CHAPTER 4

RESULTS

From September 2001, 3 months after starting the study, the government started the universal coverage policy (30-Baht project). This policy made the patients had to be treated with their community hospitals. The amount of patients was much decrease from our expectation. So we had to do the interim analysis. We planed to decrease the significant difference that occurred by chance. We decreased type 1 error by decreased the p-value to 0.01. The difference of success rate that we thought clinical significant was changed from 20 % to 40 %.

4.1 Characteristic of the study population

Forty lateral epicondylitis patients have been treated at Srinagarind hospital during the 2.5 year – period from July 2001 to January 2004. Twenty patients were allocated to each group. One patient in celecoxib group had drug allergy. She is 42 years-old woman who has no prior history of NSAIDs allergy. She had skinrash and pruritus after 12 days of celecoxib. She still had mild elbow pain and refused to continue the study. One patient in steroid group lost to follow up although being reminded by the mail. Therefore the total numbers in each group was nineteen.

The baseline characteristic of the patients in both groups were comparable regarding age, sex, affected dominant side, limitation of wrist motion and occupation as shown in table 1.

Table 1: Demographic and baseline data of the patients. Values are number (%) unless otherwise indicated.

Characteristics	Steroid Group (n = 19)	Celecoxib Group (n = 19)
Age (mean ± S.D.)	43.2 ± 10.2	44 ± 7.6
Median (range)	40.5 (27-66)	45 (31-61)
Sex male	7(36.8%)	8 (42. 1%)
Female	12 (63.2%)	11 (57.9%)
Affected dominant hand	15 (78.9%)	14 (73.7%)
Heavy worker occupation	7(36.8%)	9(47.4%)
Limitation of wrist motion	0 (0%)	1 (6.3%)
Duration of symptom (month) (mean ± S.D.)	3.74 ± 4.21	2.06 ± 2.23
Initial pain score (mean ± S.D.)	6.26 ± 2.02	5.31 ± 1.49
Pain pressure threshold of the affected side ($Kg./m^2$) (mean ± S.D.)	3.4 ± 1.44	3.98 ± 1.37
Grip strength of the affected side (Kg.) (mean ± S.D.)	23.79 ± 6.75	25.63 ±6.55

4.2 The success rate at one-month follow up

The success rate at one month follow up in steroid group was 89.5 % (17 in 19 patients) , but in celecoxib group was only 10.5 % (2 in 19 patients).This difference was statistical significant by Fisher's Exact test ($p < 0.001$).See table 2 for details. The different of success rate between the two groups was 0.79 and 95% confident interval was 0.49 to 0.90. This different was also statistically significant.

According to intention to treat analysis and worst scenario, we categorized one patient who dropped out in each group to failure. Sothe success rate in steroid group was 85 % (17 in 20 patients) , and in celecoxib group was 10 % (2 in 20 patients). This difference was still statistical significant by Fisher's Exact test ($p < 0.001$)

Table 2 : Number of patient with success of treatment in both groups at 1,2 and 3 months

Result	Steroid group (n=19)	Celecoxib group (n=19)	Difference	95% of difference
Success at 1 month	17(89.5%)	2 (10.5%)	0.79	0.49 to 0.90
Success at 2 months	18 (94.7%)	14 (73.7%)	0.21	-0.03 to 0.44
Success at 3 months	16 (84.2%)	13 (68.4%)	0.18	-0.11 to 0.40

4.3 Secondary outcomes

4.3.1 Visual analog scale, pain pressure threshold and grip strength in both groups at different times

Table 3 : Visual analog scale, pain pressure threshold (Kg./m^2) and grip strength (Kg.) in both groups at different times. Values are means (SD)

	Steroid group				Celecoxib group			
	0	1 M	2 M	3 M	0	1 M	2 M	3 M
VAS	6.26(2.02)	0.84 (1.89)	0.63(1.50)	1.47 (2.84)	5.31(1.49)	4.53 (2.55)	1.32(1.63)	1.74 (2.66)
Pain pressure threshold	3.4(1.44)	5.84(1.28)	5.45 (1.24)	4.79 (1.40)	3.98(1.37)	3.8 (1.56)	5.18 (1.34)	4.92 (1.15)
Grip strength	23.79(6.75)	28.71(7.36)	29.55 (8.05)	28.58 (8.48)	25.63(6.55)	25.47 (7.63)	30.63 (7.46)	28.71 (5.74)

