The author has no financial interests or relationships to disclose

Drug-Depository Contact Lens That Lengthen Antibiotic Corneal Contact Time in Bacterial Keratitis: A Randomized Controlled Trial

Poster # **82839**

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Background

- Up to 5% of all blindness are due to infections.
- Microbial keratitis (MK) as a cause of unilateral blindness range from 1.5 to 2 million cases per year
- Approximately 1 million clinical visits to health practitioners and 58,000 registered emergency departments per annum in the US
- Prevalence of MK are as high as 11.3 per 100,00 in South India
- Topical antibiotic eye drops in loading dose are the preferred treatment option, presently
- The pre-corneal factors and anatomical barriers negatively affect the bioavailability of topical formulations at the lesion.

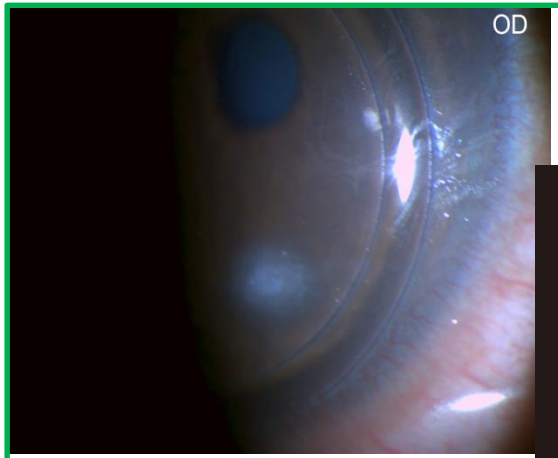
PURPOSE: To evaluate the efficacy of a novel therapeutic contact lens that increases the overall contact time of corneal antimicrobial drug (serving as a drug reservoir) in subjects with bacterial keratitis.

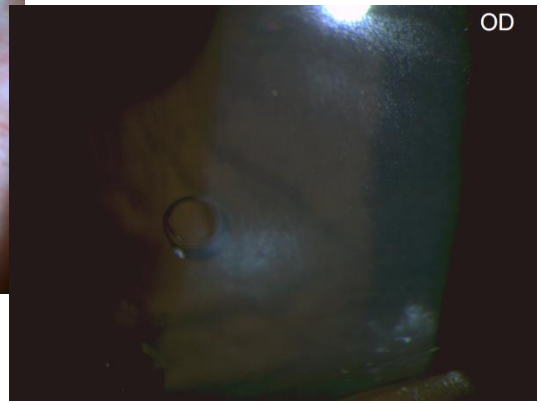
SETTING: A Randomized open-label clinical trial, at the Department of Cornea at Dr.Agarwal's Eye Hospital & Research Institute in Tirunelveli, South India

METHODS: **40 eyes of Bacterial keratitis (BK)** were randomized into Group-1, treated with a topical antimicrobial, in Group-2, a drug reservoir contact lens with characteristic dual base curves resulting in a central reservoir along with fenestrations to enable capture of topical antimicrobial, was implanted, in 1:1 ratio. 3,2 cases in Groups 1 & 2 did not complete the study & excluded from analysis. In both groups, moxifloxacin 0.5% in a standard regimen was instituted. Ulcer size, depth, AC reactions, corneal haze were studied.

Followed-up on 12 hours, Days-1,3,5 & 14. Pain evaluated on a 10 pt scale.

A study on the availability of the drug in the central reservoir was analyzed over time curve

