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Dr. Vikas RN
Ph.D. Scholar, Department of
Veterinary Surgery and
Radiology, KVAFSU, Bidar,
Karnataka, India

Dr. BV Shivaprakash
Director of Research,
KVAFSU, Bidar, Karnataka,
India

Dr. Dilip Kumar D
Director of Instructions (Post
Graduate Studies), KVAFSU,
Bidar, Karnataka, India

Dr. Bhagavantappa B
Associate Professor and Head,
Department of Veterinary
Surgery and Radiology,
KVAFSU, Bidar, Karnataka,
India

Dr. Kavitha Rani B
Professor and Head,
Department of Veterinary
Pathology, Veterinary College,
Shivamogga, Karnataka, India

Corresponding Author:
Dr. Vikas RN
Ph.D. Scholar, Department of
Veterinary Surgery and
Radiology, KVAFSU, Bidar,
Karnataka, India

Intralesional 5-fluorouracil as a therapeutic approach for ocular squamous cell carcinoma in cattle

Vikas RN, BV Shivaprakash, Dilip Kumar D, Bhagavantappa B and Kavitha Rani B

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Abstract

Bovine ocular squamous cell carcinoma (OSCC), commonly known as “cancer eye,” is an important neoplastic condition affecting cattle and has considerable clinical and economic significance. The present study was undertaken to assess the occurrence and clinical characteristics of ocular tumours in cattle and to evaluate the therapeutic efficacy of intralesional 5-Fluorouracil (5-FU). Fifteen cattle with ocular tumours presented to the Department of Veterinary Surgery and Radiology, Veterinary College, Bidar, were selected for the study. Clinical, ophthalmic, haematobiochemical, histopathological and immunohistochemical examinations were performed. All cases were confirmed as squamous cell carcinoma histopathologically. Affected animals ranged from 4 to 9 years of age, with most cases occurring in cattle above five years of age. Tumours were observed at different ocular sites, including the limbus, cornea, conjunctiva, eyelids and third eyelid, and commonly appeared as raised, irregular, fleshy or cauliflower-like masses associated with lacrimation, irritation and partial loss of vision. Immunohistochemically, tumour cells showed strong cytokeratin positivity, while EGFR and VEGF exhibited variable moderate to strong immunoreactivity. Intralesional 5-FU (50 mg/ml) was administered weekly on days 0, 7, 14 and 21. Gradual tumour regression was observed in all treated animals, with no recurrence during the six-month follow-up period. The findings indicate that intralesional 5-FU may be an effective, localized and practical therapeutic option for bovine ocular squamous cell carcinoma, particularly where preservation of the globe is desirable.

Keywords: Bovine ocular squamous cell carcinoma, cattle, 5-Fluorouracil, immunohistochemistry

Introduction

Bovine ocular squamous cell carcinoma (OSCC), commonly referred to as “cancer eye,” is one of the most frequently occurring malignant neoplasms in cattle and represents a significant economic problem in the livestock industry. The tumour arises from the squamous epithelium of the conjunctiva, cornea, eyelids or associated ocular tissues and is characterized by progressive local invasion with occasional metastasis to regional lymph nodes [1]. Several environmental and genetic factors have been associated with the development of OSCC including exposure to ultraviolet radiation, lack of periocular pigmentation, geographical location and age of the animal [2]. Viral agents such as bovine papilloma virus and bovine herpes virus have also been implicated in the etiopathogenesis of the tumour [3].

The incidence of bovine eye cancer increases with advancing age, and most cases are reported in cattle older than five years [4]. Breed susceptibility has also been reported, with crossbred cattle such as Holstein Friesian and Jersey crossbreds showing a higher incidence of ocular tumours compared to indigenous breeds [2, 5]. Female cattle are more frequently affected than males because they are generally maintained for longer periods for breeding and milk production, which increases their exposure to environmental risk factors such as solar radiation [6].

