

Clinical Studies on Bovine Papillomatosis

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Abstract

The present clinical study was conducted to study incidence, clinical symptoms and efficacy of different treatment modalities on bovine papillomatosis. Among total of 3812 cattle presented to the clinic, 52 cattle were having papillomas. No incidence of papillomas was recorded in buffaloes. Thirty cattle with bovine papillomatosis were divided into 5 groups of 6 animals each and were treated with subcutaneous administration of ivermectin, autohaemotherapy, autogenous vaccine, surgical excision and tarantula cubensis extract administration respectively. Highest incidence of bovine papillomas was observed in cattle of 3 years age. Jersey crossbred cows were the most commonly affected breed followed by HF cross breed and non – descript cows. Most of the papillomas were located on teats only (40.38%) followed by teats and udder (21.15%). Histopathologically, fibropapilloma (60%) was found to be most common papilloma followed by angiokeratotic acanthomatous papilloma (40%). Immunohistochemical studies were conducted to know the rate of proliferation of bovine papillomas. Immunopositive reaction was observed against VEGF in angiokeratotic acanthomatous papilloma. EGFR and Ki67 immunopositivity was observed in fibropapillomas. Tarantula cubensis extract was found to be efficacious in the treatment of bovine papillomatosis with no occurrence for a period of 6 months.

Keywords: Autohaemotherapy, Autogenous Vaccine, Bovine Papilloma, Ivermectin, Surgical Excision and Tarantula Cubensis Extract

Introduction

Bovine papillomatosis is a contagious disease caused by bovine papilloma virus and characterized by the presence of warts or papilloma of various sizes on the skin, either localized to the teat or generalized (Somvanshi, 2011). Papilloma viruses are classified in the family papillomaviridae. This large family of animal and human viruses generally infects epithelial cells causing hyper proliferative lesions (Dyk *et al.*, 2011). Papilloma viruses (PVs) are small, non enveloped, double stranded DNA viruses with circular genomes replicate intranuclearly in infected cells. Thirteen types of the bovine papillomaviruses (BPVs) have been characterized in cattle; namely BPV1 to BPV13, which are divided into three genera, as Delta papilloma virus (BPV 1-2 and 13), Epsilon papilloma virus (BPV5 and 8) and Xipapilloma virus (BPV 3, 4, 6, 9, 10, 11 & 12) (Jeremiah *et al.*, 2016). However, BPV1, BPV2 and BPV5 commonly cause cutaneous fibropapillomas, while BPV 3, 4 and 6 induce squamous papillomas in both the skin and upper gastrointestinal tract. In the bovine species, cutaneous papillomatosis is more common than in any other domestic animals. The disease affects young animals more often and more severely, but may also affect cattle of all age (Borku *et al.*, 2007). Papillomavirus infection in cattle could lead to weight loss and stunted growth, skin lesions are often located on the udder and impede milking, and hence results in reduced milk yield. The clinical manifestation of these disorders could incur serious economic losses, if not detected and treated in due time. The present study was carried out to study the incidence, gross, histopathological and immunohistochemical features and the efficacy of different treatment modalities of bovine papillomatosis.

Materials and Methods

The present study was conducted on thirty animals with papilloma or wart like growths anywhere on the body and divided into five groups of six animals each. Routine clinical examinations were carried out and those that found to be fit for surgery and other treatments were utilized for the present study.

- a. Group I-Animals were given ivermectin @ 200 mcg/ kg b.wt subcutaneously at 15 days intervals.
- b. Group II - Animals were given autochemotherapy 20 ml subcutaneously at weekly intervals for four weeks.
- c. Group III-Animals were administered autogenous vaccine (10 ml in adult animals and 5 ml in calves) weekly once for four weeks subcutaneously. Group IV - Animals were subjected to surgical excision.
- d. Group V- Animals were administered tarantula cubensis extract 10 ml subcutaneously at weekly intervals for two weeks.

The incidence, gross, histopathological and immunohistochemical features and the efficacy of different treatment modalities of bovine papillomatosis were studied and analyzed.

Results and Discussion

The incidence of bovine papillomatosis was found to be high in age group of above 3 years followed by 1-3 years (Sharma *et al.*, 2004). The correlations in the breed wise incidence of bovine papillomatosis revealed highest incidence in Jersey cross bred cows followed by Holstein Friesian cross bred and Non descript cows. Ozsoy *et al.* (2011) reported highest incidence of bovine papillomas in Holstein cattle. However, the availability of different breeds in a particular geographical location would predispose certain breeds to get affected. The incidence was higher in cross bred animals. This shows higher susceptibility of cross bred cattle in comparison with indigenous cattle. Sharma *et al.* (2004) also reported highest incidence of papillomas in cross bred cattle. The incidence of bovine papillomatosis was found to be high in females. The reason might be the female cattle usually under stress factors such as gestation, lactation and progression in age. On the other hand, male cattle are usually directed to fattening and meat production and are mostly slaughtered at the age of 2 years or less (Salib and Farghali, 2011). In the present study, maximum numbers of animals were having papillomas on teats only, followed by warts on udder and teats. Papillomas on other body parts (38.46%) included head, neck, eyes, eyelids, limbs, ventral abdomen and base of the tail. Generalized papillomas i.e., multiple disseminated warts on the head, ears, eyelids, neck, shoulders, limbs, abdomen and para-genital region were observed in nine animals representing an incidence of 17.30% (Turk *et al.*, 2005).