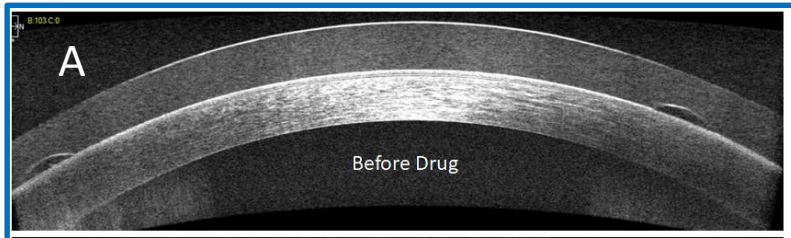


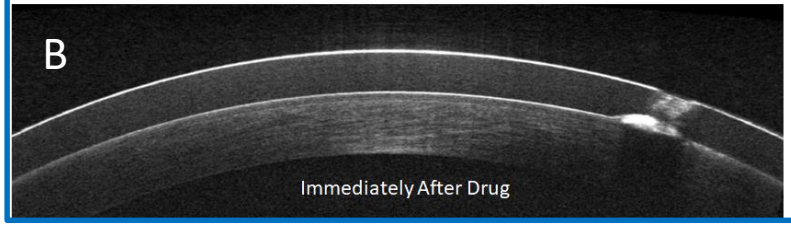


•The lens material consists of 41% Acofilcon A and 59% water in a buffered solution.

•The Lens incorporates FENESTRATIONS and a central reservoir due to DUAL BASE-CURVES .

•The lens's unique design enables the capture and maintains a drop of solution applied to the contact lens surface



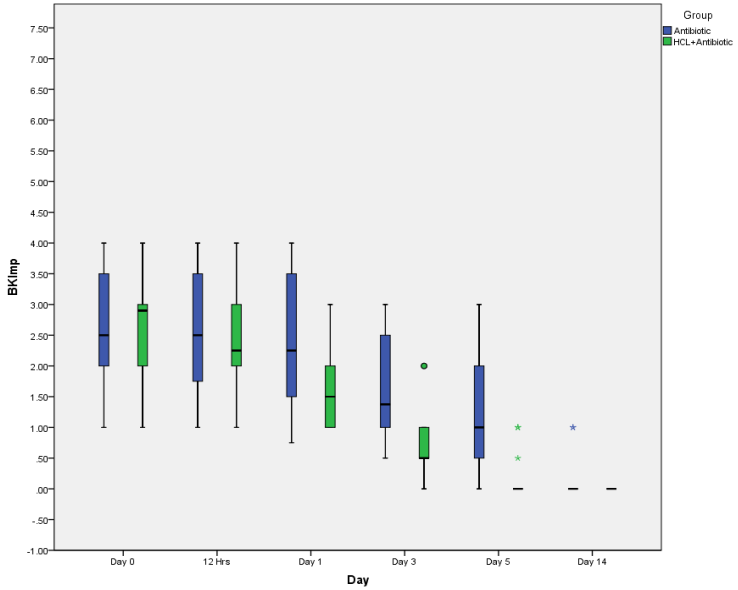


Normal Cornea + Drug Repository CL

Contact Lens Thickness – 140 microns
Tear film (Admixed with drug) -200 microns

Results

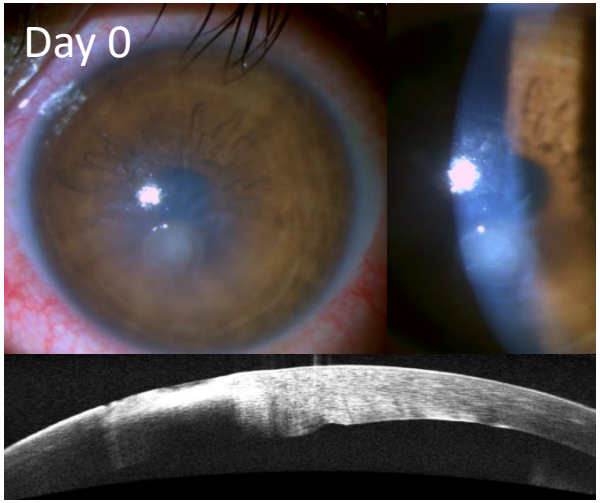
BK-Improvement Score	Group	Mean Improvement in mm	S.D	P value
12thHr	Antibiotic	0.04	0.13	<0.02
	Antibiotic + HCL	0.27	0.38	
1st Day	Antibiotic	0.18	0.27	<0.0001
	Antibiotic + HCL	0.94	0.50	
3rd Day	Antibiotic	0.93	0.39	<0.0001
	Antibiotic + HCL	1.96	0.54	
5th Day	Antibiotic	1.50	0.56	0.013
	Antibiotic + HCL	2.45	0.57	
14th Day	Antibiotic	2.51	0.95	0.62
	Antibiotic + HCL	2.66	0.75	

