DRUG THERAPY IN HYPERTENSION CHANGING TRENDS OVER THE LAST FIFTEEN YEARS

S F Tan

Department of Pharmacy
Singapore General Hospital
Outram Road
Singapore 0316

S F Tan, B Pharm (Hons)
Chief Pharmacist

SYNOPSIS

A study made on patterns of drug therapy for hypertension in the Singapore General Hospital showed that Singapore no longer use Reserpine, Guanethidine and Clonidine. The use of Reserpine dropped from 165,000 tablets in 1971 to 10,000 tablets in 1985. Guanethidine showed a similar pattern.

The 3 commonest drugs used were thiazide diuretics, methyldopa and B blockers. Thiazide diuretics, although showing a drop of 29.8% from 1980, was still one of the main stays in the treatment of hypertension. The use of Propranolol rose 15 times. Other B blockers like acebutolol, atenolol, metaprolol also saw increasing consumption but to a much lesser extent. Management with Methyldopa was still common. In 1985, 857,600 tablets were used.

The choice of step 2 management was between Hydrallazine and Nifedipine, the former being used in much higher quantities than the latter. Consumption of Hydrallazine rose 56.7 times in 1985 over 1971.

Nifedipine was first introduced in 1980 but its rise in use was meteoric. There was a hefty increase of 1,000 times from 1980 to 1985.

The choice of a Step 4 drug was Captopril. This was first introduced in 1982 with a modest beginning but rose significantly by 1985. Side effects and exhorbitant cost limited its use in the hospital.

INTRODUCTION

The Singapore General Hospital is a multi-disciplined complex comprising of 1,650 beds. The number of patient prescriptions dispensed in 1985 was 395,350, averaging 1,500 prescriptions daily during week days.

Expenditure for cardiac drugs and anti-hypertensive agents in the Singapore General Hospital in 1985 came to $239,276 against a drug bill of $5.2 million i.e. 4.6% of total drug expenditure. This ranked 5th on the list of top expenditure items after anti-microbials, cytotoxic drugs, infusion fluids and biologicals (table 1).

Expenditure on cardiac and anti-hypertensive drugs hovered around $100,000 between 1978-1982. Expenditure began to increase by 27.6% in 1983 by 39.8% in 1984 and by 28% in 1985 over each previous year (table 2).

