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Original Article

Ophthalmology Section

Ocular Toxicity due to Accidental Exposure to Plant Latex by *Calotropis procera* and *Calotropis gigantea*

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ABSTRACT

Introduction: Calotropis is a member of the milkweed or Asclepiadeae family. The latex of *Calotropis gigantea* (*C gigantea*) contains cardiac glycosides, fatty acids and calcium oxalate. The sap of *Calotropis procera* (*C procera*) produces acidic latex. Toxic effect of latex manifests after a few hours with diminution of vision due to corneal oedema with folds in Descemet's membrane.

Aim: To evaluate the ocular toxicity by the latex of *calotropis procera* and *calotropis gigantea* due to accidental exposure.

Materials and Methods: This was a prospective observational study conducted for a duration of six months (September 2018 to February 2019) on 18 patients with alleged accidental exposure to calotropis latex. The patients were examined in the Department of Ophthalmology, Mandya Institute of Medical Sciences (MIMS), Mandya, Karnataka, India. After a thorough saline wash under topical anaesthesia, visual acuity was measured by using Snellen's chart, then patients were subjected for slit lamp biomicroscopy examination, Intraocular Pressure (IOP) measurement and undilated fundus examination and the findings were noted. Demographic details like age and sex, activity at time of injury, mode of injury were noted and follow-up was done for a period of 30 days. Data were analysed using Epi info software and descriptive statistics like mean and percentage were calculated.

Results: Total 18 patients reported with calotropis associated eye toxicity, among which 11 (61.1%) were of C gigantea and seven (38.9%) were of C procera. Out of total, seven (38.9%) were males and 11 (61.1%) females. A total of 14 (77.8%) patients presented within 24 hours of injury. Eleven (61.1%) patients had involvement of both the eyes. The main symptoms were burning, irritation, foreign body sensation and diminution of vision. Best Corrected Visual Acuity (BCVA) varied from 6/9 to 6/60. Corneal oedema or striate keratopathy was the most common sign. Corneal oedema resolved in one week in case of *C procera* with use of topical corticosteroids except in three cases of *C gigantea* which took two weeks.

Conclusion: *C procera* and *C gigantea* causes significant corneal oedema and ocular morbidity. By simple health education and occupational precaution, we can prevent ocular morbidity.

Keywords: Chemical injury, Corneal oedema, Striate keratopathy

INTRODUCTION

Some plants with milky latex may cause ocular injuries in case of accidental contact with human eyes. Most commonly reported is *calotropis*. *Calotropis* is a member of small genus Apocynaceae and belongs to milkweed group, native to Indian subcontinent, distributed in Asia, tropical and subtropical Africa [1]. *Calotropis gigantea* and *calotropis procera* are two common species of *calotropis*. Flowers of *calotropis* are used to worship Lord Shiva during Shivarathri. *C procera* is perennial shrub which grows upto the height of 3-6 m, the leaves are oblong-obovate to nearly orbicular, short-pointed to blunt at the apex. It produces copious white sap which flows whenever stems or leaves are cut [2]. Plant latex of *calotropis procera* contains the cardenolide, proceraenin, while the root bark contains benzoylinesolone and benzoylisolinelone. The leaves and stalk contain calotropin, and calotropagenin while the flower contains calotropenyl acetate, and multiflavenol. The latex of *C procera* is sometimes referred to as vegetable mercury because of mercury like action on human body [2].

C gigantea is a large shrub or small tree, about 4-10 m tall. The leaves of *C gigantea* are broadly elliptical to oblong-obovate, subsessile in shape. Latex of *C gigantea* contains a- and b- amyrin, teraxasterol, gigantin, giganteol and calotropins [2]. Gigantin, a white crystalline substance, isolated from the sap is found to be poisonous [3]. Calotropis causes ocular manifestations because of the acidic nature of the milky latex and secondly due to the toxins. The clinical features occur in two stages namely, stage of acute acid injury and stage of toxicity.