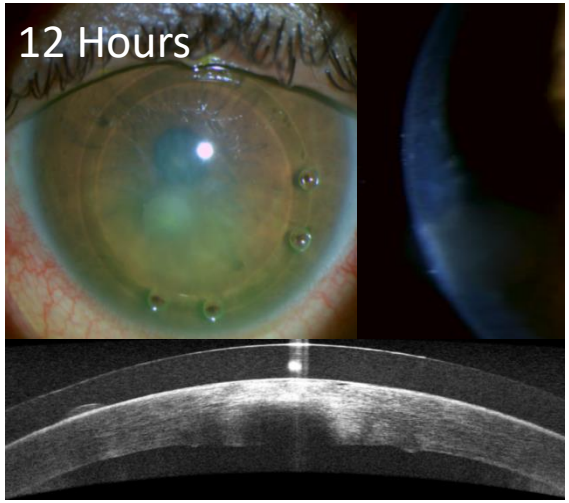


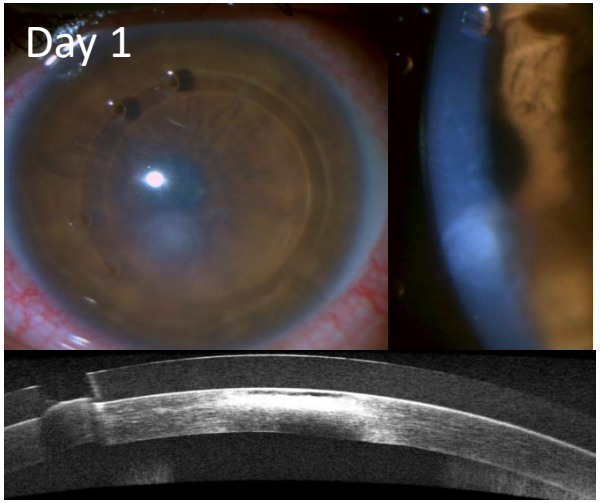
Corneal-infiltration (BK severity) on presentation in Group-1 was 2.62+/-0.82mm, in Group-2 was 2.66+/-0.39mm(p=0.92). Resolution by 12 hours in Group-2 was 0.28mm, in Group1 was 0.04mm, by Day-1 was 0.94mm in Group-2, 0.18mm in Group-1(p=0.03), by Day-3, 1.96 in Group-2 Vs 0.93 in Group-1(p<0.0001) resolved within 5 days with repository CL

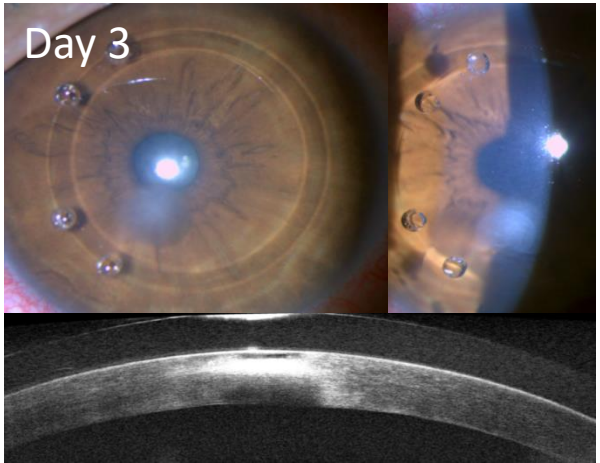
Improvement in Bacterial Keratitis Scores along timeline in both groups