TOP EXPENDITURE ITEMS ----- 1985

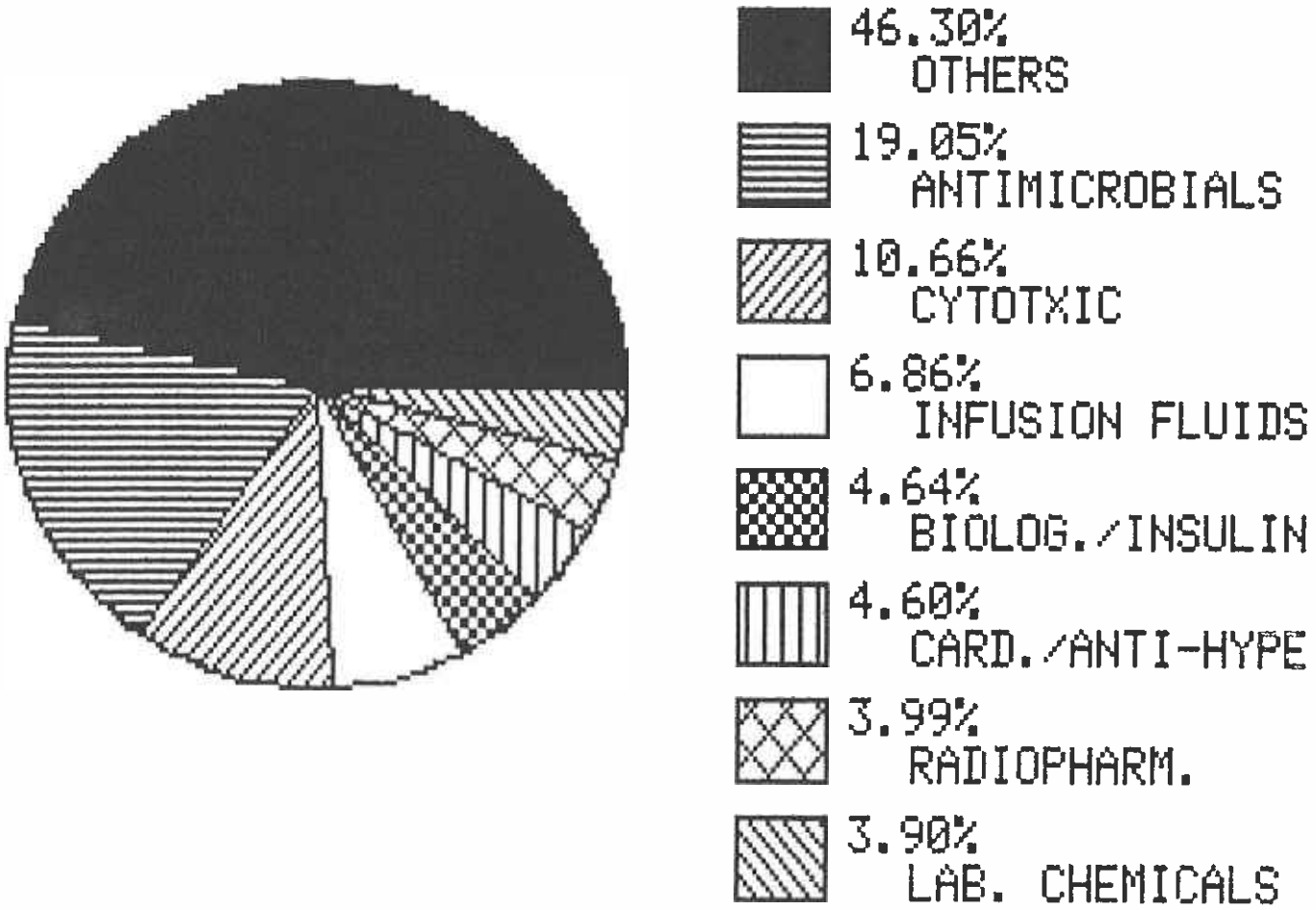


TABLE 1

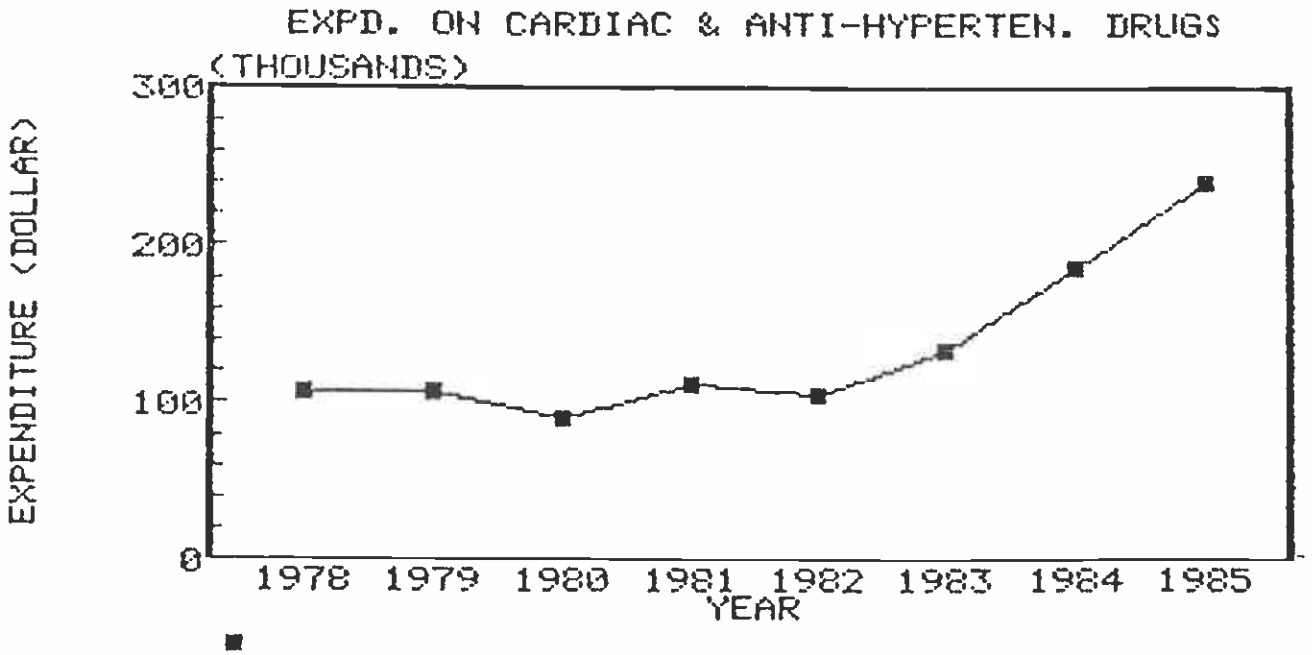


TABLE 2

STUDIES

A study was made on the usage of anti-hypertensive agents in the Singapore General Hospital. The study comprised of checking records made on the issue of drugs both to the outpatients and inpatients over a span of 15 years from 1971-1985. A second more detailed study was made on one month's prescription in the month of August from 1st-31st 1985.

RESULTS

In the treatment of hypertension over the last 15 years the study showed that the use of centrally-acting drugs fell. Reserpine dropped from 165,000 tablets in 1971 to 10,000 tablets in 1985 i.e. a 15 fold decrease (table 3). Similarly, guanethidine used in the region of 225,000 tablets in 1971 plunged to 12,500 tablets in 1985.

Use of clonidine was first started in 1973, climbed to a high of 15,600 tablets in 1975 and then dropped steeply to 1,400 tablets in 1985 (table 4).

Use of methyldopa tablets remained high, from 498,000 tablets in 1971 to 857,000 tablets in 1985. Consumption rose from 1971 to 1975, dropped in 1980 and was levelling off by 1985. The increase was only 1.7 times over a 15 year period (table 5).

The main B-blocker used was propranolol. Usage of propranolol was only 74,000 tablets in 1971 but increased 8.5 times in 1975. Usage increased by another 24.6 times in 1980 and by a further 30 times in 1985 to reach 2.2 million tablets. Usage seemed more or less levelled off by now (table 6).

Thiazide diuretics showed slight increases during the period 1971-1980. The peak consumption reached for chlorothiazide was 548,000 tablets in 1980. From 1980 consumption of the drug began to fall. In 1985, 384,000 tablets were used i.e. a drop of 29.8% in the last 5 years. On the other hand usage of frusemide tablets continued to rise. In the past its consumption was less than that of chlorothiazide. After 1980 however, consumption rose quicker to shoot past the consumption of chlorothiazide (table 7).

A meteoric rise was seen in the usage of the vasodilator hydrallazine. It began with 15,000 tablets in 1971 and up to 1975 was still not much used. From 1975 however usage shot up by leaps and bounds to reach 3 million tablets in 1985. Consumption is still rising leading to purchasing problems (table 8).

