

# Comparison of beta blockers use



## 1. 1 Background

Beta-blockers are a medication used to treat high blood pressure and heart problems. They are used by millions of people around the world everyday. In 2004, they were the fifth most widely prescribed class of medicine. Beta-blockers are effective, life-saving medicines with more than 25 years of widespread and generally safe use. There are fourteen beta-blockers are currently available. These included Acebutolol, Atenolol, Betaxolol, Bisoprolol, Carvedilol, Esmolol, Labetalol, Metoprolol, Nadolol, Penbutolol, Pindolol, Propranolol, and Timolol.

Beta-blockers are just one class of prescription medicine used to treat high blood pressure and heart disease. Four other classes are commonly used to treat high blood pressure, for example. These include the diuretics, calcium channel blockers, ACE inhibitors, and angiotensin-receptor blockers. These four plus beta blockers are often used in combination, two or more at a time. Indeed, many people with high blood pressure will require two or more high blood pressure medicines to bring their blood pressure down to a normal and healthy range.

Although they are used primarily to treat people with high blood pressure, they are also used to treat other heart conditions. These include angina (heart or chest pain), abnormal heart rhythms, coronary artery blockages, and heart failure. They are also used, along with other treatments, to help prevent repeat heart attacks in people who have already had one, to prevent migraine headaches, and to treat performance or stage-fright anxiety.

High blood pressure is one of the most significantly and persistently under-diagnosed and under-treated medical conditions. It raises your risk of heart disease, heart attack, heart failure, stroke, dementia, vision loss, and kidney failure. In most who have high blood pressure, it is a lifelong condition. Yet studies show that only 30% of people with high blood pressure getting the medicines, care, and blood pressure control they need. Uncontrolled high blood pressure is a leading cause of death. Because it has no symptoms and often goes undetected, high blood pressure is often called the nation's leading "silent killer."

Beta-blockers work by blocking adrenaline in the heart and blood vessels. Adrenaline speeds up the heart rate, makes the heart muscle contract more strongly, and constricts arteries throughout the body. All these raise blood pressure. In blocking adrenaline, beta-blockers slow down the heart and reduce its workload. That helps to decrease blood pressure.

Choosing a beta-blocker, and its dose, depends on what people need it for. Studies show that some beta blockers are more effective and safer than others for certain conditions. People respond to the various beta-blockers differently. There are important differences in how the various beta-blockers work that will affect the use of them.

In effect, beta blockers differ in the type of beta receptors they block ( $\beta_1$ ,  $\beta_2$ , and  $\beta_{\pm}$ ) and, therefore, their effects. Non-selective beta blockers, for example, propranolol, block  $\beta_1$  and  $\beta_2$  receptors and, therefore, affect the heart, blood vessels, and air passages. Selective beta blockers, for example, metoprolol primarily block  $\beta_1$  receptors and, therefore, mostly affect the

heart and do not affect air passages. Labetalol and carvedilol block beta and alpha-1 receptors. Blocking alpha receptors adds to the blood vessel dilating effect of labetalol and carvedilol.

Beta-blockers are generally safe medicines. They have not been shown to cause any serious long-term or irreversible negative consequences, even after many years of use. But side effects are common among people taking beta-blockers. The majority of people can expect to experience at least one. These include fatigue or drowsiness, dizziness or lightheadedness, slow heartbeat, low blood pressure, difficulty breathing, numbness, tinkling or coldness of fingers, toes or skin, weight gain, mental depression, disturbing dreams, reduced libido, erectile dysfunction in men, or ability to reach orgasm in both men and women. Most side effects can be avoided or minimized by starting with a low dose and increasing it gradually. Also, some of these adverse effects go away or diminish in time, after body gets used to the drug.

Overall, the strongest evidence on beta-blockers links them to a lower risk of repeat heart attack and early death in the aftermath of a heart attack. More than 60 studies have examined this, and all have found a marked benefit for the pills. There is also compelling evidence that some beta blockers lower the risk of death in people with heart failure, preventing 3.8 deaths per 100 patients in the first year of treatment. Therefore, everyone who has had a heart attack should be taking a beta-blocker.

Below are the list of beta-blockers that use in Klinik Kesihatan Greentown:

No: 1.

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Generic Name: Atenolol

Trade Name: TENORMIN®

Dosage Form: Tablet

Strength: 100mg

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No: 2.