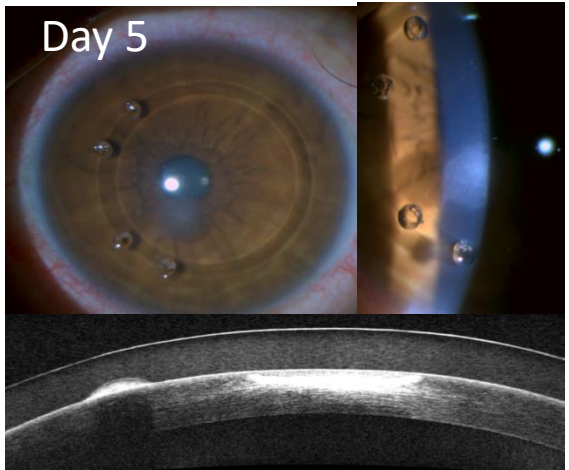
Case Ex. -1

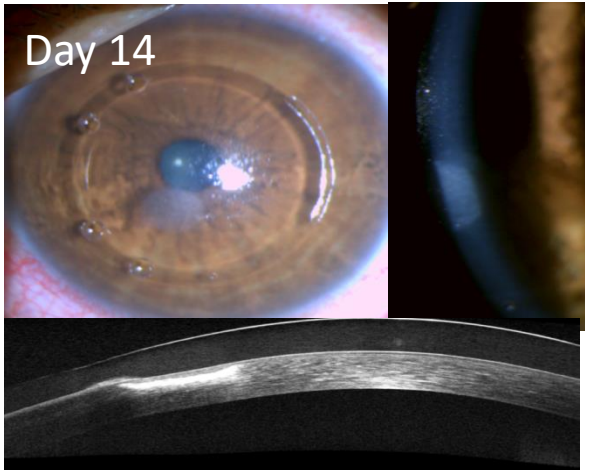












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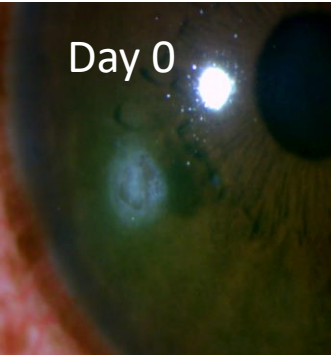
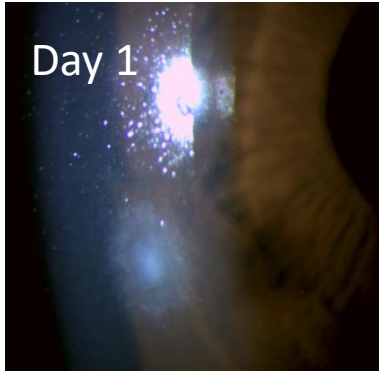
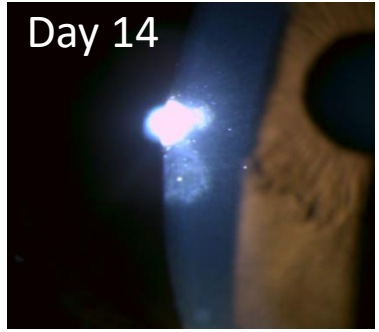

