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Lithium antimony thiomalate and acyclovir therapy for buffalo mammillitis

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Abstract

Mammillitis is a condition in she buffaloes in which there will be sudden teat inflammation, enlargement, difficulty in milking, difficult for the calf to suckle, formation of black necrotic patches with circumscribed necrotic areas on teat base. The affected teat slough off in primiparous buffaloes and the cause is suspected to be by Herpes virus. Ten buffaloes exhibiting mammillitis were treated with three injections of lithium antimony thiomalate (2 mg/kg deep IM), acyclovir (1-1.5 mg/kg slow IV in fluid), chlorphenaramine maleate (0.5-1.0 mg/kg IM), meloxicam (0.5- 1 mg/kg, IM) with two days apart along with external application of ointment containing acyclovir. Clinical recovery was seen in 8 buffaloes after 7 days of last dose of treatment. The hyperemic and edematous teats noticed earlier before treatment slowly resolved to almost normal size. Thus, the efficacy of lithium antimony thiomalate, acyclovir, chlorphenaramine maleate and meloxicam may be attributed to anti-fibrosis, antiviral, anti-allergic and anti inflammatory effect respectively in buffalo mammillitis.

Keywords: Buffalo, Mammillitis, Lithium antimony thiomalate, Acyclovir; Chlorphenaramine maleate, Meloxicam

1. Introduction

Bovine herpesvirus 2 (BHV-2) causes mammillitis of teat in cows. There will be sudden onset of inflammation, papules, skin sloughing, vesicular growth, scab forming, and ulceration. In early lactating primiparous buffaloes, there will be an acute inflammation of one or more teats leading to necrotic ring formation, gangrene and fibrosis (Mouli, 1992^[14]). The condition is less successfully treated with antibiotics, NSAIDs and glucocorticoids. The therapy by external application with herbal was moderately effective in early stage and administration of herbal capsules with external application of herbal cream (Shridhar 2005^[24]; Sundares and Janaki, 1997^[27]). Lithium antimony thiomalate was used for the condition with better cure rate in early conditions. The probable mechanism of lithium antimony thiomalate in curing the condition might be due to its anti-fibrosis activity (Shridhar *et al.*, 2014^[25]; Wadhwa *et al.*, 1992^[30]; Kachawa *et al.*, 2017^[8]) had administered amoxicillin and sulbactam combination, ketoprofen, ascorbic acid and cefoparazone for intramammary infusion in mastitis affected quarters once only for 5 days with recovery in early stage. Buffaloes with ulcerative thelitis suspected to be caused by bovine herpes mammillitis (BHV-2) infections were treated with acyclovir orally with external application for 5 days with cure rate of 62.5%. However, the treatment is unsuccessful in many cases. In the present study, an attempt is made to treat the mammillitis with combination of lithium antimony thiomalate, chlorphenaramine maleate, meloxicam with acyclovir oral and topical therapy for 5 days with good success rate.

2. Materials and Methods

2.1. Selection of the animals

Non descriptive lactating primiparous buffaloes (10) exhibiting vesicles, papules, clinical signs characterized by acute inflammation of one or more teats later leading to formation of necrotic ring and leading to sloughing off of the skin. The buffaloes were selected in Shivamogga, Uttara Kannada and Chikkamagaluru of Karnataka State for the treatment. In most of the animals the lesions were observed in hind quarters, either left or right. Most of the animals developed the condition with initial hyperemia, edema of udder, vesicles, ulceration hardness of the affected teat. (Figure 1). Calves were disallowed by the affected buffaloes to suckle and for milking indicating the severe pain and inflammation of the affected teat.

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2.2. Examination of the milk sample

The milk from the affected quarter was subjected to California Mastitis Test (CMT) and further culture and sensitivity test (Christie and Koegh, 1940^[4]). The pH of the milk samples was also recorded. The somatic cell count of milk samples was done as per the method of Schalm *et al.* (1971^[19]). Electrical conductivity was measured using conductivity meter (Sneath Peter *et al.*, 1986)^[26].



