USE OF CYCLOPLEGIC AND MYDRIATIC AMONG SUCCESSFUL POST-DCRYOCYSTORHINOSTOMY CASES: HOW SAFE IT IS!!
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ABSTRACT

BACKGROUND
In post dacryocystorhinostomy patients, absorption of topical drugs is higher due to exposed nasal mucosa. As a result, systemic side effects are more common than local effects. So, ophthalmologists must be aware of the dangers of ocular and systemic side effects of these combined drugs especially in patients with cardiovascular, renal and other morbidities which are sometimes really challenging. The main purpose of the study is to assess the safety of giving a mixture containing 0.75% tropicamide and 2.5% phenylephrine among the successful post DCR cases in normotensive and hypertensive patients, to find out whether shortening of the nasolacrimal passage which occurred after DCR surgery has any effect on the absorption and systemic effects of ocular drops and record the difference of these complications (local and systemic) in pre- and post-operative DCR sides with that of the normal sides.

METHODS
Fifty patients of successful post dacryocystorhinostomy cases were studied between February 2018 and January 2019. On admission, pupillary diameter, pulse rate, blood pressure, ECG changes were measured before and after application of drops and same procedures were done one and half month after DCR operation. This is a non-randomized control trial designed to determine the safety of use of cycloplegic and mydriatic among the successful post dacryocystorhinostomy cases.

RESULTS
The size of pupillary diameter was less in post DCR side compare to control side (p=0.000). Both blood pressure (p=<0.05) and pulse rate changes were also seen but pulse rate changes was statistically insignificant (p=0.302). Significant ECG changes were seen in hypertensive patients.

CONCLUSIONS
Removal of obstruction and shortening of nasolacrimal passage by DCR surgery causes alteration of transportation and absorption of drugs. So, before its application, pharmacodynamics and systemic adverse effects of applied drugs should be kept in mind.

KEYWORDS
Mydriatic, Phenylephrine, Tropicamide, Dacryocystorhinostomy, Systemic Effects.

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BACKGROUND
Now-a-days the topical ocular drops containing 0.75% tropicamide and 2.5% Phenylephrine are used commonly as mydriatic and cycloplegic agent for fundus examination in outdoor procedures. Parasympatholytics as well as sympathomimetics have been used to dilate the pupil. Combination of both drugs offers greater dilation of pupil than single use of any drug.

Tropicamide is the quickest and briefest acting parasympatholytic drug, blocks cholinergic action on the sphincter muscles and the ciliary muscles, thereby causes dilatation of pupil and inhibiting accommodation (cycloplegia). Phenylephrine is alpha 1- receptor stimulant, acts directly on ciliary muscle. So this is mydriatics but not cycloplegic.

Phenylephrine causes vasoconstriction of the coronary, pulmonary and systemic arteries. As a result, it causes reduction in cardiac output and renal, splanchnic, cutaneous and limb blood flow. Consequently, there is tachycardia, increased blood pressure, arrhythmia, heart failure,1,2,3

In post dacryocystorhinostomy patients, the new formed nasolacrimal passage becomes shorter and wider than normal side. As a result, absorption of topical drugs are higher due to exposed nasal mucosa. So systemic side effects like blood pressure and arrhythmia are more common than local effects.4

So, ophthalmologists must be aware of the dangers of ocular and systemic side effects of these combined drugs. The complications depend upon dosage, frequency, patency of nasolacrimal duct and systemic condition of the patients.

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Aims and Objectives
1. To record safety of giving 0.75% tropicamide and 2.5% Phenylephrine among the successful post DCR cases especially in cardiological morbid patients.
2. To find out whether shortening of the nasolacrimal passage as occurred after DCR surgery has any effect on the absorption and systemic effects of ocular drops.
3. To assess the difference of these complications (local and systemic) in pre and post-operative period of DCR surgery.

METHODS
Our study was conducted on 100 eyes of 50 patients (n=50) of unilateral nasolacrimal duct obstruction at ophthalmology outdoor, R.G. KAR medical college, Kolkata. Study time was from February 2018 to January 2019. The unaffected eye served as control. All participants have been informed about details of the study before signing the consent.

Study Design
Non randomised control trial.

Inclusion Criteria
(1) Patients between 15 to 40 years irrespective of their sex and religion.
(2) Patients given written informed consent. In patients too young to give consent, this has been obtained from their parents or guardians.
(3) Patients with history of respiratory and cardiovascular disease.
(4) The patients had to have hard stop only, thereby excluding common canalicular obstruction.

Exclusion Criteria
(1) Pregnant and lactating mother.
(2) Patients who died, loss to follow-up or transferred out.
(3) Past history of any ocular injuries or intraocular surgeries including laser treatment.

Pre-operotive Work-Up
(a) Detailed History
Following things are noted-
- Chief complaints and their duration
- Detailed family history, past history, personal history
- History of any cardiovascular, renal and respiratory diseases.
- Intake of any drugs like steroids, antihypertensive, antidiabetics.
- History of myasthenia gravis.