Day 0

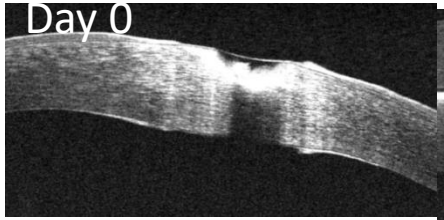

12 Hours

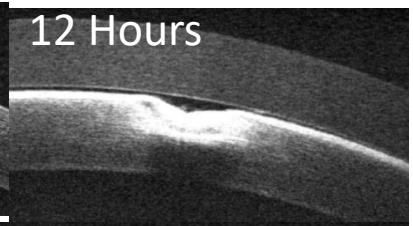

Day 1

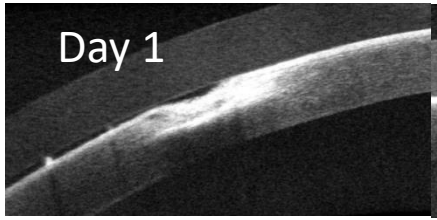

Day 3

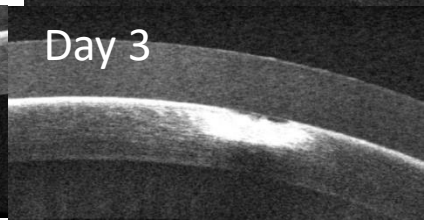

Day 5

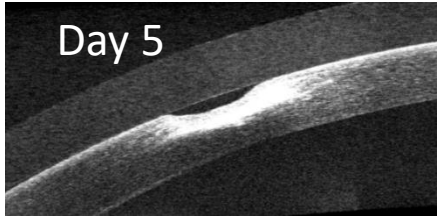

Day 14


Day 0

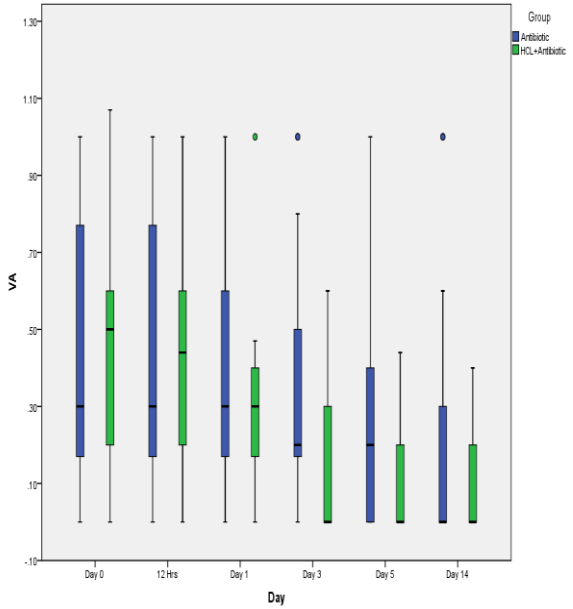

12 Hours


Day 1


Day 3


Day 5

Antibiotic only		Mean	SD	P value	Antibiotic + CL		Mean	SD	P value
Pair 1	0	0.48	0.31	n/a	Pair 1	0	0.48	0.31	0.101
	12	0.48	0.31			12	0.39	0.32	
Pair 2	0	0.48	0.31	0.08	Pair 2	0	0.48	0.31	**0.003**
	Day 1	0.45	0.24			Day 1	0.27	0.35	
Pair 3	0	0.48	0.31	0.016	Pair 3	0	0.48	0.31	0.001
	Day 3	0.33	0.08			Day 3	0.15	0.24	
Pair 4	0	0.48	0.31	0.001	Pair 4	0	0.48	0.31	0.002
	Day 5	0.31	0.09			Day 5	0.12	0.19	
Pair 5	0	0.48	0.31	<0.001	Pair 5	0	0.48	0.31	0.007
	Day 14	0.20	0.00			Day 14	0.09	0.11	



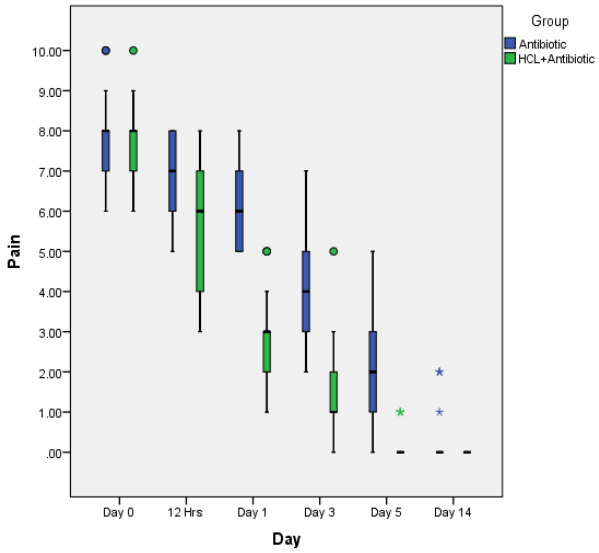
Visual Acuity (LogMAR) along timeline in both groups

A mean of 1.5line improvement in vision was noticed by Day 1 which improved by another line by Day 3 in CL group

