CHAPTER 5

RESULT

PATIENTS ACCOUNTING

There were a total of 79 perennial allergic rhinitis patients who fulfilled the eligibility criteria visiting the Ear Nose and Throat Department Kariadi Hospital during 8 months period of study. There were 40 patients in the A/B sequence (10 mg Cetirizine followed by 8 mg Chlorpheniramine) and 39 patients in the B/A sequence (8 mg Chlorpheniramine followed by 10 mg Cetirizine). Data of ten patients were incomplete. Two patients came back after 3 days taking the drug of the first period of treatment and they did not like to finish the treatment. One of them became severe headache which she thought was the effect of the treatment and the other one felt so sleepy and fatigue that she also thought was due to treatment. Three cases finished the first period of treatment with successful result, however, they did not come after the second period. The other 5 patients did not come since after the first period of treatment. It means that 5 patients did not have any data of the first period of treatment, two cases had incomplete data of the first period, while three cases had complete data of the first period only. There were 69 cases who finished the two periods of treatment,

however, two cases got acute upper respiratory tract infections during the treatment. Therefore, there were only 67 cases who finished the two periods of the two sequences of treatment without any confounders event. The dropout cases were 12.6% (10/79) (the data was in table 4).

Table 4. Characteristic of the dropped out cases compared to complete cases

		Complete	Dropped out	Stat. test
Age :	mean	29.33 year	23.30 year	t-test
	SE.	1.08	1.86	2.03 (sign.)
Sex :	male	32 (40.5%)	2 (2.53%)	Fisher exact test
	female	37 (46.84%)	8 (10.13%)	p = 0.107
	total	69 (87.34%)	10 (12.66%)	
Symptom score :				
	3	36 (45.57%)	3 (3.79)	Fisher exact test
	2	33 (41.77%)	7 (8.87%)	p = 0.16
	total	69 (87.34%)	10 (12.66)	

From this table showed that there was a significance difference of the mean age of dropped cases compared to complete cases. The mean age of dropped cases was younger than the mean age of complete cases.

DEMOGRAPHIC DATA AND CLINICAL CHARACTERISTICS

The demographic data was presented in table 5 and clinical characteristic of patients were presented in table 6. There was only one group of patients because this was a matched-pair crossover design in two-period two-treatment. From 79 cases who were enrolled into the study, there were 45.5% males and 54.5% females. Patients who have severe symptoms were almost equal to the patients with moderate symptoms (39:40). The mean age of the patients was 29.33 years (range 16-55 years SE = 1.01) and the mean duration of rhinitis was 5.6 years (range 0.5 to 15 years S.E.= 0.56). Allergic family history was found in half of cases and some of them have other allergic disease manifestations such as bronchial asthma (27%), urticaria (25%), food allergy (20%) and drug allergy (13%) besides perennial allergic rhinitis. About 83% (66/79) of cases had a positive allergic skin testing to dust mite, 70% (56/79) to house dust, 46% (37/79) to human dander and 35% (28/79) to animal dander (cat and dog). Eighty five percent (67/79) of cases had a positive skin tests result to more than one allergen.

Table 5. Demographic data

5.1. Sex	number	percentage
Male	36	45.5%
Female	43	54.5%
total	79	100%

5.2. Age

Range	16 -55 year
Mean	29.33 year
S.E.	1.01

Table 6. Clinical characteristic of patients

6.1. Duration of disease

Range	0.5 -15 year
Mean	5.6 year
S.E.	0.56

6.2. Symptom score at the entry of study

score	number	percentage
3	39	49%
2	40	51%
total	79	100%

6.3. Other allergic disease manifestation

other allergic manif.	number	percentage
No other disease	31	39.24%
Positive other dis.	48	60.76%
total	79	100%

6.4. Manifestation of disease	number	percentage (of 48)
Bronchial asthma	22	45.83%
Urticaria	20	41.66%
Food allergy	16	33.33%
Drug allergy	11	22.91%

Note: One patient might have more than one manifestation

According to the result of the taking history, the worse symptoms of allergic rhinitis mostly occurred in the early morning. Very few cases who had worse symptoms at noon time. Sneezing attack was reported as the very disturbing symptoms by 72.15% of cases, rhinorrhea was reported by 67.7% of cases, while nasal obstruction was reported as very disturbing symptoms by 46% of cases. Many cases had more than one very disturbing symptoms. The complete data of the variation of perennial allergic rhinitis symptom of the present study can be seen in table 7.