(b) General Ocular Examination
i) Best corrected visual acuity (BCVA): done with Snellen's distant vision chart.
ii) Eyelids and appendages with checking of patency of nasolacrimal passage examined by syringing.
iii) Anterior segment examination with slit lamp biomicroscopy.
iv) Fundus examination with direct and indirect ophthalmoscope, 90D lens.

(c) Special Ocular Examination
- Applanation tonometry to measure intraocular pressure.
- Slit lamp examination and Gonioscopy.

(d) Investigations Included
- Complete haemogram for Hb, TC, DC, ESR, BT, CT, Serology, blood sugar.
- Standard 12 lead ECG, ENT check-up.

(e) Blood Pressure Measurement during Admission.
Every patient has been examined two times during the whole procedure of the study.
- During the time of admission, with the help of slide calliper vertical and horizontal diameter of pupil has been measured before and after application of 0.75% tropicamide and 2.5% Phenylephrine drop.
- Recording the pulse, blood pressure, ECG (rate, rhythm, ST changes), intraocular pressure before and after application of drops.
- Six weeks after DCR surgery- when it has been ensured that the surgical anastomosis was patent- the operated eye received a similar medication as stated before. The aforesaid parameters has been noted again and compared with the baseline readings.

At the time of giving Tropicamide and Phenylephrine drops, following instructions are to be followed:
- Ocular solution should be combined of 0.75% tropicamide and 2.5% Phenylephrine.
- During the time of giving single drop(approximately 30-micron size), it has been administered in lower fornix during day time in supine position at 10 minutes interval three times and examined fifteen minutes after last drop.
- After giving drops, patient has been advised to close the eyelids.

RESULTS
This study has been done in tertiary setup over a period of one year. 100 eyes of 50 patients with unilateral nasolacrimal duct obstruction have been examined irrespective of sex and religion. The normal side selected as “Control Group” and the obstructed nasolacrimal duct side termed as “Study Group”.

Patients with cardiovascular disorder and renal disorder were high risk patients and special attention has been given to those patients. Each patient has been examined twice during the course of the study.
a) At the time of first examination on admission, the CONTROL eye was to be examined before and after application of Tropicamide 0.75% and Phenylephrine 2.5% eye drop.

b) Follow up of dacryocystorhinostomy operation done after six weeks, the STUDY eye was to be examined again after application of same ocular drop.

Socio Demographic Distribution of Patients

<table>
<thead>
<tr>
<th>Age (in year)</th>
<th>No. of Patients</th>
<th>Percentages</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-20</td>
<td>6</td>
<td>12%</td>
</tr>
<tr>
<td>21-30</td>
<td>16</td>
<td>32%</td>
</tr>
<tr>
<td>31-40</td>
<td>20</td>
<td>40%</td>
</tr>
<tr>
<td>41-50</td>
<td>8</td>
<td>16%</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 1. Age-Wise Distribution of Patients

Ocular Parameters and Cardiovascular Parameters

During examination of the normal eyes (CONTROL) vertical and horizontal diameter of pupil has been measured before and 45 minutes after application of topical combination of 0.75% tropicamide and 2.5% Phenylephrine. Similarly, blood pressure, pulse rate and ECG changes has been noted before and after 3 subsequent application of the eye drop at 10 minutes interval and 15 minutes thereafter.

The size of pupillary diameter was less both horizontal and vertical directions in post dacryocystorhinostomy side compare to control side and the difference was statistically significant.

Systolic and diastolic blood pressure changes were more in post dacryocystorhinostomy side compare to normal side and statistically significant difference was seen in post DCR side systolic BP compare to normal side.

Pulse rate changes was also seen in post DCR side compare to control side, but statistically insignificant.

Significant ECG changes were seen in cardiological morbid patients.

DISCUSSION

Following application of 0.75% tropicamide and 2.5% Phenylephrine before and after dacryocystorhinostomy operation number of ocular and cardiovascular parameters were changed significantly.

Ocular Parameters

Horizontal and vertical pupillary diameter in CONTROL side increased after application of Tropicamide and Phenylephrine eye drops and six weeks after successful DCR operation, Horizontal and vertical pupillary diameter also increased after giving same combined ocular drops. Result showed that pupillary diameters reduced in post DCR side compare to normal side in each individual due to increase systemic absorption of drugs after DCR operation via nasal mucosa.

This indicates that DCR operation causes removal of blockage site and shortage of nasolacrimal passage and as a result chance of absorption of topical drugs are higher than normal due to exposed nasal mucosa corresponding to normal side. Less dilatation of pupil causes increased incidence of complication during cataract surgery.5,6,7
Cardiovascular Parameters

After giving of Tropicamide and Phenylephrine ocular drop to normal side (CONTROL), pulse rate changed little after 45 minutes and not very much significant but in case of post DCR (STUDY) side pulse rate changed compared to normal side but this is not significant.

Blood pressure changes has also been seen significantly including both systolic and diastolic after 45 minutes application of Tropicamide and phenylephrine eye drops. Systolic blood pressure changes were statistically significant, but 95% confidence interval of the blood pressure changes was not clinically relevant.8

Minor changes of this blood pressure can occur due to-

1) Diurnal variation.9
2) White coat hypertension syndrome.
3) Anxiety
4) Usual difference observed between two BP rating.