*Significantly better early V/A gains were observed in CL group, on Days1,3

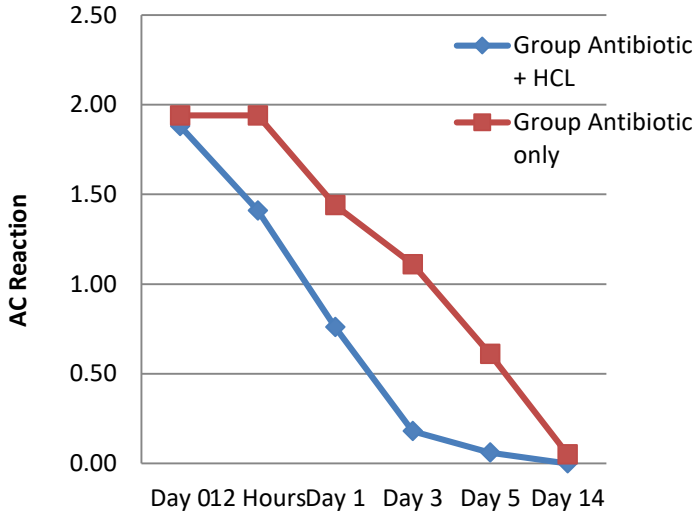
Changes in Pain, AC reaction And Corneal-Haze over time

Pain Score Drug+CL		Mean Pain	Std. Deviation
	Day 0	7.65	1.11
	12H	5.65	1.69
	Day 1	2.88	1.07
	Day 3	1.53	1.37
	Day 5	0.23	0.14
	Day 14	0.00	0.00



Presenting pain were 7.88+/- 0.70 in Group-1, 7.67+/-0.78 in Group-2, which reduced by 4.77 points in Group-2 & 1.88 points in Group-1 at Day1($p<0.001$).

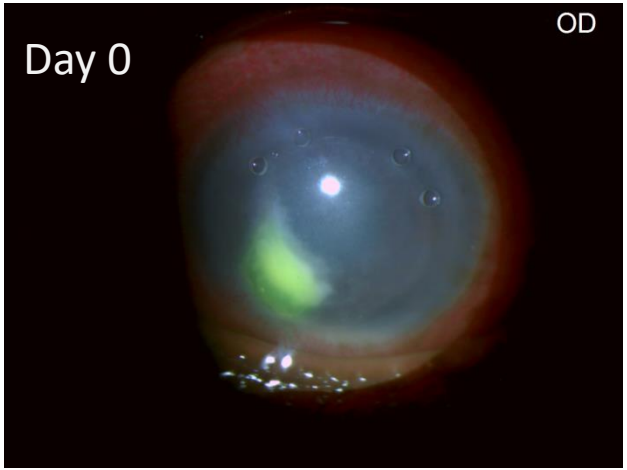
* Significantly better than drops alone

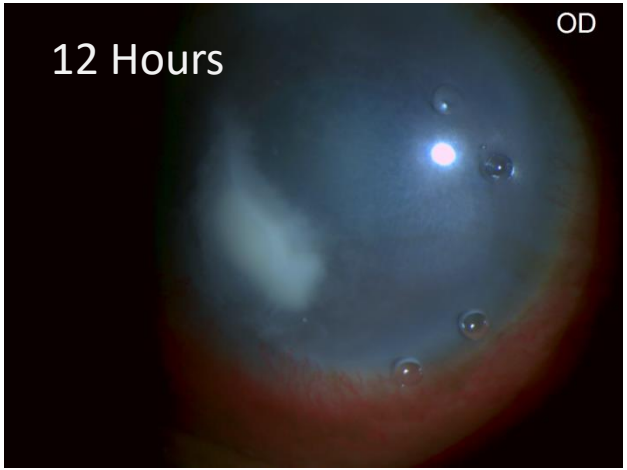


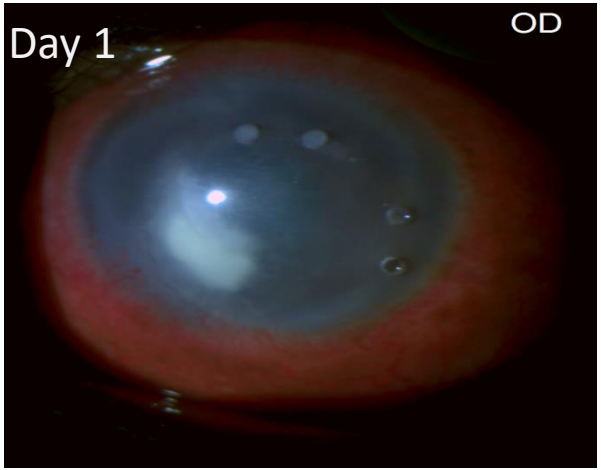
A significant reduction in AC reaction & improvements in Corneal Haze was noticed with-in the first 3 days in CL group