Fig 1: Hyperemic, edematous udder, ulceration and vesicles on the surface of the affected teats

2.3. Treatment

Lithium antimony thiomalate @ 2 mg/kg deep IM (Anthiomaline[®], 6% w/v, Novartis India Ltd, Mumbai), chlorpheniramine maleate 0.5-1.0 mg/kg IM (Anistamin[®], 10 mg/ml, Intas Animal Health, Ahmedabad), meloxicam 0.5-1 mg/kg, IM (Zobid-M[®], Sarabhai Zydus Animal Health Ltd, Mumbai), acyclovir inj @ 1-2 mg/kg slow IV in fluid (Zovinex[®], 500 mg/vial, Novo Medi Sciences Pvt. Ltd. Mumbai) were administered once in two days with external application of the ointment containing acyclovir (Herperax Ointment[®], 5 g, Micro Labs Ltd, Mumbai) to all the affected teats of buffaloes. The treated buffaloes were kept under observation for 10-15 days and the recovery signs were observed and recorded.

3. Results and Discussion

3.1. Incidence of mammillitis

Many earlier workers had also reported the incidences of mammillitis due to herpes virus in cattle and buffaloes as reported in the present study (Gourreau *et al.*, 1989^[7]; Nauriyal and Randhawa, 1992^[15]; Sehrish Firyall *et al.*, 2019^[21]).

3.2. Examination of the milk sample

In the present study, milk drawn from the affected teat revealed negativity to presence of any pathological bacteria. Similar observation was also made by many researchers who also informed that the milk will be free from pathogenic bacteria from the milk of mammillitis affected teat (Thilagar *et al.*, 2000^[29]; Kachawa *et al.* 2017^[8], Purohit *et al.*, 2014^[16]). In the present study, out of 9 animals 6 were primiparous heifers and only one hind teat is affected.

3.2. Occurrence

The reason for the occurrence in heifers is still unanswered but stated that it might be because of stress of calving particularly with udder edema and hormonal changes lead to activation of BHM virus and development of signs (Gibbs, 1984^[6]; Kemp *et al.*, 2008^[9]; Martin, 1973^[11]; Sankaram and Kotayya, 1977^[19]). The clinical condition was usually sporadic in occurrence within first two months of lactation in the heifers of first calving preferably in winter season with hind quarter infection. Similar observation also made by other researchers (Mouli, 1992^[14], Sharma *et al.*, 1998^[22]; Sharma and Singh, 2006^[23]).

Seven out of 10 animals which did reveal the early signs disease recovered uneventfully after the completion of therapy. However, those animals which showed the necrotic rings on the teat did not respond well to the treatment (Figure 2). Teat edema, hyperemia slowly resolved to normal after 7 days of therapy. Paste of *Breynia patens* and *Sclerophyllum wallichianum* moderately cure the mammillitis in buffaloes (Sundaresh and Janaki, 1997^[27]; Misra, 1991^[13]). Different parts of these plants known to possess anti-inflammatory and anti-histaminic effects might have played key role in overcoming mammillitis and preventing further damage to affected teat.