Generic Name: Bisoprolol

Trade Name: CONCOR®

Dosage Form: Tablet

Strength: 2. 5mg , 5mg

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No: 3.

Generic Name: Carvedilol

Trade Name: DILATREND®, CASLOT®

Dosage Form: Tablet

Strength: 6. 25mg , 25mg

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No: 4.

Generic Name: Labetalol

Trade Name: TRANDATE®

Dosage Form: Tablet

Strength: 100mg

-

No: 5.

Generic Name: Metoprolol

Trade Name: BETALOC®

Dosage Form: Tablet

Strength: 100mg

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No: 6.

Generic Name: Propranolol

Trade Name: INDERAL®

Dosage Form: Tablet

Strength: 40mg

## 1. 2 Objectives

- 1. 2. 1 To list down types of beta-blockers in Klinik Kesihatan Greentown.
- 1. 2. 2 To analyze the usage of each beta-blockers in Kinik Kesihatan Greentown.
- 1. 2. 3 To compare the most commonly used beta-blockers in Klinik Kesihatan Greentown based on the results.

## CHAPTER 2: LITERATURE REVIEW

From the past, beta blockers is widely use for the treatment of hypertension besides treatment such as stable and unstable angina, arrhythmias, bleeding esophageal varices, coronary artery disease, asymptomatic and symptomatic heart failure, hypertension migraine, and secondary prevention post-myocardial infarction (Mark Helfand, MD, et al., 2007). Although some study shows that beta-blockers are not first-line drugs in the treatment of hypertension (Wiysonge CS, et al., 2007) but when initiating a beta-blocker, it is proven to be as effective and safe as initiating an ACE-inhibitor first (Ferenc Follath, 2006).

Besides, beta blockers provide similar clinical outcomes and are associated with fewer adverse events than calcium antagonists in randomized trials of patients who have stable angina. (Paul A. Heidenreich, MD, et. al., 1999)

There is also evidence that suggest B-blockers are useful in managing angina and reducing mortality after myocardial infarction and in heart failure (H T Ong, consultant cardiologist, 2007) but beta blockers appear to be less effective when used as monotherapy in black hypertensives (Walter Flamenbaum, MD, 1985).

Additionally, beta-blockers may be considered as a first-line option in women of child-bearing potential because of concern about foetal renal maldevelopment with ACE inhibitors or angiotensin receptor blockers (British Hypertension Society, 2008). When starting beta blockers, it should be started at the lowest dose, with the dose increased every two to four weeks until the target dose or highest tolerated dose is reached because beta-blockers showed little evidence of useful antiarrhythmic action in the dosage used (J M Roland, et. al., 1979). It also should reconsider in the treatment of hypertension since doses smaller than those recommended are almost as effective and much cheaper. (A K Scott, et al., 1982) On the other side, when beta blocker treatment given as secondary prophylaxis after myocardial infarction it is highly cost effective (G Olsson, L A Levin, N Rehnqvist, 1987).

Among all the beta-blockers, atenolol had the most widely used in Klinik Kesihatan Greentown because study proven atenolol is more effective than placebo in lowering blood pressure but does not appear to reduce the rates of cardiovascular morbidity or mortality (Carlberg B., et al., 2004). One of the studies also shown that the use of atenolol (started 72 h before operation) is effective in reducing the incidence of supraventricular arrhythmias following elective coronary artery bypass operations in patients with good left ventricular function (R. K. Lamb, et al., 1988). When compare between atenolol versus nifedipine versus the combination, atenolol was slightly better than nifedipine on exercise time, but the combination was slightly better for decreasing the number of attacks (El-Tamimi, H. & Davies, G. J., 1992). Anyway, atenolol should be avoided in the early stages of pregnancy and given with caution at the later stages, as it is associated with fetal



growth retardation, which is related to duration of treatment. (Lydakakis C., et al., 1999)

Metoprolol, which shows the second higher usage in Klinik Kesehatan Greentown, is an effective drug for treatment of stable exercise-induced angina pectoris (Arnman K & Rydén L. 1993) where metoprolol also can reduce total mortality, sudden death, and death due to progressive heart failure and improved quality of life (Mark Helfand, MD, et al., 2007). There is also a study about 62 patients taking metoprolol 100 mg twice daily, nifedipine 10 mg three times daily and the combination in a randomised double blind crossover study, metoprolol was better than nifedipine; the combination was better again (Uusitalo, A, et. al, 1986).

