has been found as a good remedy for non-specific abortions which generally take place during early pregnancy.

Oral administration of Fertisule tablets (a combination of Homoeopathic drugs such as *Alteris Farinosa 30*, *Aurum Met.30*, *Apis Mel. 30*, *Borex 30*, *Calc. Phos. 30*, *Colocynthis 30*, *Folliculinum 30*, *Iodine 30*, *Murex 30*, *Oopherinum 30*, *Palladium 30*, *Platinum 30*, *Pulsatilla 30* and *Sepia 200*) showed very good response in repeat breeding buffaloes and better response

as compared to repeat breeding cattle (Chandel *et al.*, 2009).

Immunotherapy (Immunomodulators)

Many antibiotics such as Ciprofloxacin, gentamicin, enrofloxacin, OTC and cephalirin either intrauterine or parenterally and iodine preparations (prolonged cases of endometritis of fungal origin) have been used along with PGF₂ alpha and sometimes estrogen to combat post-partum endometritis. But, many reports indicated that intrauterine and systemic treatment with antibiotics either inhibited or destroyed leucocytic activity in bovine uterine secretions (Jayappa and Luken, 1983) or led to the development of antibiotic resistant strains (Whitemore and Anderson, 1985) or detected as antibiotic residues in milk for longer time (36-120 hrs) after intra uterine infusion (Hualand *et al.*, 1984). One important drawback is their activity is greatly reduced in presence of blood, pus and necrotic tissues, so, not very effective in the treatment of uterine infections (Olson *et al.*, 1984). PGF₂a is only effective when active corpus luteum is present. Estrogen seldom used because of their appreciable levels detected in milk that make it unfit for human consumption or higher doses may lead to the development of ovarian cysts. Mild endometritis cases should be left untreated to heal by "self cure" phenomena at least for 4 weeks post-partum.

Lysosubtilin (more precisely lysosubtilin G10x) obtained from *Bacillus subtilis* SK-52 act as lytic enzyme capable of degrading proteinaceous components of microbial cell wall and is found to be effective against post-partum endometritis in cattle when 2 x 10⁶ U lysosubtilin in 100 mL of distilled water administered at intervals of 3-4 days (Biziulevichius and Lukauskas, 1998). Immunomodulators as an alternative to antibiotic therapy have been shown to be of great value in treatment of endometritis. They act mainly by three ways (1) contains immunoglobulins mimic humoral immunity. Examples are (i) Autologous blood plasma. Dose:

40-50 ml IU 2 times at 24hrs interval (Methai, 1999) (ii) colostrum whey. Dose: 40-50 ml IU 2 times at 24hrs interval (2) chemo-attractants boost cellular immunity. Examples are (i) 100µg or 200 µg E. coli LPS in 20 ml distilled water IU 2 times at 24hrs interval (Saini *et al.*, 1999) (ii) Mycobacterial Cell Wall Extracts : Mycolic acid (Rogan *et al.*, 2007) (iii) Granulocyte macrophage colony stimulating factor (GM-CSF) (Hughes and Couto, 1988) (iv) Leucotriene B₄ (LTB₄): an arachidonic acid metabolite. Dose: 50 ml of 30 nmol/L solution IU once (Zerbe *et al.*, 1996; Dhaliwal *et al.*, 2001) (v) Oyster glycogen 500 mg IU once (Singh *et al.*, 2003) (3) Antimicrobial activity like antibiotics. Examples are (i) PMN extracts called defensins (Ganz *et al.*, 1985) (ii) Probiotic cultures derived from the vaginal microflora of healthy women (iii) Alcoholic extracts of chamomyle, marigold, comfrey, salvia and yarrow plants (Borowieck, 1989) (iv) Neem oil. Dose: 40-50 ml IU 2 times at 24hrs interval (v) *Tinospora cordifolia* (aqueous extracts). Dose: 50ml (3000 mg total dose) IU for 3 consecutive days (Kumar *et al.*, 2004) (vi) Turmeric and garlic extracts (vii) Antifungal agents *i.e.* *Rosemarinus officinalis* and *Thymus vulgaris* against mycotic endometritis (Hanafi *et al.*, 2010).

CONCLUSION

Therapeutic management of bovine reproductive disorders significantly improves reproductive health and productivity of animal. Today, veterinarians prefer herbal remedy, immunotherapy and homeopathic treatments over antibiotics because of their minimal side effects and milk residues which are important from public health point of view. On the other aspect, herbal preparations and immune modulators have the potential to boost immunity and enhancing the body's natural healing process to combat disease conditions. But along with medicinal therapy, nutrition and other aspects of management also play an important role in livestock production system. Trace mineral supplements or chelated mineral

mixture along with concentrate ration should be given as per the requirement of the animal in different physiological states. Deworming calendar of animals should be strictly followed as it is shown to jeopardize fertility of the animal. Most of the periparturient diseases can be prevented if dry cow nutrition and management are well attended during transition period.

CONFLICTS OF INTEREST

Authors declare no conflicts of interest.

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