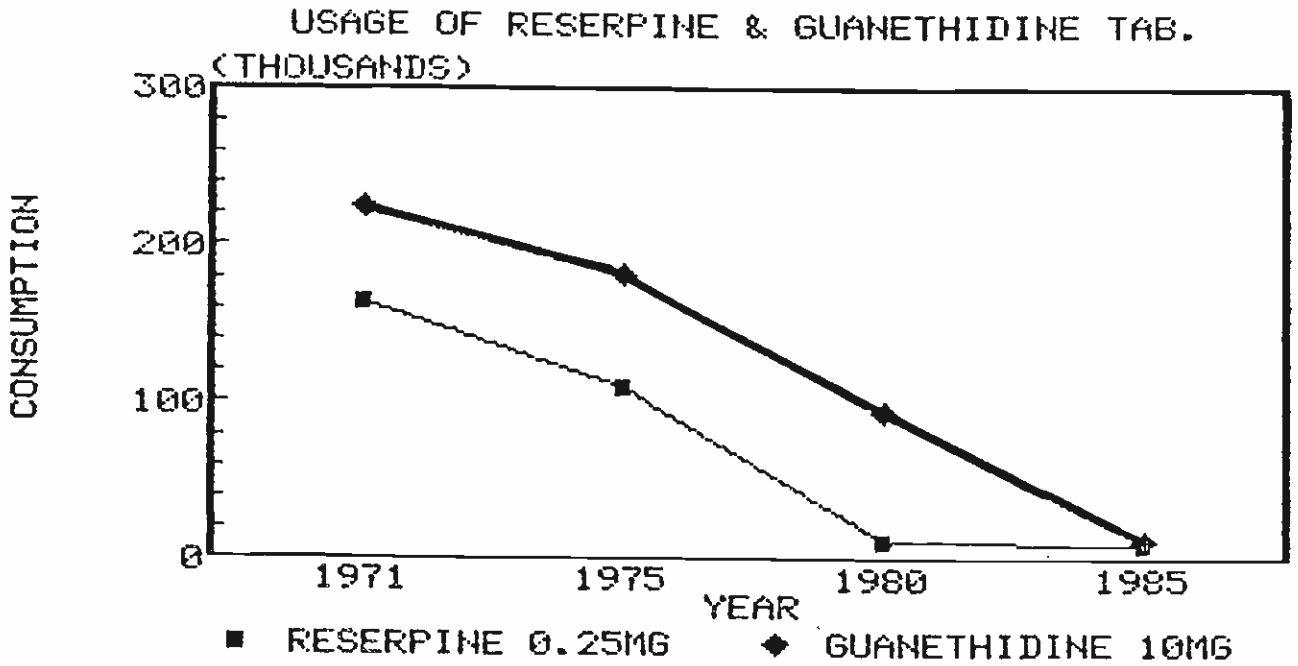
A similar upward trend was seen in the usage of another vasodilator prazosin. It was first used in the hospital in 1977 (38,500 tablets) but consumption fell drastically and only picked up again after 1980. There was a 10 fold increase in 1985 over 1980 (table 9).

1980 also saw increased uses in metoprolol and acebutolol. About twice the amount of metoprolol than acebutolol was used in 1985 (table 10). The usage of atenolol also began to show its presence felt after 1980. Approximately 5,000 tablets were used. Tenoretic was used to a lesser extent (1,000 tablets) (table 11).

Moduretic was first used in 1976. Between then and 1980, less than 1,000 tablets were prescribed. However between 1980 and 1985 there was a 3 fold increase. About 1,500 tablets were used in 1985 (table 12).

After 1980 saw the advent of calcium antagonists and an ACE inhibitor captopril. Nifedipine began with 270 tablets in 1980 and rose to 205,470 tablets in 1985, an increase of 205,200 times or 76,000% (table 13).

Captopril was first used in 1982. Usage was only 100 tablets a year until 1985 when it shot to 1,500 tablets i.e. a 15 times increase (table 14).



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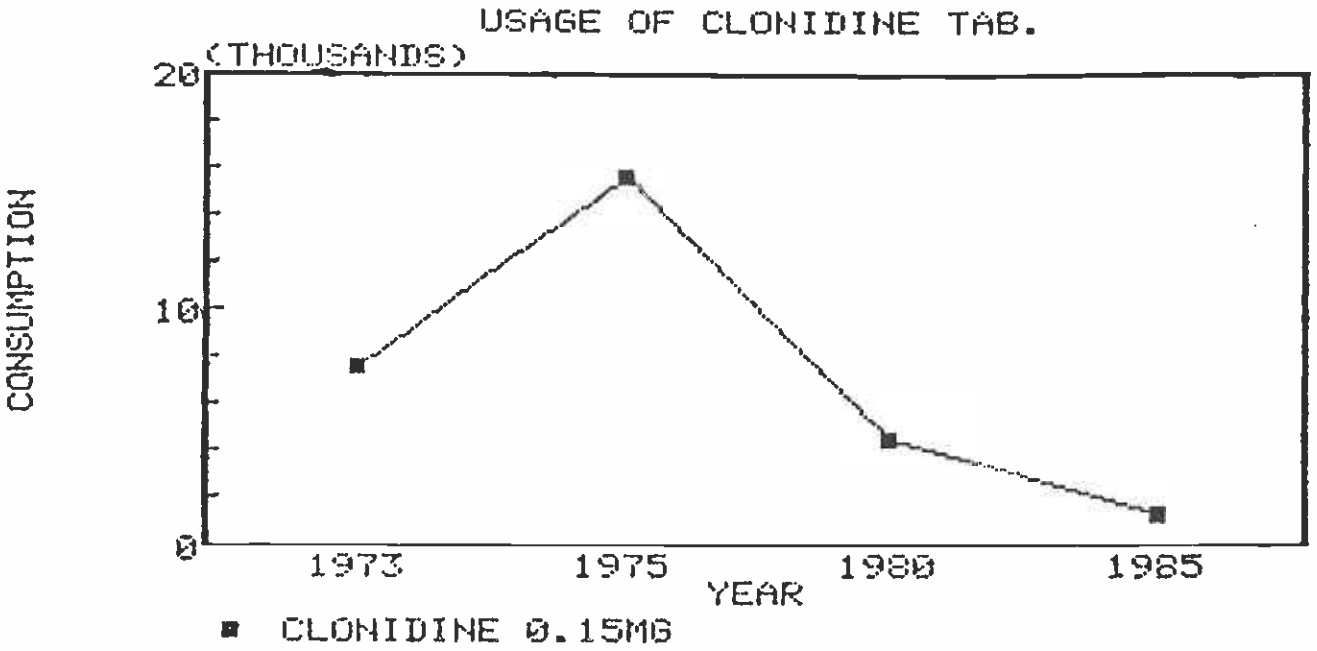