Several treatment methods have been reported for the management of ocular squamous cell carcinoma including surgical excision, cryotherapy, radiation therapy and chemotherapy [7]. Among chemotherapeutic agents, 5-Fluorouracil (5-FU) is widely used due to its antineoplastic activity against epithelial tumours. 5-Fluorouracil is a pyrimidine analogue that inhibits thymidylate synthase, thereby interfering with DNA synthesis and preventing proliferation of rapidly dividing tumour cells [8].

Intralesional administration of the drug enables direct delivery to the tumour mass, producing localized cytotoxic effects while minimizing systemic toxicity. Therefore, the present study was undertaken to evaluate the prevalence of bovine ocular tumours and assess the therapeutic efficacy of intralesional 5-Fluorouracil in affected cattle.

Materials and Methods

The present study was conducted on clinical cases of cattle affected with ocular tumours presented to the Department of Veterinary Surgery and Radiology, Veterinary College, Bidar. A total of fifteen cases were randomly selected for the study. Relevant data pertaining to each animal, including history, clinical signs, age, sex and breed, were systematically recorded. Diagnosis of ocular tumours was established based on clinical examination and was further confirmed through histopathological and immunohistochemical findings. All animals were subjected to detailed clinical, haematobiochemical and ophthalmic

examinations prior to treatment.

Intralesional therapeutic procedures were performed under proper restraint, with animals maintained in a standing position. Regional anaesthesia was achieved by administering auriculopalpebral nerve block and Peterson block using 2% lignocaine hydrochloride to ensure painless intervention. The size of the tumour was measured using a digital Vernier calliper for assessment and monitoring of treatment response.

All affected cattle were treated with intralesional administration of 5-Fluorouracil (50 mg/ml). The drug was injected directly into the tumour mass until saturation was achieved, as indicated by resistance to further injection or leakage of the drug from previous injection sites due to the friable nature of the tissue. The volume of drug administered varied depending on the size of the tumour. Treatments were given at weekly intervals on day 0, 7, 14 and 21, resulting in a total of four injections.

Table 1: Clinical profile of bovines with ocular squamous cell carcinoma treated with intralesional 5-Fluorouracil

Cases	Age	Sex	Breed	Tumour location	Eye affected	Tumour surface appearance	Volume (mm ³)	Duration of tumour
1	7 yr	M	Deoni	Limbus	Left	Colliflower like	3600	2 month
2	8 yr	F	Deoni	Bulbar conjunctiva	Left	Irregular, nodular and ulcerated	4000	1 month
3	5 yr	M	Deoni	sclera	Left	highly vascular, dome-shaped irregular surface	486	1 month
4	7 yr	M	Deoni	cornea	Left	pedunculated, cauliflower-like	3818.28	15 days
5	5 yr	M	Deoni	Upper eye lid	Right	smooth, fleshy, dome-shaped mass	16465.40	1 month
6	7 yr	F	Hf x	Bulbar conjunctiva	Left	reddish, smooth, glistening,	18513	2 months
7	6yr	f		Limbus	Right	Nodular mass	786.50	3 months
8	5 yr	F	Hf x	Third eye lid	Left	Cauliflower like granulomatous fleshy	198	2 months
9	8 yr	F	Deoni	Third Eyelid	Left	Soft pedunculated mass	210.50	3 months
10	5 yr	F	Jr x	Limbus	Right	Cauliflower growth	323.44	1.5 months
11	6 yr	F	Deoni	Nictitating membrane	Left	Irregular, ulcerative mass	1706.70	2 months
12	9yr	F	Hf x	Lower eye lid	Left	Cauliflower-like, proliferative	1440	3 months
13	4 yr	F	Deoni	Cornea	Right	Small nodular, smooth surface	1306.80	20 days
14	6 yr	F	Jr x	Bulbar conjunctiva	Left	Reddish irrerugar	4752.10	1.5 months
15	7 yr	M	Deoni	Limbus	Right	Fleshy ulcerated mass	2136.20	2 months



Results and Discussion

In the present study, ocular tumours appeared as raised, irregular and fleshy masses involving different parts of the eye including the limbus, third eyelid and eyelids. The lesions were typically pink to reddish in colour and were associated with lacrimation, irritation and partial loss of vision. Tumour growths varied in size and often presented as cauliflower-like proliferative masses, which is consistent with earlier reports [16, 17].

