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Comparison of ketorolac tromethamine 0.4% and nepafenac 0.1% for the prevention of cystoid macular edema after phacoemulsification: Prospective randomized double-masked study

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- ✓ **Purpose**: To compare the anti-inflammatory efficacy of Ketorolac of tromethamine 0.4% and Nepafenac 0.1% eye drops for prophylaxis of cystoid macular edema (CME) after small-incision cataract extraction.

- ✓ **Design**: Randomized double-masked single center clinical trial.

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✓ Pacients and Methods:

- Prospective randomized clinical trial study ,
- Patients older than 40 years with age-related cataract,
- Normal ophthalmologic examination besides senile cataract.
- Patients were assigned to 3 groups :

Group 1: Topical artificial tear substitute (Placebo);

Group 2: Ketorolac tromethamine 0.4% (Acular LS, Allergan);

Group 3: Nepafenac 0.1% (Nevanac, Alcon).

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✓ Methods: Study Protocol

Pre and postoperatively measurements:

- Corrected distance visual acuity (CDVA);
- Central corneal thickness (CCT) (Pentacam, Oculus, Inc.);
- Corneal endothelial cell count by noncontact specular microscopy (Noncon Robo, Konan).
- A baseline spectral-domain optical coherence tomography (SD-OCT) before surgery and postoperatively after 1 wk, 4wks, and 12 wks. Heidelberg Spectralis OCT devise (Heidelberg, Germany). Calculates retinal volume over the entire 6-mm ETDRS grid.Central subfield thickness (CST) and total macular volume (TMV)

✓ Statistical Analysis

- Data were entered into a Microsoft Excel spreadsheet and analyzed using SPSS (version 17.0, SPSS, Inc.).
- Quantitative variables are described using mean ± standard deviation (SD) or median as well as minimum and maximum value where appropriate.
- To test whether the 3 medications had comparable baseline values concerning the target variables a **1-way repeated measures analysis of variance** or **Kruskal-Wallis test** were applied depending on sample distribution.
- The 1-way repeated measures analysis of variance was used to check quantitative variables for changes over time.
- Any differences showing a P value of < 0.05 (i.e., at the 5% level) were considered to be statistically significant.

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✓ Results

Table 1. Baseline characteristics of 97 study eyes (75 patients) by treatment group.				
	Group 1 Control (n=17)	**Group 2 Ketorolac (n=35)**	**Group 3 Nepafenac (n=23)**	**P. Value**
Age (y) **Mean ± SD** **Range**	58.97 (16.80) 50-90	66.33 (6.96) 50-81	67.22 (7.88) 53-90	.08
Sex, n (%)				.61
Male	06 (35%)	17 (48.5%)	10 (43.5%)	
Female	11 (65%)	18 (51.5%)	13 (56.5%)	
Medical history				
Diabetes	9 (52.9%)	5 (14.3%)	5 (21.7%)	.01
AL (mm) **Mean ± SD**	23.53 (1.37)	23.62 (1.24)	23.65 (1.27)	.42

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Table 2. Preoperative and 30 days postoperative data.

	Group 1 Mean ± SD		Group 2 Mean ± SD		Group 3 Mean ± SD		P Value	
	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop
CDVA (logMAR)	0.13 (0.17)	0.01 (0.05)	0.16 (0.13)	0.06 (0.12)	0.17 (0.20)	0.04 (0.10)	.74	.44
CCT (µm)	529.93 (32.37)	527.10 (32.93)	517,78 (40.84)	518.09 (39.07)	535.81 (39.85)	531.76 (38.89)	.15	.33
ECD (cells/mm^2)	2495.35 (323.69)	2323.23 (320.70)	2288.11 (415.11)	2164.90 (493.86)	2340.75 (425.64)	2168.75 (539.17)	.24	.48

CDVA: corrected distance visual acuity; CCT: central corneal thickness; ECD: endothelial cell density.

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Table 3. Between-group comparison of central subfield thickness (CST, µm) measured with SD-OCT.

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		Postoperative		
Group	Baseline	1 Wk	4 Wk	12 Wk
Group 1 – Control				
Mean ± SD	259.93 (30.84)	268.86 (30.51)	270.71 (30.73)	274.82 (30.45)
Group 2 – Ketorolac				
Mean ± SD	269.78 (34.69)	271.46 (37.42)	278.85 (45.43)	282.26 (45.21)
Group 3 – Nepafenac				
Mean ± SD	270.44 (33.68)	274.01 (33.48)	279.00 (33.82)	289.73 (54.80)
P value	.56	.89	.77	.54

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Table 4. Between-group comparison of total macular volume (TMV, mm^3) measured with SD-OCT.