The means and standard deviations of VAS , PPT, and grip strength were shown in table3. We compared the mean of VAS between groups of treatment at different times using repeated ANCOVA by the VAS at baseline as the covariate. After the assumptions (normality, homogeneity, compound symmetry) were met, the baseline VAS had no interaction effect with the VAS at different times. But the time and treatment had interaction with VAS as shown in table 4

Table 4: ANOVA table of VAS

ANOVA Table of VAS					
Source	df	SS	MS	F	p-value
Between subject					
VAS0	1	8.794	8.794	1.645	0.208
GRP	1	76.255	76.255	14.267	0.001
Subject within group	35	187.066	5.345		
Within Subject					
TIME	2	2.556	1.278	0.269	0.765
TIME * VAS0	2	13.984	6.992	1.473	0.236
TIME * GRP	2	77.587	38.794	8.170	0.001
Error(TIME)	70	332.367	4.748		

Then we analyzed the difference between VAS of two treatment group at different time using unpaired t-test to solve which pairs was different. The VAS at one month in steroid group was lower than celecoxib group ($p<0.001$). The mean different was -3.68, 95% CI of the different were -5.16 to -2.21

By comparing the mean VAS of steroid group at different time using repeated ANOVA. We found that the VAS at 1,2 and 3 months were not statistically difference. The same analysis was done for celecoxib group. The VAS at 1 month was more than VAS at 2 months ($p<0.001$). The mean difference was 3.21, 95% CI of the difference were 1.31 to 5.11. And the VAS at 1 month was more than VAS at 3 months ($p=0.005$). The mean difference was 2.79, 95% CI of the difference were 0.79 to 4.79.

We compared the mean of PPT between groups of treatment at different times using repeated ANCOVA by the PPT at baseline as the covariate. After the assumptions were met, the baseline PPT had interaction effect with the PPT at different times. The time and treatment had interaction with PPT as shown in table 5.

Table 5: ANOVA table of PPT

ANOVA Table of PPT					
Source	df	SS	MS	F	p-value
Between subject					
PPT_0	1	30.730	30.730	11.833	0.002
GRP	1	24.391	24.391	9.392	0.004
Subject within group	35	90.895	2.597		
Within Subject					
TIME	2	7.652	3.826	4.059	0.021
TIME * PPT_0	2	4.284	2.142	2.273	0.111
TIME * GRP	2	25.267	12.634	13.403	0.000
Error(TIME)	70	65.980	0.943		

Then we analyzed the difference between difference of PPT and PPT at baseline of two treatment groups at different time using unpaired t-test to solve which pairs was different when adjusted the baseline PPT. The PPT at one month in steroid group was higher than celecoxib group ($p<0.001$). The mean difference was 2.6, 95% CI of the different were 1.63 to 3.61.

By comparing the mean PPT of steroid group at different time using repeated ANOVA by the PPT at baseline as the covariate.. The PPT at 1 month was more than PPT at 3 months ($p<0.001$). The mean difference was 1.05, 95% CI of the difference were 0.20 to1.91. The same analysis was done for celecoxib group. The PPT at 1 month was lower than PPT at 2 months ($p=0.009$). The mean difference was –1.38, 95% CI of the difference were -2.45 to -0.32.

We compared the mean of grip strength between groups of treatment at different times using repeated ANCOVA by the grip strength at baseline as the covariate. The compound symmetry assumption was not met. The values of grip strength in different time were shown in table 3 and figure 2.