In the present study, a total of fifteen clinical cases of ocular tumours in cattle were examined, and all cases were confirmed as squamous cell carcinoma based on histopathological findings. The occurrence of OSCC in the present study supports earlier reports indicating that it is the most common malignant ocular tumour in bovines [1, 2]. Moulton JE, 1961. Fazili MR *et al.*, 2001. The age of affected animals in the present study ranged from 4 to 9 years, with the majority of cases observed in cattle above 5 years of age. The highest incidence was recorded in animals between 6-8 years. This finding is in agreement with earlier reports which state that OSCC is predominantly a disease of older cattle due to prolonged exposure to ultraviolet radiation and cumulative carcinogenic effects [3-5]. Russell WO *et al.*, 1956. Hawkins CD *et al.*, 1981. Rhadostits OM *et al.*, 2000.

Histopathological examination confirmed the diagnosis of squamous cell carcinoma in all cases. Microscopic examination revealed proliferation of squamous epithelial cells arranged in nests and sheets with formation of keratin pearls, cellular pleomorphism and presence of mitotic figures. These findings are in agreement with previous studies on bovine OSCC [18, 19].

Intralesional administration of 5-Fluorouracil resulted in gradual regression of tumour masses in all fifteen treated animals. The antitumour effect of the drug is attributed to its ability to inhibit DNA synthesis and induce cytotoxic effects in rapidly proliferating tumour cells [14]. Similar successful outcomes with intralesional 5-FU therapy have been reported in both veterinary and human oncology studies [15, 24, 25].

The localized delivery of the drug directly into the tumour mass ensured a high drug concentration at the lesion site, enhancing its therapeutic efficacy. Furthermore, the procedure was simple, economical and suitable for field conditions when compared to more invasive surgical procedures.

On day 0, the affected bovines presented with proliferative neoplastic masses involving the corneal, limbal or third eyelid region, showed loss of vision at the tumour region, mild lacrimation, slight corneal opacity around the tumour and distortion of the palpebral fissure. From day 7 to day 14 following of intralesional 5-Fluorouracil therapy, gradual regression of the tumour mass was observed, characterized

by reduction in tumour size, shrinkage of proliferative margins and improvement in ocular appearance. Mild lacrimation and corneal opacity progressively subsided during this period. By day 21, a significant healing and marked reduction in tumour volume were evident. The lesions appeared as small localized regressing nodules near the limbal or corneal margins with mild residual congestion at the treatment site. Restoration of corneal transparency was observed in the surrounding ocular tissues and vision was preserved in all the animals as evidenced by normal palpebral, corneal and pupillary reflexes. Between day 28 and day 35, complete macroscopic regression of the neoplastic mass with satisfactory healing of the ocular surface was observed in most cases. Restoration of normal palpebral architecture, minimal corneal scarring and clear ocular media were evident by day 35, indicating good therapeutic efficacy and satisfactory healing following intralesional chemotherapy. No recurrence or major ocular complications were observed during the follow-up period. No recurrence of tumour was observed in any of the treated cases during the six-month follow-up period. Similar findings have been reported in previous studies where intralesional 5-Fluorouracil showed effective tumour control with minimal or no recurrence, indicating its efficacy as a reliable therapeutic modality for squamous cell carcinoma [Maxfield L *et al.*, 2021. and Reisinger J *et al.*, 2023. 15 out of 15 cases cured 100% success rate.

