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Corneal alkali burn in rabbit: An experimental model for study of corneal ulcer

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Abstract
Rabbit models of ocular diseases are particularly useful since rabbits can be easily handled, while sharing more common anatomical and biochemical features with animals including longer life span and larger eye size. In the present study rabbit eye model was used to access the effect of corneal alkali burn. In all the eyes, approximately 5-6 mm in diameter, full thickness corneal defect was created by placing a filter paper soaked in 1N NaOH (pH 13±0.6) solution at axial cornea for 30 secs. The eyes were treated by giving conventional medicinal treatment of eye drop Moxifloxacin and Flurbiprofen for 07 days post alkali burn induction. Post induction of alkali burn there was significant increase in STT values from 6.3±0.49 to 9.00±1.00mm/min between day 03 and 30. Size of corneal alkali burn increased from 6.00± 0.00 to 7.50 ± 0.50 mm in all animals from day 03 to 30 along with marked retention of fluorescein dye indicative of corneal ulceration.

Keywords: Alkali burn, corneal ulceration, rabbit

Introduction
Corneal stroma is highly specialized connective tissue containing cells and intercellular substance, consisting of fibrillar elements and amorphous material. Substantial components of the latter are glycosaminoglycan's, proteins and water (Cejkova *et al.*, 1975)[2].Development of novel drugs and drug delivery mechanisms, as well as advanced ophthalmological techniques requires experimental models including animals, capable of developing ocular diseases with similar etiology and pathology, suitable for future trials of new therapeutic approaches (Kang *et al*., 2019) [3]. Rabbit models of ocular diseases are particularly useful in this context, since rabbits can be easily handled, while sharing more common anatomical and biochemical features with animals including longer life span and larger eye size. In the present study rabbit eye model was used to access the effect of corneal alkali burn. An alkali burn of the cornea causes a recalcitrant keratitis characterized by frequent blister formation, recurrent epithelial breakdown, stromal cell death, inflammatory cell infiltration and endothelial dysfunction (Kim *et al*., 2000) [4].

Material and Methods
The present research work was carried out at Department of Veterinary Surgery and Radiology, Department of Veterinary Anatomy and Histology, Central Laboratory Animal House, College of Veterinary Science and A.H., Jabalpur, M.P and Animal Biotechnology Centre, Adhartal, Nanaji Deshmukh Veterinary Science University, Jabalpur (M.P). Jabalpur is situated at 23.17˚latitude and 79.57˚ East longitudes at 410.87 mean sea level in the southern part of second agro-climatic zone, including Satpura Plateau and Kymore hills. It has a tropical climate having average rainfall of 1241 mm.
The clinical observations were recorded for a period of one month. The study was conducted on 04 clinically healthy adult New Zealand white rabbits (08 eyes) of either sex, reared in Animal House, College of Veterinary Science and A.H., Jabalpur. Rabbits were acclimatized for 7 days in the new environment. Standard diet and water *adlibitum* was provided throughout the research period. The study protocol was approved by IAEC.
In all the eyes, approximately 5-6 mm in diameter, full thickness corneal defect was created by placing a filter paper soaked in 1N NaOH (pH 13±0.6) solution at axialcornea for 30 secs. The eyes were treated by giving conventional medicinal treatment of eye drop Moxifloxacin and Flurbiprofen for 07 days post alkali burn induction.

Grading of corneal ulcer was done according to score card of Thatte *et al*. (2017) [15] as described in table 01

Table 1: Grading of corneal ulcer

Grade	Type of corneal ulcer
I	Epithelial defect only
II	Mild stromal thinning, <50% corneal thinning
III	Deep stromal thinning, >50% corneal thinning
IV	Desmetocele
V	Corneal perforation, full thickness defect in cornea

Clinical Observations

1. General behavioural changes: General behavioral changes and feeding pattern were observed in all the animals, immediately after complete recovery from anesthesia. Animals were found slightly dull and depressed as evident by their isolation and reduced interest in feeding. This remained for initial 4-6 hours after surgery and thereafter, normal feeding resumed. All rabbits maintained their regular diet without any deterioration in body condition. Body weight of animals in both the groups was within a range of 1-2.5 kg and did not show any significant difference.

