The Pharma Innovation Journal 2022; SP-11(5): 1236-1239

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277-7695
ISSN (P): 2349-8242
NAAS Rating: 5.23
TPI 2022; SP-11(5): 1236-1239

www.thepharmajournal.com
Received: 26-02-2022
Accepted: 30-03-2022

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Promising role of micronutrient zinc in reducing the clinical severity in contagious ecthyma (ORF) affected sheep and goats

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Abstract
Contagious ecthyma (CE), known as ORF, a specific disease of sheep, goats and many other wild small ruminants is caused by a parapox virus of the family poxviridae. The disease mostly affects young animals 3-6 months of age, but older animals may also be affected. It is an economically important disease of sheep and goat raising countries and is worldwide in distribution. Clinically the disease is characterized by proliferative lesions on lips, mucosa of the mouth, nostrils, face, scrotum, teats and feet. Complications can arise due to secondary infections resulting in mortality.

A clinical trial for evaluating the therapeutic potential of topical application of zinc (zinc oxide paste) in reducing the clinical severity of ORF lesions was conducted. Young affected lambs (N=30) from a single outbreak in an organized farm (MRCSG, Shuhama Alusteng, SKUAST-K) were enrolled for the trial. Animals were divided into 3 groups of 10 each. The lesions were treated topically with zinc oxide paste, boric acid paste and combination of the two.

The mean number of days taken for recovery in group A (zinc oxide), B(boric acid) and C(zinc oxide + boric acid) were $11.70^{a} \pm 1.46$, $17.90^{b} \pm 1.96$ and $14.70^{ab} \pm 0.84$ respectively. Besides no complication, or mortality was observed in group A. The results showed that zinc oxide was significantly ($P<0.05$) better compared to other treatment regimens, considering the number of days taken for clinical recovery, mortality observed and complications developed. The study concluded that zinc oxide offers a novel, viable and non-antimicrobial alternative in alleviating the severity of ORF lesions and a need to refine the existing farmers' practice of using boro-glycerin.

Keywords: Clinical severity, contagious ecthyma, lambs, zinc

Introduction
Contagious ecthyma is an acute, contagious and economically important zoonotic disease of sheep, goats and many species of wild ruminants (Spyrou *et al*., 2015) [1], caused by epitheliotropic ORF virus of the genus Parapoxvirus and family Poxviridae (Gallina *et al*., 2006) [2]. ORFV is related to bovine papular stomatits virus (BPSV), Pseudocowpox virus (PCPV), and Parapoxvirus of red deer in New Zealand (PVNZ) (Hosamani *et al*., 2006).Clinically the disease (CE) is characterized by proliferative and often self-limiting lesions on the skin of lips, oral mucosa and around the nostrils of affected animals.

Sometimes the lesions can also occur on teats/udder of nursing mothers and rarely on internal organs (esophagus, abomassum and rumen mucosa), and tongue and gums of the affected animals (Bouznach *et al*., 2013) [4].

In an outbreak, management of the affected animals includes separation of sick animals, disinfection of animal houses and potentially infected equipments and treatment of the sick animals. The latter involves parental antimicrobials (Nandi *et al*., 1999) [5], topical application of $KMnO_4$ and Boric acid (Rao *et al*., 1994) [6], levamisole (Wilson *et al*., 2002) [7], combination of sucralfate (15% w/w) and cidofovir (1% w/w) as a spray and Vaseline mixed with Iodine (Sonvico *et al*., 2009) [8]. Battling with the threat of growing antimicrobial resistance, a research for non-antimicrobial alternatives has to be prioritized. Yet one should balance the ethical obligations regarding patient benefits versus public health risks. Micronutrient zinc, having antimicrobial, anti-inflammatory and pro-healing properties, offers a novel approach and a new boulevard for alleviating the severity of lesions. The present study reports evaluating efficiency of micronutrient (zinc) in reducing the severity of the lesions and hastening the recovery.

Materials and Methods

For evaluating the efficiency of zinc (zinc oxide) in alleviating the severity of lesions and hastening the recovery, young affected lambs (N=30) from a single outbreak in an organized farm (MRCSG, Shuhama Alusteng, SKUAST-K) were enrolled for the trial. Animals were divided into 3 groups (Group A, Group B, Group C) of 10 each. The lesions as depicted in Figure 1 were treated topically with zinc oxide paste, boric acid paste and combination of the two as depicted in Figure 2 and 3. Group A was treated with zinc oxide paste (ZnO @ X conc. in glycerine @Z), Group B treated with Boric acid paste (Boric acid @ X conc. in glycerine @ z) and Group C treated with Zinc oxide & Boric acid paste (ZnO @ 1/2 X conc. & Boric acid@1/2X conc. in glycerine) (where *X* = 60 grams; Z = 40 ml). The group homogenity with respect to age, severity of lesions was ensured. The comparative efficacy of the treatment interventions was assessed on average number of days taken for resolution of clinical signs, complications developed during the trial. Different criteria for the trial are given in Table 1.