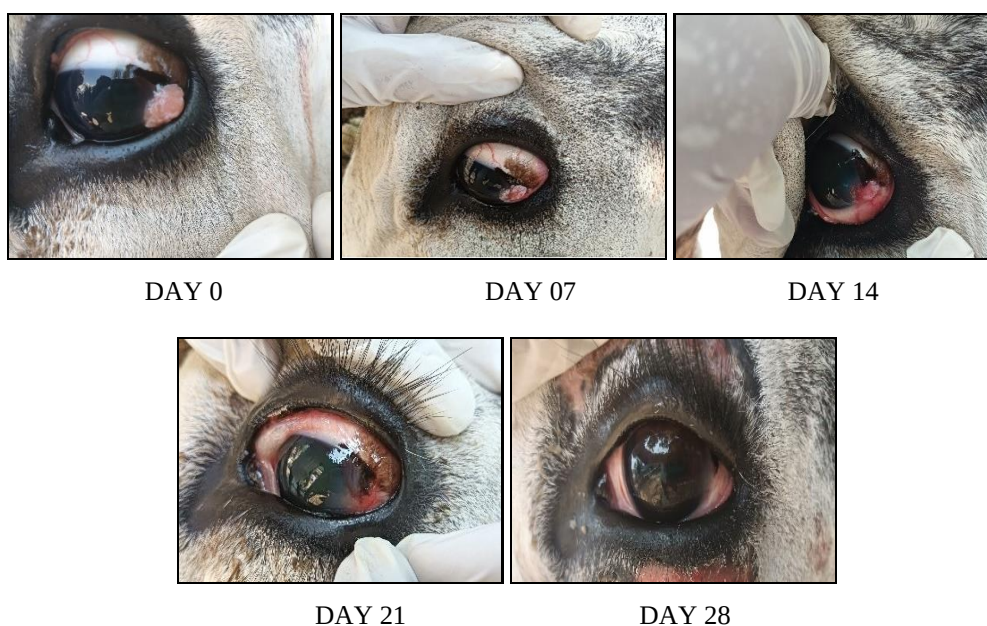


Fig 1: Sequential clinical response of (case 4) bovine ocular squamous cell carcinoma following intralesional 5-Fluorouracil therapy (Day 0, 7, 14, 21 and 28)





Fig 2: Sequential clinical response of (case 9) bovine ocular squamous cell carcinoma following intralesional 5-Fluorouracil therapy (Day 0, 7, 14, 21 and 28)

Table 2: Age-wise Distribution of Affected Cattle

S. No	Age Group (Years)	Number of Cases	Percentage (%)
1	4-5	5	33.33%
2	6-7	6	40.00%
3	8-9	4	26.67%
	Total	15	100%

Table 3: Sex-wise Distribution of Affected Cattle

S. No	Sex	Number of cases	Percentage%
1	Male	5	33.33%
2	Female	10	66.67%
	Total	15	100%

Table 4: Eye Involvement in OSCC

S. No	Eye affected	Number of cases	Percentage%
1	Left eye	10	66.67%
2	Right eye	5	33.33%
	Total	15	100%

Table 5: Location of Tumour on Eye

S. No	Tumour location	Number of cases	Percentage%
1	Limbus	4	26.27%
2	Bulbar conjunctiva	3	20.00%
3	Cornea	2	13.33%
4	Eye lids (upper/lower)	2	13.33%
5	Third eyelid (nictitating membrane)	3	20.00%
6	Sclera	1	6.67%
	Total	15	100%

Table 6: Breed-wise Distribution of Affected Cattle

S. No	Breed	Number of cases	Percentage%
1	Deoni	9	60.00%
2	Hf crossbred	3	20.00%
3	Jersey crossbred	2	13.33%
4	Non described	1	6.67%
	Total	15	100%

Conclusion

Bovine ocular squamous cell carcinoma is a common ocular tumour affecting cattle, particularly older animals and crossbred breeds. The present study demonstrated that intralesional administration of 5-Fluorouracil is an effective and economical treatment option for the management of ocular tumours in bovines. Early diagnosis and timely intervention are essential to prevent progression of the disease and preserve ocular function in affected animals.

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