Table 7. Variation of perennial allergic rhinitis symptoms

7.1. The time of worse symptom

Time	number	percentage
morning and night	42	53.16%
morning or night	32	40.50%
noon time	5	6.34%
total	79	100%

7.2. Very disturbing symptom

Symptom	number	percentage
sneezing	10	12.65%
rhinorrhea	15	18.98%
nasal obstruction	4	5.06%
sneezing & rhinorrhea	20	25.31%
sneezing & nasal obst.	12	15.18%
sneezing, rhinorrhea & nasal obstructions	18	22.78%
total	79	100%

7.3. Frequency of sneezing

frequency	number	percentage
less than 3 times	4	5.06%
3 to 5 times	29	36.70%
6 to 8 times	27	34,17%
more than 8 times	19	24.07%
total	79	100%

7.4. Frequency of nasal blowing

frequency	number	percentage
1 time	2	2.54%
many times	38	48.10%
profuse nasal secretions	39	49.36%
total	79	100%

7.5. Nasal obstruction

severity	number	percentage
no obstruction	4	5.07%
mild obstruction	50	63.29%
severe/total obstr.	25	31.64%
total	79	100%

7.6. Duration of the worse symptoms

time	number	percentage
less than 0.5 hour	7	8.86%
0.5 to 1 hour	28	35.44%
more than 1 hour	44	55.69%
total	79	100%

7.7. Other symptoms

symptom	number	percentage (of 79)
headache	31	39.24%
sleepy	18	22.781%
fatigue	11	13.92%
Difficult to concentrate	13	16.45%

EFFECTIVENESS OF TREATMENT

PATIENT ASSESSMENT

Since this study was a match paired design, so only cases who finished the two treatments were analyzed to inference the result of the treatment. Data of patients who dropped out during or after the first period of treatment were not analyzed since they did not have any comparison.

This study followed a principle of intention to-treat, therefore, all data were analyzed twice. First including all cases with confounder event, non compliant and then excluded them from the analysis.

Table 8.1. Treatment result based on patient assessment included cases with confounder event

		10 mg CETIRIZINE		
		success	failure	TOTAL
8mg CHLORPHENIRAMINE	success	43 (62.32%)	5 (7.24)	48 (69.56%)
	failure	10 (14.49%)	11 (15.95%)	21 (30.44%)
	TOTAL	53 (76.81%)	16 (23.19)	69 (100%)

The difference of 7.25% was not statistically significance. Mc Nemar statistic = 1.066 .

The 90% Confidence Interval was - 0,179 < 0.0725 < 0.034 .

Table 8.2. Treatment result based on patient assessment Excluded cases with confounder event

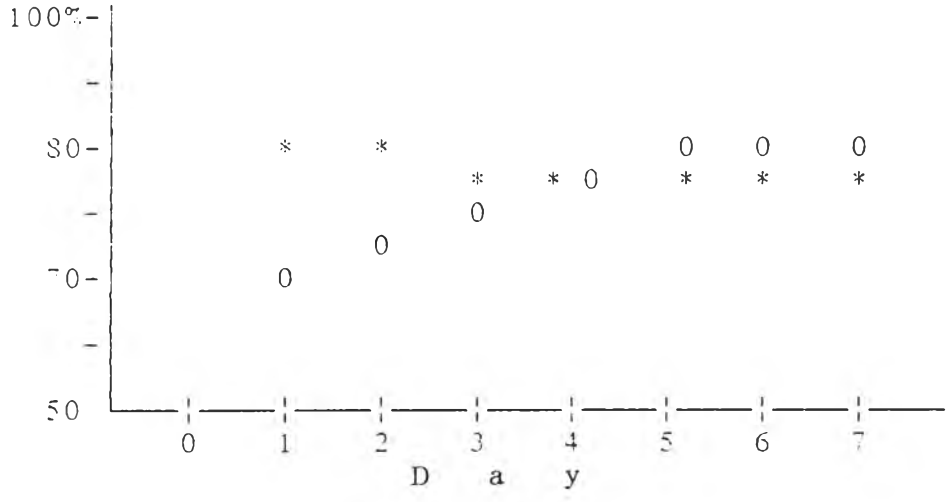
		10 mg CETIRIZINE		
		success	failure	TOTAL
8mg CHLORPHENIRAMINE	success	43 (64.1%)	5 (7.45%)	48 (71.55%)
	failure	9 (13.42%)	10 (15.03%)	19 (28.45%)
	TOTAL	52 (77.52%)	15 (22.48%)	67 (100%)

The difference of 5.97% was not statistically significant. Mc Nemar = 0.64, the p value > 0.10. The 90% Confidence Interval was - 0.1163 < - 0,0597 < 0.0469.