2. Rectal temperature

Mean values of rectal temperature in all rabbits up to day 30 is depicted in Table 02. There was no significant difference in values post alkali burn induction. Minimum value was recorded as 101.99±0.27 on day 03 and maximum value on day 20 as 102.53±0.25.

Table 02: Mean values of rectal temperature (ºF)

Group / Day	03	10	20	30
I	101.99±0.27	102.13±0.15	102.53±0.25	102.20±0.20

Difference in rectal temperature may be due to environmental variation and stress. However, temperature fluctuated within normal physiological limits in all the animals which may be due to absence of infection or any other systemic reactions affecting the physiological status of the animal. These findings are in corroboration with Tembhurne *et al.* (2010) [14], Rajhans (2013) [12] and Jain (2017) [11].

3. Ophthalmic examination

Gross ophthalmic examination was performed for all rabbits. The examination revealed corneal opacity and vascularization of various grades at different intervals of study period in all rabbits. Intraocular pressure was normal. Neuro-ophthalmic reflexes were also normal. Mild blepharospasm and slight photophobia was observed on day 30.

Blepharospasm and photophobia may be due to corneal ulcer formation on day 30 in all the rabbits causing ocular pain. These findings were in accordance with findings of Soontornvipart *et al.* (2003) [13], Williams and Burg (2017) [17]and Myrna and Girolamo (2019) [8].

4. Fluorescein dye test

Fluorescein dye was used as ancillary diagnostic aid to examine corneal abrasion and size of the induced corneal alkali burn. Damaged corneal epithelium exposed underlying layer of collagen or hydrophilic stroma which retained fluorescein stain. It gave fluorescent green stain or apple green stain to cornea for better visualization. Similarly, Lin and Lee (2002) [5], Ollivier (2003) [10], Moore (2003) [7] and Amol (2016) [1] stressed the use of fluorescein dye for diagnosis and assessment of corneal epithelial defect.

5. Schirmer Tear Test value

Post induction of alkali burn there was significant increase in STT values from 6.3±0.49 to 9.00±1.00 mm/min between day 03 and 30. However, all the values varied within normal physiological limit (Table 03).

Table 3: Mean values of Schirmer′s tear test (mm/min)

Group / Day	03	10	20	30
I	6.38^{b}±0.49	5.17^{b}±0.30	5.75^{b}±0.48	9.00^{a}±1.00

Mean value within same group (a,b) with different superscript varied significantly(p<0.05) at different time intervals

These findings are in concurrence with Lima *et al.* (2015) who reported mean STT value of 4.8 ± 2.9 to 5.3 ± 2.9mm/ min in ten New Zealand White rabbits. Significant increase in STT values in group I may be due to progression of corneal alkali burn to corneal ulceration in all the animals leading to ocular pain and increased lacrimation.

6. Size of corneal alkali burn

Size of corneal alkali burn increased from 6.00± 0.00 to 7.50±0.50mm (table 04) in all animals from day 03 to 30 along with marked retention of fluorescein dye indicative of corneal ulceration.

Table 4: Mean values of size of corneal alkali burn (mm)

Group / Day	03	10	20	30
I	6.00^{b} ±0.00	6.00^{b} ±0.00	7.75^{a} ±0.25	7.50^{a} ±0.50

Mean value within same group (a,b) with different superscript varied significantly(p<0.05) at different time intervals

These findings may be credited to the pathophysiological changes that occur in corneal tissue post alkali burn. Similar findings were reported by Nasisse (1995) [9], Wilkie and Whittaker (1997) [16] and Miller (2001) [6].

7. Grading of corneal ulcer

All cases of corneal alkali burn showed corneal epithelial

abrasion on day 03 and grade II corneal ulceration on day 30 on ophthalmic examination as depicted in Fig 01.

(a) **(b)**

Fig 01: Alkali burn on cornea a) at day 0 b) day 30

Conclusion

From the present study it can be concluded that corneal alkali burn causes damage to corneal stroma leading to formation of corneal ulcer up to grade IIin due course of time. Medicinal treatment of antibiotic and anti-inflammatory agent alone is insufficient in stopping the cascade of pathophysiological changes in alkali burnt cornea.

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