On the other side, both carvedilol and metoprolol also showed parallel beneficial effects on symptoms, exercise, ejection fraction, and oxidative stress in heart failure (Marrick L. Kukin, MD, et. al, 1999). Treatment with metoprolol will resulted in lower all-cause mortality than treatment with a thiazide diuretic (Mark Helfand, MD, et al., 2007) but metoprolol did not benefit mortality or ischemic events in a longer-term (Mark Helfand, MD, et al., 2007). Although carvedilol and immediate release metoprolol had similar effects on quality of life, but metoprolol improved exercise capacity more (Mark Helfand, MD, et al., 2007). Yet, the chronic use of the more selective beta-1 selective blockers such as atenolol and metaprotenol has been shown in several studies to not significantly increase asthma or worsen pulmonary function (J Respir, 2003).

Among all the beta blockers, labetalol is among the physician's choice because the efficient hypotensive action, together with apparent freedom from maternal and fetal side-effects, and consequent improved perinatal mortality, suggest that it is a suitable drug for use in pregnancy complicated by hypertension (C A Michael, 1979). Besides, labetalol appears to be better able to prevent the appearance of fetal growth retardation compare to atenolol (Lardoux H, et al., 1983).

The most significant effect is when comparing side-effect liabilities, it is clear that quantitatively labetalol produces no greater burden of side-effects than drugs of the  $\beta^2$ -adrenoceptor-blocking group (B. N. C. Prichard & D. A. Richards 1982). It also may be considered relatively safer than pure non-selective beta-adrenoceptor blocking drugs in patients with airways obstruction (S H Jackson & D G Beevers 1983). Among the incidence of side-effects, was similar with atenolol, metoprolol and pindolol but was slightly less with labetalol (J J McNeil & W J Louis 1979). Of all this reason, labetalol become one of the common prescribe drug for pregnant women. For the next drug, propranolol, it should be used with care in patients with known vascular disease (P D McSorley & D J Warren 1978).

Carvedilol which is other beta blockers has a powerful antiarrhythmic effect, where a study shows after AMI, even in patients already treated with an ACE inhibitor, carvedilol suppresses atrial as well as ventricular arrhythmias in these patients (McMurray, J., et al., 2005). It also may adversely affect recovery from severe hemorrhagic shock (Taniguchi T., et al., 2009). Next, carvedilol is the only beta blocker shown to reduce mortality in post-MI

patients who are already taking an ACE inhibitor (Mark Helfand, MD, et al., 2007).

In one of the study also shown that administering carvedilol in addition to conventional therapy reduces mortality and attenuates myocardial remodelling in patients with left ventricular dysfunction following acute MI. Mortality was significantly lower with carvedilol than with metoprolol in patients with mild to severe CHF, suggesting that carvedilol may be the preferred beta-blocker (Keating GM & Jarvis B. 2003). However, patients with CHF and asthma tolerated carvedilol poorly and because of that asthma still remain a contraindication to beta-blockade (Kotlyar E, et al., 2002). For bisoprolol, neither dose of bisoprolol showed any obvious influence on reducing attack duration or severity (Mark Helfand, MD, et al., 2007).

## **CHAPTER 3: METHODOLOGY**

### **3.1 Study Design**

A case control study is conducted from 1st Mac 2009 till 8th May 2009. We will identify the usage of Beta Blocker drugs in Klinik Kesihatan Greentown. Inclusion criteria for this study are based on the date noted on the cupon. Exclusion criteria is the date for the part supply prescriptions which we will take the last date the patient comes to collect the their medication. A total of 3 months prescription (October 2008 till December 2008) will be taken to be analyzed. Comparison between all beta blockers is then done when all data has been analyzed.

### **3.2 Data Collection**

Each month of prescription is divided among us group members to evaluate and count the frequency usage of those Beta Blocker drugs. Time that given <https://assignbuster.com/comparison-of-beta-blockers-use/>

to finished the evaluation of the prescription is 1 month from the date the prescription is given. The Beta Blocker drugs that has be taken count for this study is between Metoprolol Tartrate, Atenolol, Carvedilol, Propanolol HCL, Bisoprolol Fumarate, and Labetolol HCL.