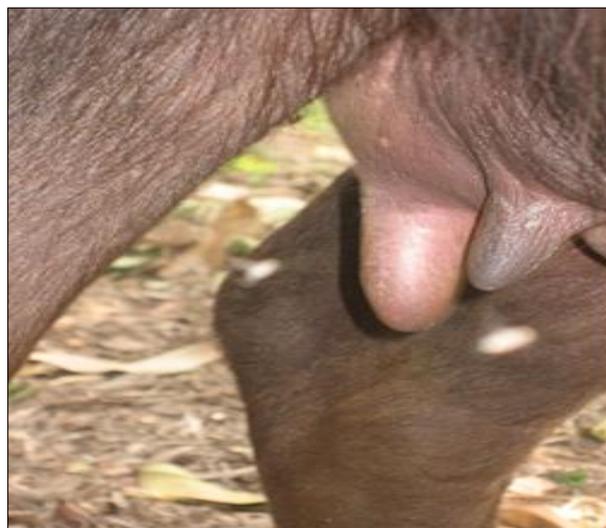


Fig 2: Recovery stage after treatment

3.3. Treatment

A twin treatment with Whisprec ointment application and Teburb Capsule oral administration in early stages had the cure (Shridhar, 2005^[24]). Therapy with different drugs and auto immune therapy was with little success (Rao, 2009^[17]). In the present study the buffaloes which did not respond positively to the treatment and developed necrosis of the affected teat and later fallen off from the udder (Figure 3 and 4). Once the necrosis start developing, the tissue will not have the active cells to respond. The efficacy of lithium antimony thiomalate will reduce the fibrosis with mechanism not well understood. Chlorpheniramine maleate is an antihistamine with known anti allergic property. Meloxicam is an NSAID with well known anti inflammatory activity (Shridhar *et al.*, 2014^[25], Syed *et al.*, 2009^[28]). Lokanadhamu *et al.* (2005)^[10] studied the efficacy of oral and topical use of acyclovir a well established anti-herpes drug in buffalo mammillitis. It acts by converting to its triphosphate form, acyclovir triphosphate (ACV-TP), which competitively inhibits viral DNA

polymerase, incorporates into and terminates the growing viral DNA chain, and inactivates the viral DNA polymerase. The anti-herpes activity against bovine herpes mammillitis (BHV-2) virus is explained by Watson (1989^[31]).

The oral kinetics of acyclovir is not well established in ruminants. In horses, the oral administration of acyclovir did not achieve the required plasma concentration where as its pro-drug valacyclovir did it after IV administration in equine herpes virus infection (EHV-1). Valacyclovir is a prodrug of acyclovir that may be an attractive and valuable candidate for the treatment of EHV-1 infections in horses. Acyclovir given orally to horses @ 20 mg/kg did not eradicate EHV-1 plasma concentrations of the same could not be achieved at site of action. Hence oral treatment of horses with acyclovir was proved not effective for EHV1 infection in horses (Bentz Garré *et al.*, 2006^[1]). But acyclovir could abolish virus titre of BHV-1 and progression of cytopathic effect in cell culture studies (Enan *et al.*, 2012^[5]). It was confirmed that acyclovir had good efficacy on BHV-2 infection. Hence, in the present study parenteral administration of acyclovir was preferred to assure the good plasma concentration for better anti viral activity based on earlier observations (Watson, 1989^[31]; Rollinson, 1992^[18], Sehrish Firyall *et al.*, 2019^[21]). Chlorpheniramine meclizate is a H1 receptor antagonist antihistamine used to treat many conditions in cattle and buffaloes. It is used to treat the allergies in cattle and buffaloes. In the present study also, it is used as anti allergic drug to reduce the allergic reactions as reported to be efficacious in earlier studies (Lokanadhamu *et al.*, 2005^[10]; Vardanyan and Hruby, 2006^[32]; Neelesh Sharma *et al.*, 2006^[2]). In the present study Meloxicam was used as analgesic and anti-inflammatory agent to reduce the inflammation and pain. It is a well known NSAID that is used commonly in bovine mastitis therapy. It has got low ulcerogenic property as it is a preferential COX-2 inhibitor with long half life of 17 hours in cattle (Mathews, 2002^[12]; Breen, 2017^[3]).

In the present study, calves were not allowed to suckle the affected teat as suckling and forced milking may cause more damage to the teat. Infusion of intramammary preparations is not suggested as forceful insertion will cause more damage as there will not be any bacterial infection (Sehrish Firyall *et al.*, 2019^[21]).

Further studies on finding a better medication or an effective vaccine to prevent the occurrence of the disease are much needed to avoid the loss due to a reduction in the milk yield of the affected buffalo due to the development of teat deformity or teat loss which would reduce the market price of buffalo causing significant economic loss to farmers.



Fig 3: Formation of black necrotic ring at the base of the teat



Fig 4: Fallen off teat with remnant

4. Conclusion

Primiparous buffaloes in first calving do suffer from a condition known as mammillitis in which there will be characteristic teat inflammation, enlargement, difficulty in milking, difficult for the calf to suckle followed by black necrotic ring formation and finally the teat will slough off from udder. The disease is caused by bovine herpes virus (BHV-2). The buffaloes suffering from the mammillitis were treated with lithium antimony thiomalate, acyclovir, chlorpheniramine meclizate and meloxicam with good recovery rate which indicates the efficacy of these drugs in the therapy of buffalo mammillitis.

5. Conflict of interest

No conflict of interest.

6. Acknowledgement

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