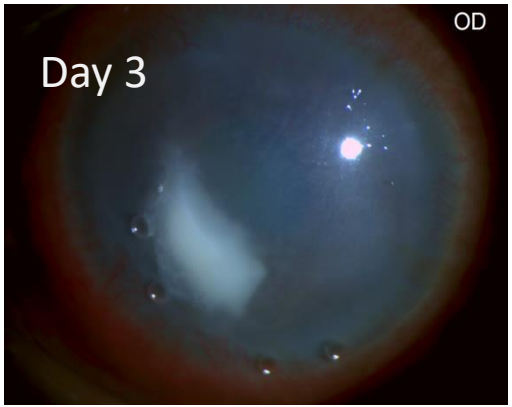
Patients treated with Repository CL were relieved of pain very early

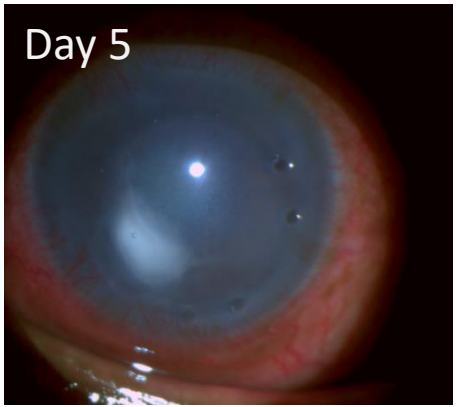
Case Ex. (Over 4mm)