### **3. 3 Statistical Methods/Data Analysis**

Data has been analysis using Microsoft Excel which the results is shown through bar and pai chart.

### **3. 4 Ethical Consideration**

Permission to conduct this study is obtained from the chief pharmacist and our local preceptor of Hospital Raja Permaisuri Bainun and Klinik Kesihatan Greentown.

## **CHAPTER 4: RESULTS**

Graph 1 show the total usage of each type of Beta-blockers used in October 2008 at Klinik Kesihatan Greentown. From the graph, we found that atenolol is among the most frequently used Beta-blocker drug used by Klinik Kesihatan Greentown on October 2008 which is 449 patients, followed by metoprolol, 404 patients, propranolol, 20 patients, labetalol and carvedilol, 1 patient each, while no patient was prescribed with Bisoprolol.

Graph 2 shows the total usage of each type of beta-blockers in November 2008 at Klinik Kesihatan Greentown. The graph indicates that atenolol is the most highly used if compared with other Beta-blockers which have 358 patients, followed by metoprolol, 324 patients, propranolol, 35 patients, bisoprolol, 4 patients, labetalol, 2 patients and carvedilol, have 1 patient only.

Graph 3 shows the total usage of each type of Beta-blockers in December 2008. From the graph we can conclude that atenolol rated as the most widely used where there are 377 patients, followed by metoprolol, 303 patients, then propranolol, 27 patients, bisoprolol, 14 patients, labetalol, 3 patients and carvedilol, 8 patients.

Graph 4 shows the overall usage of each beta-blocker used in Klinik Kesihatan Greentown based on total amount of prescriptions prescribed on October, November and December 2008. From types of beta-blocker, we can conclude that atenolol is the most widely used which have 1184 patients compared with other beta-blocker drugs. While metoprolol is the second beta-blocker drug that commonly used which have 1034 patients, followed by propranolol, 82 patients, bisoprolol, 18 patients, carvedilol, 10 patients and labetalol, 6 patients.

Graph 5 displays the total usage of beta-blockers based from October, November and December in year 2008 at Klinik Kesihatan Greentown. From the overall, the month of October 2008 shows the highest percentage of beta-blockers used in Klinik Kesihatan Greentown which are 38% or total usage are 875, followed by December 2008 which are 31% or total usage are 732 and November 2008 are 31% or total usage are 724.

## **CHAPTER 5: DISCUSSION**

### **5.1 Atenolol**

Beta-blockers work by blocking adrenaline in the heart and blood vessels. Adrenaline speeds up the heart rate, makes the heart muscle contract more strongly, and constricts arteries throughout the body. All these raise blood

pressure. In blocking adrenaline, beta-blockers slow down the heart and reduce its workload. That helps to decrease blood pressure (Houghton T, Fremantle N, Cleland JG. 2002). Atenolol in this case is a beta blocker used not only to treat hypertension but also is the primary medication treatment for angina and after an heart attack (American Academy of Family Physician, 2000). Based on our study, at Klinik Kesehatan Greentown the most used beta blocker from October 2008 till December 2008 was atenolol. This could be due to many factors; one of it to be the effective treatment towards treating hypertension.

It is also widely use because doctors nationwide has been prescribing this drug for a long time and it is shown by patient age on the prescription studied, geriatric patients prefer sticking to atenolol than changing to other beta blockers as they safe and satisfied with the treatment of atenolol. Atenolol also has very less adverse effects compared to other beta blockers . It is also known to effectively lower blood pressure to its normal range by decreasing the heart rate. It easy to consume as the daily dosing is usually 1 tablet a day(100mg) or half a tablet a day(50mg) ( Shekelle, P. G., et al., 2003 ).

According to a study it has chosen four of the five indicated beta blockers as Best Buy drugs for people with angina, based on price. They are atenolol, metoprolol tartrate, and propranolol. Generic acebutolol is substantially more expensive than these four and no more effective. Taking a beta-blocker after a heart attack lowers the risk of a repeat attack and death by 15% to 25%. Five beta-blockers -atenolol, carvedilol , metoprolol tartrate, propranolol, and timolol- have been proven in studies to reduce deaths in people who've had

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heart attacks. The evidence is somewhat stronger for atenolol, however. On that basis, and because they are available at lower cost than carvedilol (Coreg) and timolol, atenolol is chosen as one of the best buys around. Studies of carvedilol are complicated by its use therefore atenolol is a much suitable drug to be considered alongside its market price (Houghton T, Fremantle N, Cleland JG. 2002).