Stage of acute acid injury cases manifest immediately with burning sensation, pain and photophobia with epithelial defects on local application or accidental exposure like any other chemical injury to the eye. It is known to produce contact dermatitis. The latex of this plant produces intense inflammation when injected locally in animal models due to the presence of histamine in the latex itself and also due to the release of mast cell histamine by the latex [3,4]. The key mediators of inflammatory response are histamine and prostaglandins. These mediators are produced due to induction of Cyclooxygenase 2 (COX2) enzyme [3]. In stage of toxicity, the effect manifests after a few hours with diminution of vision due to corneal oedema with folds in Descemet's membrane. Corneal oedema with Descemet's membrane folds is predominant feature due to toxicity to corneal endothelium by plant latex [5]

The first confirmed report of Calotropis induced ocular toxicity was by Muthayya RE, in 1949 from India [6]. Previous studies have reported only on *Calotropis procera*, however there are no case reports on *C gigantea*. Thus, the present study was done to assess the ocular manifestation of accidental eye injury by *C procera* and *C gigantea.*

MATERIALS AND METHODS

This hospital-based prospective observational study was conducted for six months duration from September 2018 to February 2019 at Mandya Institute of Medical Sciences (MIMS), Mandya, Karnataka, India in accordance with tenets of the Declaration of Helsinki. Ethical clearance was obtained from Institutional Ethical Committee (IEC) of MIMS, Mandya (MIMS/IEC/RP/2018/266). Informed consent was taken by all patients who participated in the study.

Inclusion criteria: A total of 18 patients with alleged accidental exposure to plant latex by calotropis were examined in the Ophthalmology Outpatient Department (OPD).

Exclusion critera: Patients with pre-existing corneal opacity and conjunctival scar were excluded from the study.

After a thorough saline wash under topical anaesthesia (using proparacain) patient was subjected for visual acuity measurement by Snellen's chart, Slit lamp biomicroscopic examination, IOP measurement by Goldmann Applanation Tonometer (GAT) and undilated fundus examination. The demographic details like age, sex, occupation were noted. A detailed history of activity at time of injury, mode of injury was taken. First follow-up was done on 3rd day, 2nd follow-up after one week of presentation and further follow-up was done depending on the recovery of patient till one month after presentation. In each follow-up visual acuity was recorded, and the patient was looked for corneal oedema and Descemet Membrane Folds (DMF).

STATISTICAL ANALYSIS

Data was entered in Microsoft Excel and analysed using Epi-info software. Descriptive statistics like mean and percentage were calculated.

RESULTS

Total 18 cases presented to the Opthamology Department in six months of study period by accidental exposure to *calotropis*. Among 18 cases, 11 were by *C gigantea* and seven were by *calotropis procera*. Out of total, seven were males and two were female children aged 10 and 14 years. A total of seven (38.9%) patients were aged between 41 to 60 years, nine (50%) patients were aged between 21 to 40 years and two (11.1%) aged between 1 to 20 years, the mean age of presentation was 30 years. A 14 (77.7%) patients presented within 24 hours of accidental exposure, three (16.7%) patients on 2nd day (24 to 48 hours) and one (5.6%) patient on 3rd day. Twelve (66.7%) patients got injured while plucking flowers, five (27.8%) of patients while doing gardening work, one (5.6%) patient while applying sap for thorn injury to foot. Eleven (61.1%) patients had involvement of both the eyes, only Right Eye (RE) in four (22.2%) and Left Eye (LE) in three (16.7%). Burning sensation, foreign body sensation and redness was common presenting complaints in all patients, six patients had additional complaint of blurring vision [Table/Fig-1].

BCVA on presentation in *C gigantea* was 6/9 to 6/18 in six patients, 6/ 24 to 6/36 in three patients, 6/36 to 6/60 in two patients. On 3rd day of follow-up BCVA improved to 6/6 in seven patients, three patients improved to 6/9 to 6/18 and one patient improved to 6/24 to 6/36. After one week of treatment, eight patients improved to 6/6 except in three patients. Among these three patients, two patients improved to 6/6 after 15 days except in one male patient aged 60 year who had pre-existing nucleus sclerosis grade 2 with cataract with BCVA of 6/60 on presentation, which improved to 6/18.

Circumcorneal congestion with conjunctival congestion was seen in all patients of *C gigantea*. Corneal epithelium was intact in most eyes, except two corneas which had corneal abrasion confirmed by fluorescein staining. Corneal oedema with DMF was noted in all patients. On 3rd day, only six patients had corneal oedema; after one week, three had persisting corneal oedema which resolved after 15 days. Endothelium was normal by specular reflection in slit lamp biomicroscopy. IOP was within normal range (12 to 18 mmHg) and in two cases it was deferred because of epithelial defect in the cornea. Patients were prescribed 1% Prednisolone eye drop 6 times daily, except in two cases of corneal epithelial defect. Epithelial defect was completely healed after treatment with topical oflaxacin 0.3% antibiotic eye drops and 1% carboxy methyl cellulose eye drops on 3rd day follow-up Table/Fig-2].