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		Postoperative		
Group	Baseline	1 Wk	4 Wk	12 Wk
Group 1 – Control				
Mean ± SD	8.56 (.64)	8.57 (.56)	8.69 (.58)	8.72 (.61)
Group 2 – Ketorolac				
Mean ± SD	7,99 (1.31)	8.17 (1.20)	8.33 (1.23)	8.38 (1.25)
Group 3 – Nepafenac				
Mean ± SD	7.89 (1.32)	8.16 (1.23)	8.21 (1.23)	8.21 (1.23)
P value	.20	.47	.43	.37

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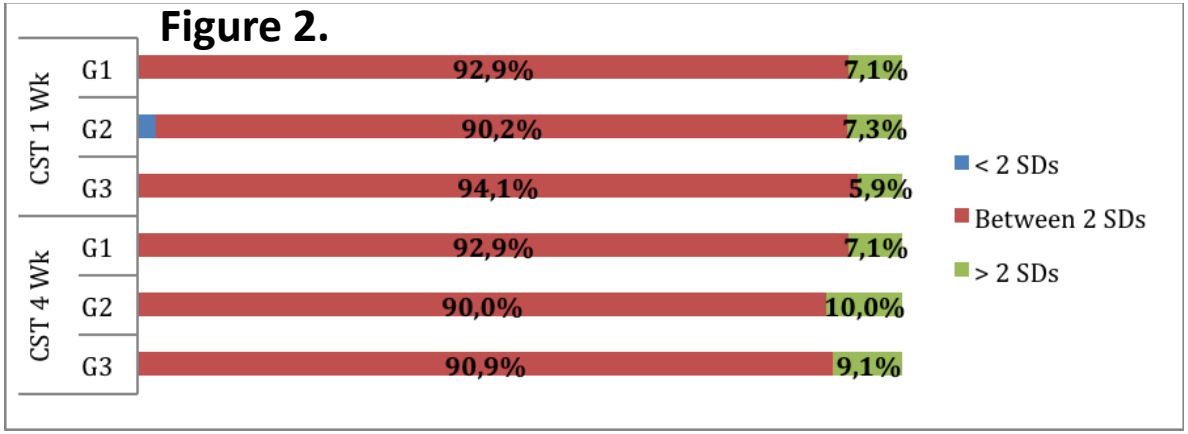
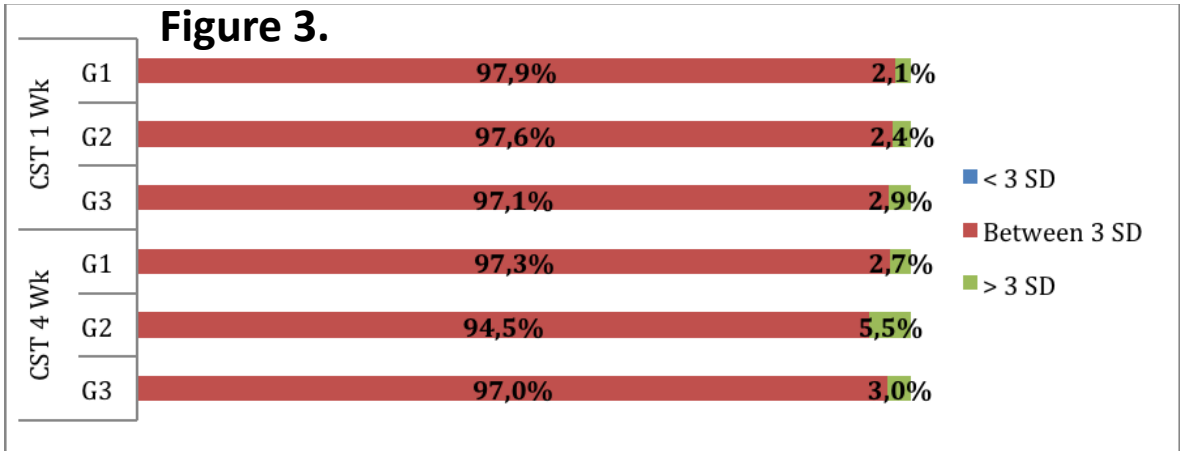
Figure 2 and 3. Percentage of patients in whom we defined macular edema using an upper cutoff of 2 and 3 SDs above the mean baseline CST by treatment group.





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Discussion

Incidence of EMC

Reduce	Not reduce
1-Almeida at al 2008 Ketrolac x placebo(uveitis,diabetes,macular desease) decrease macular volume.	1-Our results show there no was diference in CST and TMV
2-Donnenfeld at al 2006 . Ketrolac X Placebo .They have a hypothesis that NSAIDS may be able to reduce the EMC incidence	2-Almeida at al 2012- Prophilactic NSAID x placebo on macular volume 1 month after phacoemulsification
	3-Biro at al 2008 measured foveal and perifoveal thickness
	4-Chatziralli et al 2011.The study demonstrated that the frequency of inflammation related signs did not differ between the two groups at any time . There was no evidence of clinically significant CME in either group.

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Discussion

- There is no consensus on OCT parameters for identifyng the presence of CME after cataract surgery.
- Perene at al 2007. they studied 110 eyes of 102 healthy pacients - peak of incidence CME 10,9% using OCT. The author defined CME as 2 SDs preoperative-(CTS).
- Kusbeci et al 2012,defined as three SDs above preoperative mean CMT.(5.5 % and 4.44% incidence rate of CME at postoperative 12th weeks and 24weeks)
- Our reseach we using 2 SDs we observed higher incidence rate 7.1%, 10%, 9.1%of CME at postoperative 4 weeks in placebo, ketrolac and nepafenac. When we used 3 SDs – 2.1%, 2.4%, 2.9%.

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✓ Conclusion

- Visual recovery, central corneal thickness, endothelial cell density, macular foveal thickness and total macular volume were statistically similar between the placebo group, keterolac group and the nepafenac group;

- Establishing normal incidence ranges of CME using OCT and clarifying its correlation with vision will become increasingly important.

- Future studies with larger sample sizes are necessary to better define these associations.