## **5. 2 Metoprolol**

Metoprolol is the second commonly used in Klinik Kesihatan Greentown after atenolol. It is a first-line therapy for hypertension, angina, congestive heart failure, coronary artery disease, secondary prevention of heart attack (Bradley HA, et al., 2006). Besides that, metoprolol is also used to treat migraine headaches, panic disorder, anxiety and hyperthyroidism (Cleland JGF, et al., 2002). It is a selective beta-1-blocking agents which do not significantly affect respiratory function or antagonize salbutamol effects in patients with COPD (Fogari R, et al., 2001). Metoprolol does not significantly affect FEV1 or FVC at a dose of 200 mg daily when compared with placebo in patients with moderately severe COPD and significant reversible component (Fenster PE, et al., 1990). Metoprolol is used to decrease symptoms such as rapid heart rate, sweating and tremor which are associated with thyrotoxicosis. It is also used to prevent migraine, although it is not fully understood how metoprolol works in this area (Erdmann E, et al., 2005). At low doses, cardioselective beta blockers such as metoprolol selectively block the beta receptors found in the heart and are less likely to cause side effects. These medications may be better than nonselective beta blockers for people with obstructive lung disease, asthma, poor circulation, diabetes, and

depression (Torp-Pedersen C, et al., 2007). Based on the analysis of the COMET (Carvedilol Or Metoprolol European Trial) study, metoprolol patients had a 34% lower risk of death than placebo patients. Metoprolol reduced mortality and all-cause hospitalization by 19%. All-cause mortality plus hospitalization for heart failure went down 31%. All-cause hospitalization alone was lowered by 13%, hospitalization for all heart-related causes by 20%, and hospitalization for worsening CHF by 32% ( Woolfenden J, et al, 2003). Selective beta-1-adrenergic blockade is routinely preferred to non-selective blockade in patients with coexistent COPD and CHF to minimize the risk of inducing bronchoconstriction (Abraham T, et al, 1983). Compared to metoprolol tartrate, carvedilol reduced the total days lost. This effect was mostly due to increased longevity. Metoprolol tartrate has been shown to improve well-being after myocardial infarction (Olsson G, et al, 1993). Beneficial effects of metoprolol in idiopathic dilated cardiomyopathy, indicating that the effect of carvedilol was in addition to that of an active control (Waagstein F, Bristow MR, Swedberg K, et al, 1993).

### **5. 3 Propranolol**

From the graph, propranolol is one of the least used in Klinik Kesehatan Greentown. Propranolol is used most often for the treatment of high blood pressure, angina, and abnormal heart rhythms. It is also used to treat the symptoms of anxiety. Propranolol was the first beta-blocker available in the United States. Beta-blockers are drugs that interfere with nerve signals transmitted by the chemical norepinephrine. They reduce the force and speed of the heartbeat and prevent dilation of certain blood vessels. These actions reduce the work load on the heart, relieve the muscle tremors that



often accompany anxiety, and reduce the blood pressure in the brain to prevent migraines. ( Division of Simon and Schuster 1230, avenue of the Americans New York, NY 10020).

Because of the risk of side effects, propranolol should be used with caution in people with impaired kidney or liver function (Division of Simon and Schuster 1230, avenue of the Americans New York, NY 10020). It works by affecting the response to nerve impulses in certain parts of the body, like the heart. As a result, the heart beats slower and decreases the blood pressure. When the blood pressure is lowered, the amount of blood and oxygen is increased to the heart. Propranolol is also affects the body's sugar metabolism, it should be used with caution in people with diabetes or hypoglycemia (low blood sugar). Propranolol may mask certain clinical signs of thyroid disease and interfere with thyroid-function tests. Similarly, propranolol may interfere with tests for glaucoma ( Division of Simon and Schuster 1230, avenue of the Americans New York, NY 10020).