BCVA on presentation in *C procera* was 6/9 to 6/18 in five patients, 6/ 24 to 6/36 in two patients. On 3rd day of follow-up BCVA improved to 6/6 in six (85.7%) patients, one patient improved to 6/9 to 6/18. After one week of treatment, all patients of *calotropis procera* improved. Circumcorneal congestion with conjunctival congestion was seen in all patients of *procera*. In one patient of *calatropis procera*, eyelid oedema was noted. Corneal oedema with DMF was noted in all patients. Treatment with 1% prednisolone eye drop six times daily was given. On 3rd day only one patient had corneal oedema which resolved at one week. Intraocular pressure was within normal range (12 to 18 mmHg) in all patients [Table/Fig-3]. Patients follow-up was done till 30 days after exposure in both *procera* and *gigantea*. On 30th day, all patients recovered completely, there were no fresh complaints and no scaring even in conjunctiva and cornea.

Sl. No.	Patient profile	*Calotropis gigantea*	*Calatropis procera*	Total	Percentage
1.	**No. of patients**	11 (61.1%)	07 (38.9%)	18	100
2.	**Gender**				
	Males	04 (22.2%)	03 (16.7%)	07	38.9%
	Females	07 (38.9%)	04 (22.2%)	11	61.1%
3.	**Age group (years)**				
	1 to 20	02 (11.1%)	00	02	11.1%
	21 to 40	04 (22.2%)	05 (27.8%)	09	50%
	41 to 60	05 (27.8%)	02 (11.1%)	07	38.9%
4	**Occupation**				
	Farmer	05 (27.8%)	02 (11.1%)	07	38.9%
	Flower vendor	04 (22.2%)	01(5.6%)	05	27.8%
	House hold work	00	04 (22.2%)	04	22.2%
	Student	02 (11.1%)	00	02	11.1%
5.	**Presentation**				
	Within 24	08 (44.4%)	06 (33.3%)	14	77.7%
	24 to 48	02 (11.1%)	01(5.6%)	03	16.7%
	>48	01(5.6%)	00	01	5.6%
6.	**Eye**				
	RE only	02 (11.1%)	02 (11.1%)	04	22.2%
	LE only	02 (11.1%)	01 (5.6%)	03	16.7%
	Both eye	07 (38.9%)	04 (22.2%)	11	61.1%
7	**Activity at the time of injury**				
	Plucking flowers	10 (55.5%)	02 (11.1%)	12	66.6%
	Gardening work	00	05 (27.8%)	05	27.8%
	Applying sap on injured wound by thorn	01 (5.6%)	00	01	5.6%
8	**Presenting complaint**				
	Burning sensation and foreign body sensation	11 (61.1%)	07 (38.9%)	18	100%
	Blurring of vision	04 (22.2%)	02 (11.1%)	06	33.3%

[Table/Fig-1]: Demographic profile and clinical presentation Calotropis chemical injury.
h: Hours; RE: Right eye, LE: Left eye

Patient profile		Presentation	3 days after treatment	1 week after treatment
BCVA	6/6	00	07 (63.6%)	08 (72.7%)
	6/9 to 6/18	06 (54.5%)	03 (27.3%)	02 (18.2%)
	6/24 to 6/36	03 (27.3%)	01 (9.1%)	01 (9.1%)
	6/36 to 6/60	02 (18.2%)	00	00
Eye lid oedema		05 (45.4%)	00	00
Conjunctival congestion		11 (100%)	03 (27.3%)	00
Corneal abrasion and epithelial defect		02 (18.2%)	00	00
Corneal oedema with descement membrane folds		11 (100%)	06 (54.5%)	03 (27.3%)

[Table/Fig-2]: Clinical presentation of calatropis gigantea exposure.
n=11, BCVA: Best corrected visual acuity

Patient profile		On presentation	3 days after treatment	7 days after treatment
Visual acuity	6/6	00	06 (85.7%)	07 (100%)
	6/9 to 6/18	05 (71.4%)	01 (14.3%)	00
	6/24 to 6/36	02 (28.6%)	00	00
	6/36 to 6/60	00	00	00
Eye lid oedema		01 (14.3%)	00	00
Conjunctival congestion		07 (100%)	02 (28.5%)	00
Corneal abrasion and epithelial defect		00	00	00
Corneal oedema with descemet membrane folds		07 (100%)	01 (14.3%)	00