Results and Discussion

The experimental findings obtained with respect to the clinical trial conducted revealed significantly ($P<0.05$) better results with topical application of zinc oxide alone compared to other treatment regimens tested in terms of number of days taken for resolution of clinical signs, complications developed and mortality observed during the trial (Table 2). A typical severe case of ORF treated successfully during the trial is shown in Figure 4.The potential role of zinc oxide in reducing the clinical severity of ORF lesions could be attributed to its antimicrobial activity (Bhat IA. 2016), immunomodulatory and mucosal protective role (Turner RB and Cetnarowski WE. 2000) [10]. The encouraging results obtained in the present study have opened up newer and non-antimicrobial window for management of ORF through topical application of zinc oxide paste. Although ORF is a self-limiting disease, symptomatic treatment with local antiseptics is very helpful (Nandi *et al*., 2011) [11]. Topical and systemic antimicrobials can be used to prevent secondary bacterial complications. Local application of $KMnO_4$ (1:100-1:10000) and Boric acid (1:10) has been found helpful (Rao *et al*., 1994) [6]. Use of Levamisole as an immunostimulant has been indicated in ORF (Wilson *et al*., 2002) [7]. Cidofovir (1% w/w) as anti-viral alone or in combination with sucralfate (15% w/w) as wound healant has shown promising results in treatment of human ORF, however, the costs involved have proven prohibitive for use in animals (Dal Pozzo F.2007) [12].

Present study revealed that topical application of zinc oxide with suitable vehicles can help in early resolution of the lesions, offering a viable non-antimicrobial alternative for clinical management of contagious ecthyma.

Table 1: Inclusion and exclusion criteria for the therapeutic trial

S. No.	Inclusion criteria	Exclusion criteria
1.	Lambs of either sex	Kids of either sex
2.	Age < 3 months	Of any age
3.	No initial clinical evidence of bronchopneumonia or gastroenteritis	Death during the trial
4.	Affected during a particular time period and in a single farm.	Time zero evidence of systemic involvement.

Table 2: Evaluation of different therapeutic regimens tested

Group (n=10)	No. of days taken for recovery (Mean±SE)	Complications Developed
A	$11.70^{a} \pm 1.46$	Nil
B	$17.90^{b} \pm 1.96$	1. Death due to inanition 2. Wool ball on PME*
C	$14.70^{ab} \pm 0.84$	1. Bronchopneumonia 2. Gastroenteritis 3. Wool ball on PME*

*****PME= Postmortem examination

Figures bearing different superscripts differ significantly (P<0.05)

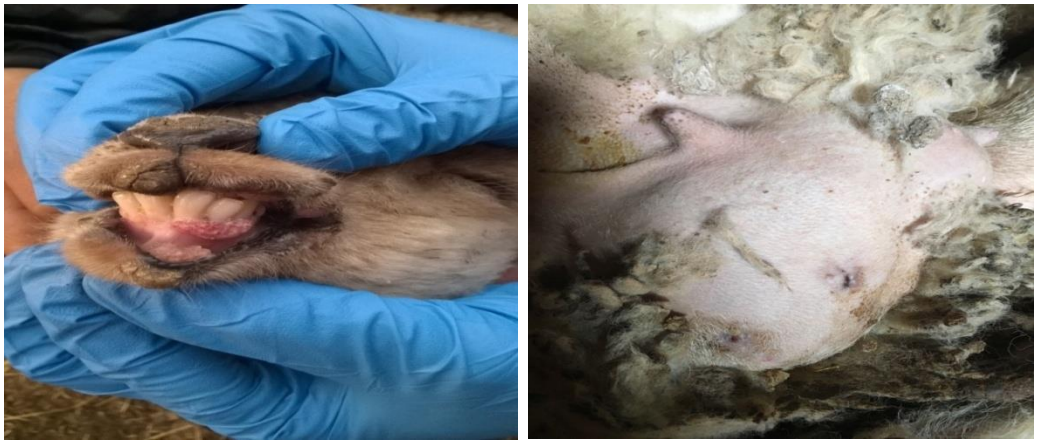

Fig 1: Proliferative lesions of ORF on gums, lips, muzzle, nostrils and udder

Fig 2: Different therapeutic agents used in the clinical trial

Fig 3: Topical application of medicine over the lesions

I II III

Fig 4: A typical case of ORF: I) Pre-treatment, II) during treatment and III) Post-treatment

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