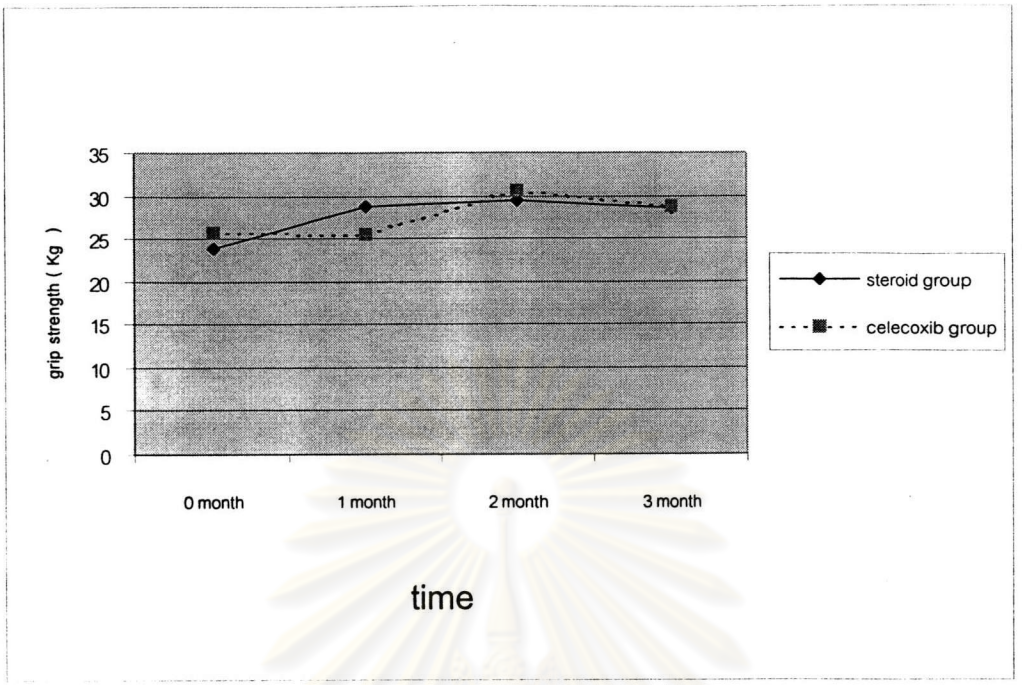

Figure. 2 Comparative grip strength between steroid group and celecoxib group

4.3.2 Recurrent rate

In 17 patients of steroid group who had successful treatment in first month follow up, 4 patients had recurrent of symptoms. Recurrent rate was 4 in 17(23.5%) Duration of pain free symptoms in steroid group was 7.29 weeks. But in 2 patients in celecoxib group who has successful treatment in first month follow up , no one had recurrent of symptoms so duration of pain free symptoms in celecoxib group was 8 weeks. This was not statistically significant difference by Log Rank test (p=0.47).

4.3.3 Adverse effects

The major adverse effects in steroid group was post injection pain ; severe pain in 6 patients, moderate in 5 patients and mild in 3 patients. But all resolved within 3 days. The local skin atrophy was observed in two patients. In the celecoxib group the GI symptoms which were abdominal pain and dyspepsia were comparable with the steroid group. There was no patient who had GI bleeding. Two patients had skin rash and pruritus, one had severe symptoms so that she withdrew from the study. The overall side effects were shown in table 6.

Table 6: Number of patients with adverse effects in both groups.

Adverse effects	Steroid Group (n = 19) (%)	Celecoxib Group (n = 20) (%)
GI bleeding	0(0)	0(0)
Abdominal pain	1(5.3)	1(5)
Dyspepsia	2(10.5)	2(10)
Nausea and vomiting	1 (5.31)	0(0)
Post injection pain: severe	6(31.6)	0(0)
Moderate	5(26.3)	0(0)
Mild	3(15.8)	0(0)
Local skin atrophy	2(10.5)	0(0)
Skin rash and pruritus	0(0)	2 (10)

4.3.4 Amount of rescue drug used in steroid group was 9.8 $\pm$ 9.7 tablets whereas in celecoxib group was 10.7 $\pm$ 11.5 tablets. There was not statistical significant difference by unpaired student t test (p=0.785). The mean difference was -0.95, 95%CI of the difference were -7.95 to 6.05 which was not statistical significant.