Propranolol is thus used for the symptomatic relief of thyrotoxicosis (hyperthyroidism). It has no direct effect on the cause, namely overproduction of thyroid hormones, which requires to be treated concurrently. This is clearly shown at Klinik Kesehatan Greentown because most of propanolol usage was to treat thyrotoxicosis. Scores on various subjective rating scales showed that propranolol had a larger mood elevating effect than atenolol. Heart rate and blood pressure were significantly reduced 24 h after atenolol medication; these effects were absent or reduced after propranolol had been given (A. A. Landauer, et al., 1978 ).

#### **5. 4 Bisoprolol**

From the graph we know that the total usage of bisoprolol is only 6 patients out of the 3 month that we have evaluated. It shows that bisoprolol is also less than one of the least used in Klinik Greentown Ipoh. This is due to the price of the medicine. As in a journal, the greatest absolute cost discrepancy for both groups was under-estimation of linezolid (\$800 and \$400) and over-estimation of clopidogrel (\$60) and bisoprolol therapy (\$62) by residents and pharmacists, respectively (Wilbur K., 2009). It shows that bisoprolol is one of the expensive Beta blocker drugs compared to the others of Beta blocker drugs. Perhaps it can't give the same effect of atenolol which the most used Beta blocker.

Based on a journal, serious adverse effects (e. g. serious bradycardia or hypotension) occurred in 3. 1% of patients switching from metoprolol tartrate to carvedilol, and 2. 3% experienced worsening heart failure. In the metoprolol to bisoprolol group, worsening heart failure occurred in about 2% of patients. Serious adverse effects also occurred in about 2% of the metoprolol to bisoprolol patients. Adverse effects were higher in patients switched to the equivalent dose rather than half the equivalent dose. (Pharmacist's Letter / Prescriber's Letter, 2009) Other than that, bisoprolol is also difficult to get the stock of drugs because it is the List A drug and have its own procedures to make the ordering from the company.

#### **5. 5 Carvedilol**

From the graph we can conclude that carvedilol have the least favorable number of usage compare to others beta blockers but then its still a preferable drug for physician to prescribe due to its beneficial effect. First of

all, carvedilol is proven to lower mortality in patients with mild to severe congestive heart failure (Keating GM, 2003), besides it also suppresses atrial as well as ventricular arrhythmias (McMurray et. al 2005) and it is the only beta blocker shown to reduce mortality in post-MI (Mark Helfand et. al, 2007). But then on the other side, when compare to metoprolol, it is lack in improved exercise capacity (Mark Helfand et. all 2007) and it may adversely affect recovery from severe hemorrhagic shock (Taniguchi T et. all 2009). Between, patients with CHF and asthma tolerated carvedilol poorly and yet, asthma still remains a contraindication to beta-blockade. All the prescribing for beta blockers in Klinik Kesihatan Greentown also mostly due to the restriction of cost where carvedilol is listed as A list drug therefore it needs a specialist to start and indirectly reduce A listed drug.

### **5. 6 Labetalol**

From the graph, we can see that labetalol shows the least usage in Klinik Kesihatan Greentown. This is because the main indication of labetalol is for use in pregnancy complicated by hypertension with apparent freedom from maternal and fetal side-effects, and consequent improved perinatal mortality (C A Michael, 1979). Beside that, labetalol should be avoided in asthmatic patient because it produced more bronchial blockade than atenolol (A D Mackay, et al., 1981) and reduced the effect of inhaled salbutamol on FEV1 (S H Jackson & D G Beevers, 1983). Furthermore, labetalol was associated with a significant less reduction or increase in cardiac output than on pure beta blockers (Lund-Johansen P, 1983) and probably induced SLE syndrome (R. C. Brown, et al., 1981). Lastly, considerable differences in dose (atenolol 138 +/- 13 mg daily; labetalol 308 +/- 34 mg daily; metoprolol 234 +/- 22 mg

daily), labetalol will required a higher dose to produce similar antihypertensive effects (J J McNeil & W J Louis, 1979) and the cost for labetalol is higher than atenolol and metoprolol.

## **CHAPTER 6: CONCLUSIONS**

Finally, we can conclude that atenolol have the highest usage among beta-blockers in Klinik Kesihatan Greentown followed by metoprolol, propranolol, bisoprolol, carvedilol and the least usage which is labetalol. Commencing from this study, we found that further studies is needed so that physician can prescribe more convincingly and led to a better life for patients.