Since zero value was in these intervals it means that the difference between proportions may be zero. It could not be concluded, therefore, that there was a difference in the proportions of success result during the treatment of 10 mg Cetirizine and 8 mg Chlorpheniramine.

When the response of the treatment was evaluated every day, it was found that initially 10 mg Cetirizine produced good response (the symptom score was 0 or 1) more than 8 mg Chlorpheniramine. Similar result was achieved after day 3 of the treatment. While at day [illegible], 8 mg Chlorpheniramine produced good response little bit more than 10 mg Cetirizine but not more than maximal good response of Cetirizine at the first day of treatment. The percentage of the good response achievement during seven days treatment of 10 mg Cetirizine were 80%, 80%, 77%, 76%, 77%, 77%, 77%, while good response of 8 mg Chlorpheniramine were 71%, 73%, 74%, 76%, 80%, 80%, 80%. The summary is shown in figure 1.

Fig 1. Good response during 7 days treatment of 10 mg Cetirizine and 8 mg Chlorpheniramine based on 67 cases



PHYSICIAN ASSESSMENT

The result of the treatment based on the physician assessment was summarized in table 10 and table 11. The data was analyzed including patient with confounder event in the analysis and then excluding them from the analysis.

Table 9.1. Treatment result based on physician assessment. excluding patients with confounder event.

		10mg CETIRIZINE		
		success	failure	TOTAL
8mg CHLORPHENIRAMINE	success	52 (75.37%)	9 (13.05%)	61 (88.41%)
	failure	4 (5.79%)	4 (5.79%)	8 (11.60%)
	TOTAL	56 (81.16%)	13 (18.84.%)	69 (100%)

The difference of 7.25% was not statistically significance. Mc Nemar statistic was 1.06. The 90% Confidence interval was - 0.027 < 0.0725 < 0.1727.

Table 9.2. Treatment result based on physician assessment. excluding -patients with confounder event.

		10mg CETIRIZINE		
		success	failure	TOTAL
8mg CHLORPHENIRAMINE	success	52 (77.61%)	9 (13.43%)	61 (91.04%)
	failure	4 (5.97%)	2 (2.99%)	6 (8.96%)
	TOTAL	56 (83.58%)	11 (16.42%)	67 (100%)

The difference of 7.46% was not statistically significance. The Mc Nemar statistic was 1.23 . The 90% Confidence interval was - 0027 < 0.074 < 0.175. The zero value was also found in these intervals, so the difference

SUBGROUP ANALYSIS

From the overall data analysis there was no significance different of the success result between 8 mg Chlorpheniramine and 10 Cetirizine in term of relieving perennial allergic rhinitis symptoms. To see whether there was a difference of the treatment result between the severe and the moderate groups, Mantel - Haenzsel statistic was used. Data analysis was done based on the 67 patients assessment. The data can be seen in table 12.

Table 10.1. Sub-group analysis based on the patients assessment of moderate and severe symptoms group

Severe group.

	success	failure	total
10 mg CETIRIZINE	25	11	36
8 mg CHLORPHENIRAMINE	25	11	36
Total	50	22	72

Chi -square (Yates correction) = 0.07 , p value = 0.79.

Moderate group.

	success	failure	total
10 mg CETIRIZINE	27	4	31
8 mg CHLORPHENIRAMINE	23	8	31
Total	50	12	62

Chi-square (Yates correction) = 0.93, p value = 0.33

Mantel-Haenzsel statistic Chi- square = 0.03

p value = 0.85 (not significance).

EVALUATION OF ADVERSE EFFECTS

Adverse effects event during the treatment were evaluated based on the experienced reported by patients during the treatments which were recorded in the patient diary symptoms card. About dry mouth sensation, visual disturbance, urinary problem and headache were recorded qualitatively while the severity of sedation effect was measured using 7 point Stanford sleepiness scale. The data was summarized table 13.