ECG Changes

After application of Tropicamide and Phenylephrine eye drop ECG changes has not been seen significantly in control and study side as well as post DCR side in most of the patients but ten (32%) patients had significant ECG changes which included atrial fibrillation and ventricular bigeminy (twelve patients) in study side. Those were previously diagnosed as post CVA patients.

It is usually considered to be safe, but certain reports have appeared in the literature suggesting definite side effects such as acute episodes of systemic hypertension. British National Formulary recommends caution in use of phenylephrine ocular drops, particularly in elderly patients and those with hypertension.10 Symons et al reported no significant change in the mean systolic and diastolic blood pressure in 126 patients receiving phenylephrine.5 Chin et al in their study on 89 patients concluded that significant hypertensive effects can arise after topical phenylephrine.6 Samantary and Thomas (1975) reported a definite increase in blood pressure after topical use of phenylephrine in all of their cases.

Summary

The study has been conducted on 100 eyes of 50 patients having unilateral nasolacrimal duct obstruction (NLO) of different ages ranging from 15-50 years. The unaffected eye noted as control and the eye with NLO served as study group.

Among 50 patients, 32 were males and 18 patients were females. A number of variety of patients including cardiovascular, respiratory and renal morbidity has been included in the study.

The patients have been examined twice during the course of the study- during the time of admission, normal eye has been monitored before and after application of

### Table 3. Mean changes of the vertical, horizontal pupillary diameter on the normal side and post DCR side. systolic, diastolic and pulse rate mean changes also seen.

<table>
<thead>
<tr>
<th>Pair</th>
<th>Difference normal pupillary vertical diameter</th>
<th>N</th>
<th>95% Confidence Interval of the Difference</th>
<th>T</th>
<th>df</th>
<th>Sig.(2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pair 1</td>
<td>Difference normal pupillary vertical diameter-Difference post- DCR vertical pupillary diameter</td>
<td>1.400</td>
<td>.4120</td>
<td>.06230</td>
<td>1.29077</td>
<td>1.5920</td>
</tr>
<tr>
<td>Pair 2</td>
<td>Difference normal pupillary horizontal diameter-Difference post- DCR horizontal pupillary diameter</td>
<td>1.320</td>
<td>.38809</td>
<td>.05488</td>
<td>1.20971</td>
<td>1.43029</td>
</tr>
<tr>
<td>Pair 3</td>
<td>Difference normal side systolic blood pressure-Difference post- DCR systolic blood pressure</td>
<td>2.900</td>
<td>7.65386</td>
<td>1.08242</td>
<td>-5.07520</td>
<td>-.72480</td>
</tr>
<tr>
<td>Pair 4</td>
<td>Difference normal side diastolic blood pressure-Difference post- DCR diastolic blood pressure</td>
<td>1.380</td>
<td>4.95239</td>
<td>.70037</td>
<td>-2.78745</td>
<td>.02745</td>
</tr>
<tr>
<td>Pair 5</td>
<td>Difference normal pulse rate-Difference post DCR pulse rate</td>
<td>.7200</td>
<td>5.2684</td>
<td>.74507</td>
<td>-.77728</td>
<td>2.21728</td>
</tr>
</tbody>
</table>

### Table 4. Paired Samples Test
Tropicamide and phenylephrine drop and secondly six weeks after DCR operation study eye has been examined before and after application of Tropicamide and phenylephrine drop.

After half an hour rest in supine condition, each time a single drop (30 micron. Size) of Tropicamide 0.75% and Phenylephrine hydrochloride 2.5% has been administered in the eye 10 minutes interval and reading has been taken 15 minutes after the last dose and the following changes has been seen.

In control eye, the mean increased vertical pupillary diameter was 4.8000 mm and mean horizontal diameter was 3.4300 mm after 45 minutes. So pupillary diameters were found to be significantly altered.11,12

Blood pressure has been measured before and after giving ocular drops and blood pressure changes seen were statistically significant(p<0.05) but no clinically significant.

Pulse rate changes were also seen in the study but no statistically or clinically significant (p=0.339).

No significant ECG changes were detected in the normal eye (CONTROL) and significant ECG changes (in 32% cases) were seen in the post DCR side (STUDY) especially patients with cardiovascular morbidity.

CONCLUSIONS

DCR surgery offers an altered nasolacrimal anatomy and it causes alteration of transportation and absorption of drugs. So, pharmacodynamics and systemic adverse effects of applied drugs should be kept in mind before application.

Abbreviation

NLD- Naso Lacrimal Duct
IOP- Intraocular pressure
DCR- Dacryocystorhinostomy
PPBS- Post Prandial blood sugar
BT- Bleeding time
CT- Clotting time
BP- Blood pressure
ECG- Electrocardiogram
OPD- Out Patient Door
HBsAg- Hepatitis B surface antigen
HIV- Human immunodeficiency virus
ESR- Erythrocyte sedimentation rate
Hb%- Haemoglobin
TC- Total count
DC- Differential Count
ENT- Ear, Nose & Throat

REFERENCES