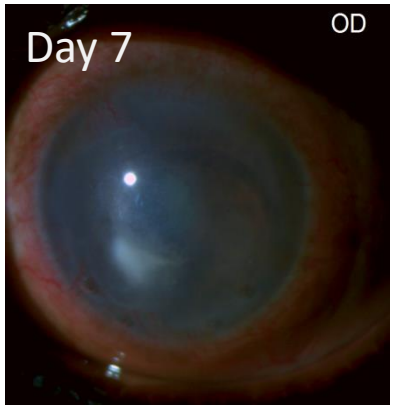


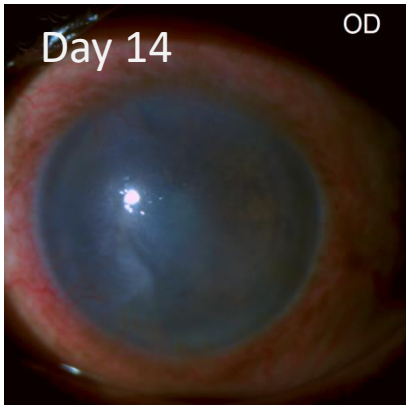






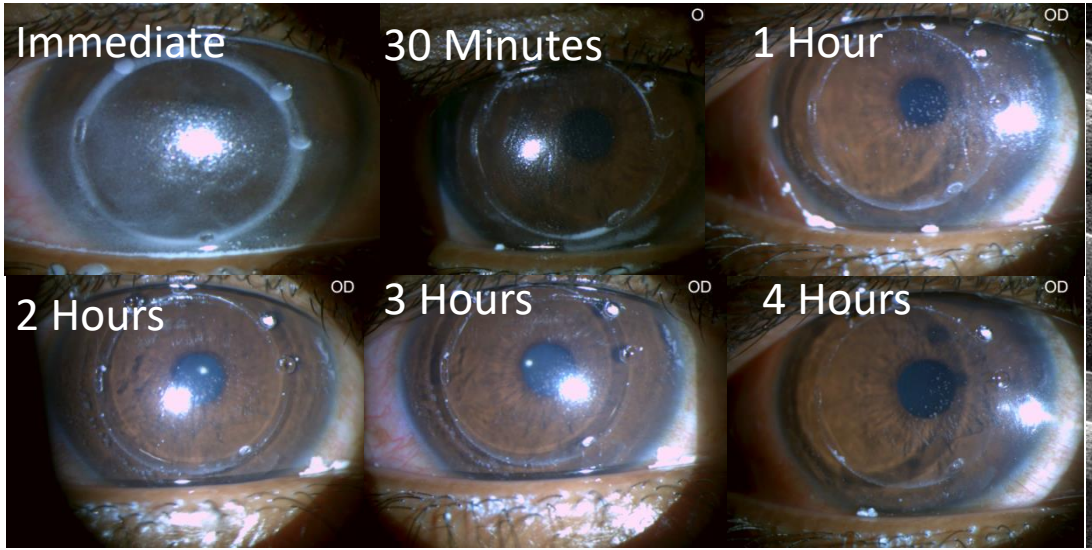


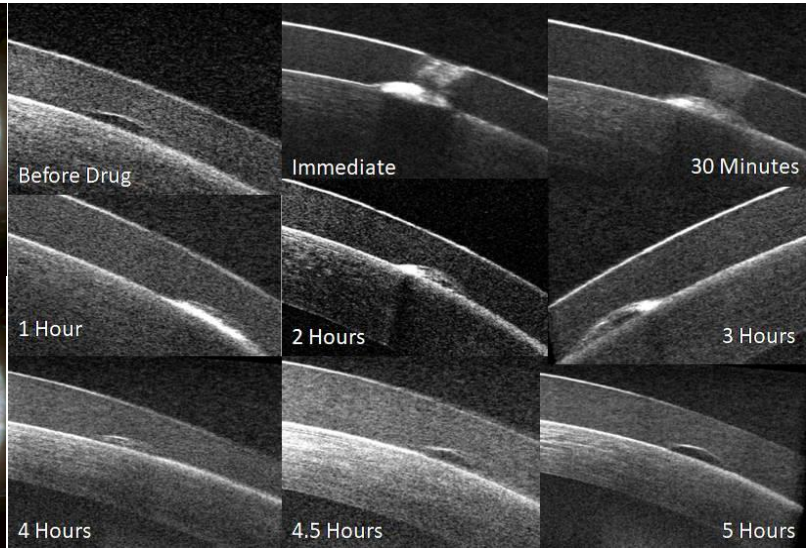




Ulcer over 4 mm, the effective healing started in 1 to 3 days and resolved by 14 days

Drug Retention Studies





Drug retention over time curve studies, using triamcinolone acetonide reflected drug availability in the central reservoir, peaking immediately on instillation and detected in the potential pre corneal space up to a period 4 hours, thus favoring an extended drug-corneal contact time

* Triamcinolone used to stain vitreous without staining the IOL during cataract surgery, is used as a testing agent in this study

- Poor drug bioavailability is a major concern associated with ocular dosage forms
- We in our study aimed in retaining the drug in the pre-corneal space, by using a very highly specified Depo-CL with dual base curves which resulted in a central antimicrobial lake for drug retention properties rather than the sustained release properties.
- Also, the fenestrations in the lens enabled the capture of every time applied topical antimicrobial to refill the central reservoir with the drug for a prolonged corneal contact time.
- Resolution of corneal infiltration was observed significantly before the 3rd day & we recommend that the treating physicians may remove Lens after a significant clinical healing response is noticed preferably after 3 days
- We noted a significant reduction in pain by 12 hours of treatment
- Our study reported no treatment-emergent adverse events
- Further studies may be evaluated with larger cohorts, comparison of large-sized ulcer groups, studies aiming reduced frequency of topical applications, and extension of this management strategy for protozoal and mycotic keratitis which requires longer drug-lesion contact periods than bacterial keratitis.

CONCLUSIONS:

- The Drug Repository Contact Lenses may be indicated for therapeutic use to promote effective corneal healing and pain relief during the treatment of bacterial keratitis.
- The concept of using novel drug repository contact lens over the lesion is effective in prolonging corneal antimicrobial availability, which can affect the overall outcomes in bacterial keratitis.
- Employing a drug-depo contact lens may reduce the regimen of antibiotics, decrease treatment burden on the medical staff, improve patient tolerance, reduce drug toxicities, and may change present practice patterns of loading dose concepts.