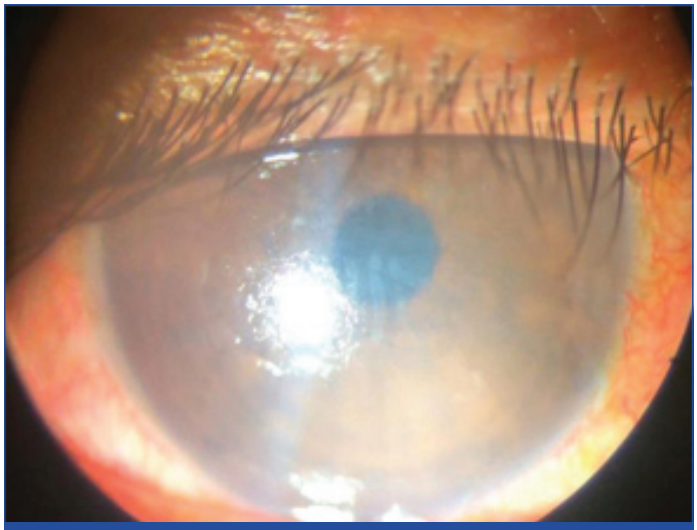
[Table/Fig-3]: Clinical presentation of Calatropis procera exposure.
BCVA: Best corrected visual acuity

Calotropis procera and *gigantea* had similar clinical presentation. Male to female ratio was high in *C gigantea* (4:7) than *C procera* (3:4). Complete recovery of vision in C gigantea on 3rd day was less (63.6%) compared to *C procera* (85.7%). At the end of 1 week 100% recovery of vision was noted in *C procera* compared to *C gigantea* which was only 72.7%. Eyelid oedema was seen in 45.4% of patients in *C gigantea* and it was more compared to *procera* corneal epithelial defect was seen in two cases in *C gigantea* exposure, whereas it was not seen in *C procera*. The healing of corneal oedema or striate keratopathy was faster within a week in *C procera* whereas in *C gigantea*, three patients took two weeks for complete recovery of corneal oedema.

[Table/Fig-4,5] shows *C procera* and *C gigantea* leaves and flowers respectively. [Table/Fig-6] shows corneal oedema with DMF.

[Table/Fig-4]: *Calotropis procera* leaves and flowers.

[Table/Fig-5]: *Calotropis gigantea* leaves and flowers.



[Table/Fig-6]: Corneal oedema with DMF.

DISCUSSION

Calotropis is toxic to skin and mucous membrane because of irritant and pro-inflammatory property of milky latex. Shivkar YM and Kumar VL study on rat paw oedema model, found that the injection of dried latex produces an intense inflammatory response involving oedema formation and cellular infiltration due to the presence of histamine in the latex itself and also due to the release of mast cell histamine by the latex [4]. *C gigantea* also belongs to *calotropis* group of plant, exhibit similar manifestation in eye but there are no case reports on *C gigantea*. Accidental contact with *C gigantea* is more compared to *C procera* [7]. This could be because *C gigantea* is found commonly in southern Karnataka. Pandey N et al., reported male predominance whereas in the present study female predominance (61.1%) was seen [8]. In the present study, 77.7% of patients presented within 24 hours of accidental contact with sap regained vision completely within three days of treatment as compared to patients who presented late after 24 hours to 48 hours. In this study, patients took one to two weeks for complete recovery.

Pandey N et al., reported eight cases of corneal abrasion and epithelial defect whereas in the present study corneal epithelial defect was seen in only in two eyes [9]. Increase in IOP was not seen in this study on the day of presentation and also on subsequent follow-up, whereas in a study by Basak SK and Bhaumik A they reported seven cases of secondary glaucoma and increased IOP after sap exposure to eye [7]. Toxic iridocyclitis due to calotropis was first reported by Basak SK and Bhaumik A and Tomar VP et al., study also reported 9 cases of toxic iridocyclitis, whereas in our study no cases of iridocyclitis was noted after exposure [7,10]. The present study compared the ocular toxicity of both and found that the recovery is delayed in *C gigantea*.

Limitation(s)

C gigantea and *C procera* belongs to same family, and both presents with clinically similar features. Five patients of *C gigantea* had eyelid oedema and these patients also had persistent corneal oedema and descemets membrane folds even after three days. These patients need further evaluation by specular microscopy for endothelial count and pachymetry for corneal thickness measurement. This study has a limitation of small sample size, thus further studies are needed with adequate sample size.

CONCLUSION(S)

Accidental contact with calotropis causes burning sensation and irritation of ocular surface. Diminution of vision is transient for three days to one week. *Calotropis gigantea* produce severe clinical features compared to *Caltropis procera*. The recovery is comparatively faster in *Caltropis procera*. Simple health education

and occupational precautions can prevent ocular morbidity. Further studies are needed to know the presence of toxins in anterior chamber and penetration of corneal layers by toxins.

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