Sedation effects was classified as positive when they have scale of 3 or more in at least two days of the 7 days treatment.

Table 11. Adverse effects event based on 67 cases.

	Cetirizine	Chlorpheniramine	Mc Nemar	90% C.I.
dry mouth	14	18	0.04	0.05 to 0.06
visual prob.	10	8	0.08	-0.09 to 0.06
headache	15	22	0.56	-0.24 to 0.23
urinary prob.	3	5	0.08	-0.06 to 0.09
sedation	22	32	3.11	0.009 to 0.289

Critical value for significance of Mc Nemar stat.= 2.70

From this table showed that there was no significance difference of anticholinergic adverse effect between 8 mg Chlorpheniramine and 10 mg Cetirizine. Sedation adverse effect of 8 mg Chlorpheniramine, however, it was significantly more than sedation effect of 10 mg Cetirizine. The layout data of sedation adverse effect was showed in table 14.

Table 12.1. Sedation effect during the treatment including patient with confounder event

		10 mg CETIRIZINE sedation (+)	sedation (-)	TOTAL
8 mg CHLORPHENIRAMINE	sedation (+)	14	19	33
	sedation (-)	9	27	36
	TOTAL	23	46	69

The difference of 14.4% of sedation adverse effect during 8 mg Chlorpheniramine treatment from 10 mg Cetirizine treatment was statistically significance. The Mc Nemar statistic was 2.89 and the 90% Confidence Interval was $0.004 < 0.144 < 0.280$.

Table 12.2.. Sedation effect during the treatment
Excluding cases with confounder event

		10 mg CETIRIZINE		
		sedation (+)	sedation (-)	TOTAL
8 mg CHLORPHENIRAMINE	sedation (+)	14	18	32
	sedation (-)	8	27	35
	TOTAL	22	45	67

From the second step of analysis it was also found a significance difference. where Mc Nemar statistic was 3.11. where the critical value of significance was 2.70. The 90% Confidence Interval was 0.009 < 0.149 < 0.289. From the two steps of analysis were found a similar result (there were significance difference). From the 90% confidence limits there were not found zero value in the intervals. So it can be concluded that there were a real difference.

COST- EFFECTIVENESS ANALYSIS

The variable of economic study is the cost. The cost of health treatment includes the health service. on patients. their family and other public sector agency. It is very difficult and complicated to calculate of the exact cost for each patient.

In this study, the patients are perennial allergic rhinitis with the age range between 16 -55 years. They are out patients since perennial allergic rhinitis which is a non fatal chronic disease.

The value of the outcome is successful result, where patients are free of symptoms or free of disturbing symptoms. During the treatment there was adverse effect of the drug, however, all patients still work or do their daily activity. Therefore it is too hard to estimate how much the lost of patients' productivity because of their sleepiness. In this study is appropriate to calculate only the direct medical cost, not including the direct non-medical cost, indirect cost and intangible cost.

According to the procedure of treatment, following are the items of cost calculated :

1. Cost of screening and diagnosis
   - E.N.T. examinations
   - Allergic skin testing
   - Liver function test
   - Renal function test
   - Cytologic nasal smear examination
2. Cost of the drug

Point of view of patient was taken into account in the analysis.

Table 13. DATA OF TOTAL COST-ITEMS

Cost factors	Treatment 1 10 mg Cetirizine (79 cases)	Treatment 2 8mg Chorphen. (72 cases)
1. a. E.N.T. Examinations	158 000.-	144 000.-
b. Allergic skin testing	1185 000.-	1080 000.-
c. Liver function test	197 500.-	180 000.-
d. Renal function test	197 500.-	180 000.-
e. Cytologic examinations	197 500.-	180 000.-
2. Drug for 7 days treatment	774 200.-	50 400.-
Total	Rp. 2709 700.-	Rp.1814 400.-

Table 14. COST-EFFECTIVENESS ANALYSIS

	treatment 1 (10 mg Cetirizine)	treatment 2 (8 mg Chlorphen.)
1. Number of cases	79	72
2. Number of success (patient assessment)	56	48
3. Effectiveness of treatment	70.88%	66.66%
4. Cost / success	Rp. 48 387.50	Rp. 37 800.-
	$ 21.03	$ 16.43

Note : The value is in Rupiah, $ 1.- = Rp 2 300.-

From the cost effectiveness analysis the data showed that 8 mg Chlorpheniramine was more cost effective.