CHAPTER VI

DISCUSSION, CONCLUSION AND RECOMMENDATION

6.1 Discussion

This study shows that latanoprost monotherapy can lower IOP significantly more than the combination of pilocarpine and timolol therapy. The mean diurnal IOP reduction from baseline was greater in the 36 latanoprost group than that in the 35 pilocarpine plus timolol group (7.34±2.02 (SD) VS 5.29±2.91 mmHg, the mean difference in diurnal IOP reduction between the two groups was 2.1 mmHg with 95% CI 0.632 to 3.553, p=0.005, 3 way ANOVA). Latanoprost lowered the mean diurnal IOP from 24.4 to 17.0 mmHg, a reduction of 30.1%. The corresponding figure for pilocarpine plus timolol group was a reduction from 24.2 to 18.9 mmHg (-21.9%). The result of previous study of latanoprost monotherapy versus pilocarpine in combination with timolol, also showed the same superior result of latanoprost monotherapy to the combination of pilocarpine and timolol.[13]

The mean difference in diurnal IOP reduction between the two treatments was 2.1 mmHg. It has not been proved whether this difference will have a clinically significant effect on the progression of optic nerve damage, but it will certainly increase the odds of reaching the designed target IOP.

From Table 5.2.1.1 GMEANB1 (stratified patients into 2 groups, baseline IOP $\leq$ 25 and > 25 mmHg) also shows statistically significant difference effect (p=0.017). This demonstrated that patients with baseline IOP $\leq$ 25 and > 25 mmHg had a significant difference in mean IOP at final visit (17.35 $\pm$ 2.08 (SD) VS 19.31$\pm$ 4.38) which was consistent with our expectation.

For success rate and response rate of treatment, this study shows that more patients in the latanoprost group, reached a target IOP$\leq$18 mmHg and reached a reduction in diurnal IOP from baseline $\geq$ 30%, than in the control group. However, in this circumstance it should be interpreted carefully. There are two aspects of result. Firstly, positive result, there is significant difference between the two groups. Considered this aspect, if we did multiple testing, in every 20 parameters testing at least one parameter testing resulted in significant difference ($p < 0.05$) by chance alone. Secondly, negative result, there is no significant

difference between the two groups. This can also occur from small sample size.

Regarding safety, latanoprost resulted in more conjunctival hyperemia and eye discomfort than did pilocarpine plus timolol group, which is consistent with past studies.[12,13,19]

Other known ocular side effects of latanoprost; changes of eyelashes, iris hyperpigmentation and presence of cystoid macular edema, were not found in this study. However, the treatment period was most likely too short to demonstrate these findings. Pilocarpine plus timolol resulted in more decreased vision than did latanoprost, as expected from known miotic effect of pilocarpine.[3]

Systemic side effects were reported in very few number of patients in both groups. Only one patient in latanoprost group reported severe insomnia that made the patient withdrawn from the study. Two patients in pilocarpine plus timolol group reported headache and browache. In general, both treatments were well tolerated during the 3-month study period. But side effects occurring after treatment longer than three months can not be evaluated from this study.

Cost-effectiveness Analysis (Table 5.3.4.1)

1. Cost-effectiveness ratio

- *When target IOP≤ 15 mmHg* (The CE ratio of both groups were nearly equal.)

Both treatment groups appeared to have the same cost-effectiveness, hence it would be wise to decide to use latanoprost as the first choice of treatment in patients who need very low IOP as target pressure, since it has less ocular and systemic side effects and gives better quality of life with very good compliance.

- *When target IOP≤18 and ≤21 mmHg* (The CE ratio of combination group was less than that of latanoprost group.)

Combination of pilocarpine and timolol were more cost-effective. So from the health provider's point of view, it will be worth while to decide to use the combination drug as the first choice of treatment in patients who need target IOP≤18 and ≤21 mmHg. This conclusion is based on assumption that the quality of life and compliance are the same in the two groups. If we asked the patients about their quality of life and compliance, the answer might be different.

2. Incremental analysis

The result of incremental CE ratio shows that if we want to cure (IOP control) one more patient by changing from the combination drug to latanoprost, we have to spend 48,872 Baht, 30,418 Baht and 93,225 Baht more for target IOP≤15, ≤18 and ≤21 mmHg, respectively.

3. Sensitivity analysis with IOP≤18 mmHg

When varying the price of latanoprost, it shows that if the price of latanoprost is 360 Baht/bottle, latanoprost will be more cost effective. But if varying the price of timolol to 100 Baht/bottle, latanoprost will be more cost effective only if it's price is 280 Baht/bottle.

6.2 Conclusion

In summary, this study confirms that in patients with inadequately controlled IOP with timolol, latanoprost monotherapy can lower IOP significantly more than the combination of pilocarpine and timolol. It can also achieve higher success rate in target IOP ≤ 18 mmHg and higher response rate of treatment in IOP reduction from baseline ≥ 30%, than the combination group, with no serious ocular and systemic side effects.

For economic consideration, this paper shows that when aiming for target IOP ≤15 mmHg, both groups have nearly equal cost effectiveness but when aiming for target IOP≤18 and ≤21 mmHg, the combination of pilocarpine and timolol was more cost effective.

6.3 Recommendation

1. In open angle glaucoma patients, medication is the first line of treatment. Beta-blockers are still the first agents used because they are not expensive and have high efficacy in lowering IOP with relatively few ocular side effects. But clinician should be aware of the possibility of significant systemic side effects. They are contraindicated in patients with actual or suspected compromised cardiovascular or pulmonary function.

2. When target pressure is not achieved, a second medication, adding on previous medication or switching to the new drug, may be considered.

3. To decide what drug should be used, clinician should assess not only cost-effectiveness but also the quality of life and compliance of the patients.

4. Most new glaucoma drugs are very expensive. Apart from considering medication as first line of treatment, further study comparing medication and surgery, in term of cost-effectiveness, compliance and quality of life will be very interesting and very beneficial not only for individual patient, but also for national health care cost.