Flat type papillomas were found to be most common type of papilloma followed by filliform and cauliflower like papillomas. The wart size ranged from 1 cm to 15 cms. Grey and brown colored papillomas were most commonly recorded followed by black, white and black and brown. Papillomas with rough surface were most commonly observed with an incidence of 55.76% in our study. Papillomas on teat and udder were mostly multiple, disseminated and non pedunculated with a size ranging from 0.5 cm to 1 cm. In group I, animals affected with papillomatosis were given ivermectin injection at the rate of 200 mcg/ kg bodyweight subcutaneously. Ivermectin was effective in young calves with mild and early papillomatosis. Warts disappeared between 45 to 60 days after the second injection. Out of 6 cases, 3 animals responded well to the treatment thus giving efficacy in only 50% of cases (Fig. 1). In our study, improvement obtained upon subcutaneous injections of ivermectin for the treatment of papillomatosis might have occurred due to immunostimulatory effect of ivermectin (Jameel *et al.*, 2011).

GROUP I



Figure 1: Animals treated with Ivermectin

In the present study, efficacy of autohemotherapy was 66.66% by the end of six weeks of treatment. Out of 6 cases, four animals responded well to the treatment. After 3rd injection, the papilloma growths showed signs of regression (Fig. 2). Autohemotherapy was believed to stimulate the reticulo-endothelial system and to increase population of macrophages in circulating blood which might be responsible for enhancing regression of the papillomas (Ranjan *et al.*, 2013).

GROUP II



Figure 2: Animals treated with autohaemotherapy

Administration of autogenous vaccine in group III animals caused sloughing of warts from the affected areas. Regression of papillomas occurred in about 3 weeks after the commencement of the treatment and complete regression was observed after 15-20 days of last injection, with a success rate of 83.33% (Fig. 3). The autogenous vaccines stimulate the immune system against the papilloma viruses. The variation of response might be attributed

to type of virus involved, developmental stages of papillomas, method of collection of papilloma tissues and preparation of vaccine, schedule of administration and immune function of the patient.

GROUP III



Figure 3: Animals treated with autogenous vaccine

In our study, surgical excision was the more appropriate solution with success rate of 100% as the shape, size and location of papillomas permitted their easy removal. The therapeutic effect was more rapid and definitive after surgery (Fig. 4).

GROUP IV



Figure 4: Animals treated by surgical excision

In the present study, tarantula cubensis extract has been used to treat bovine papillomatosis in group V animals. The extract of tarantula cubensis is a homeopathic drug used widely in veterinary medicine. It is effective through the spider venom it contains. Tarantula cubensis extract stimulates the absorption and demarcation of many types of ulcers and necrosis as well as treating mammary gland tumors and proliferative cases in animals (Gultiken and Vural 2007 and Gultiken *et al.*, 2015 in canine mammary tumors, Icen *et al.*, 2011 in canine oral papillomatosis). In this study, tarantula cubensis extract was found to be effective in decreasing clinical lesions in bovine papillomatosis and the post treatment observations for 6 months. Papillomas regression was verified after the second week evidenced by papillomas necrosis, detachment and fall (Fig. 5). There was no recurrence in any animal, with no adverse reaction. Although the mechanism of action of tarantula cubensis extract was not completely clear, it is thought to stimulate the defence mechanism of the body to aid spontaneous remission (Cam *et al.*, 2007). Histologically, fibropapillomas and angiokeratotic acanthomatous papillomas were the different types of papillomas diagnosed in the present study. The findings of the present study were in agreement with the observations of the Jelinek and Tachezy (2005).

GROUP V



Figure 5: Animals treated with *Tarantula cubensis* extract

In the present study immune positive expression of VEGF in the cytoplasm of endothelial cells of blood vessels and the basal layer of epidermis in angiokeratotic acanthomatous papilloma cases was observed, suggesting a possible role in papilloma development through angiogenesis (Martano *et al.*, 2018). EGFR Immunopositive reaction was noticed in different layers of epidermis in the cytoplasm of fibroblasts present in dermis which established that dysregulation of EGFR receptor signaling pathway is associated with the development and progression of malignancy. In the present study, immunohistochemistry for the proliferation marker Ki67 displayed mild immunopositivity in the nuclei of basal layer of epidermis in fibropapillomas (Beytut, 2017). This was in agreement with the findings of Ozsoy *et al.* (2011)

On the basis of our results, the success rate of bovine cutaneous papillomatosis through surgical excision was higher than after autohemotherapy, autogenous vaccine and ivermectin. The therapeutic effect was more rapid and definitive after surgery, but only in cases where clinical symptoms (size, shape and location) were appropriate for total excision. The surgical excision could not be possible in all cases, where papillomas have spread on a large body area, (generalized papillomatosis) when their shape and size do not allow excision as in disseminated, sessile papillomatosis (in udder and teat papillomatosis). In such instances, alternate method of treatments were appropriate among which was the tarantula cubensis extract which decreased lesions of papillomas with no adverse reactions. Due to the ease of use and availability in preparatory form it is concluded that tarantula cubensis extract can be used in the treatment of bovine papillomas effectively under field conditions.

Conflict of Interests

There is no conflict of interest.

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