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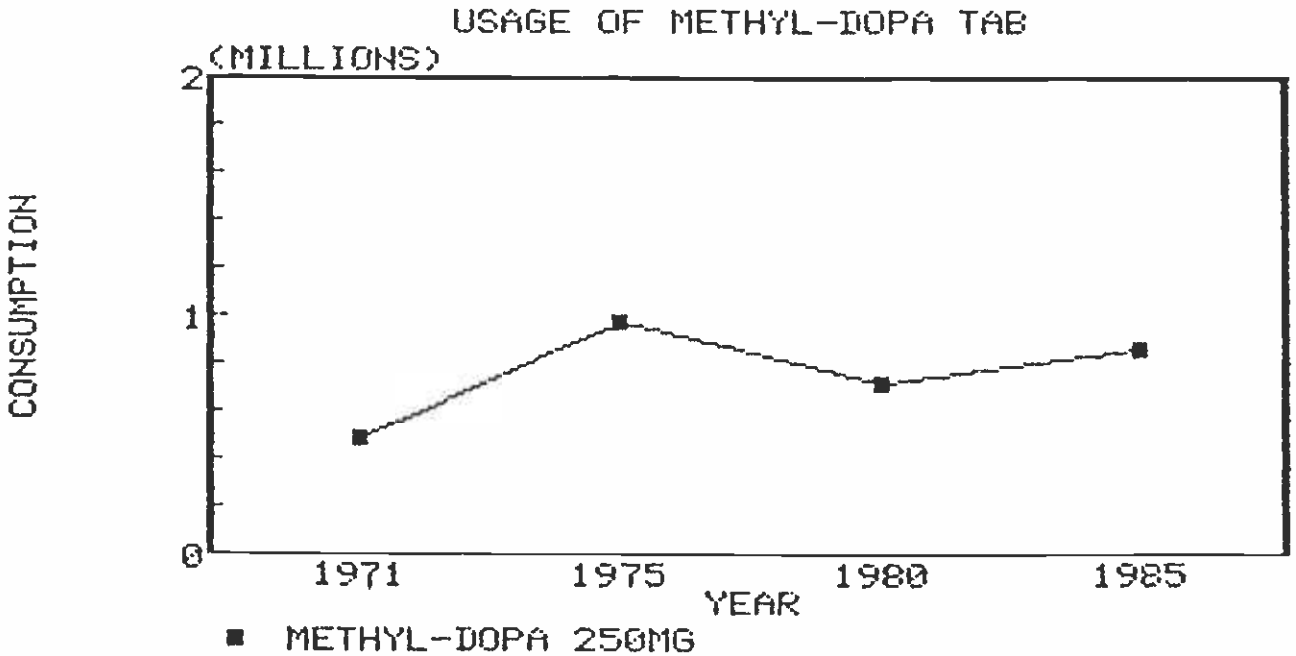

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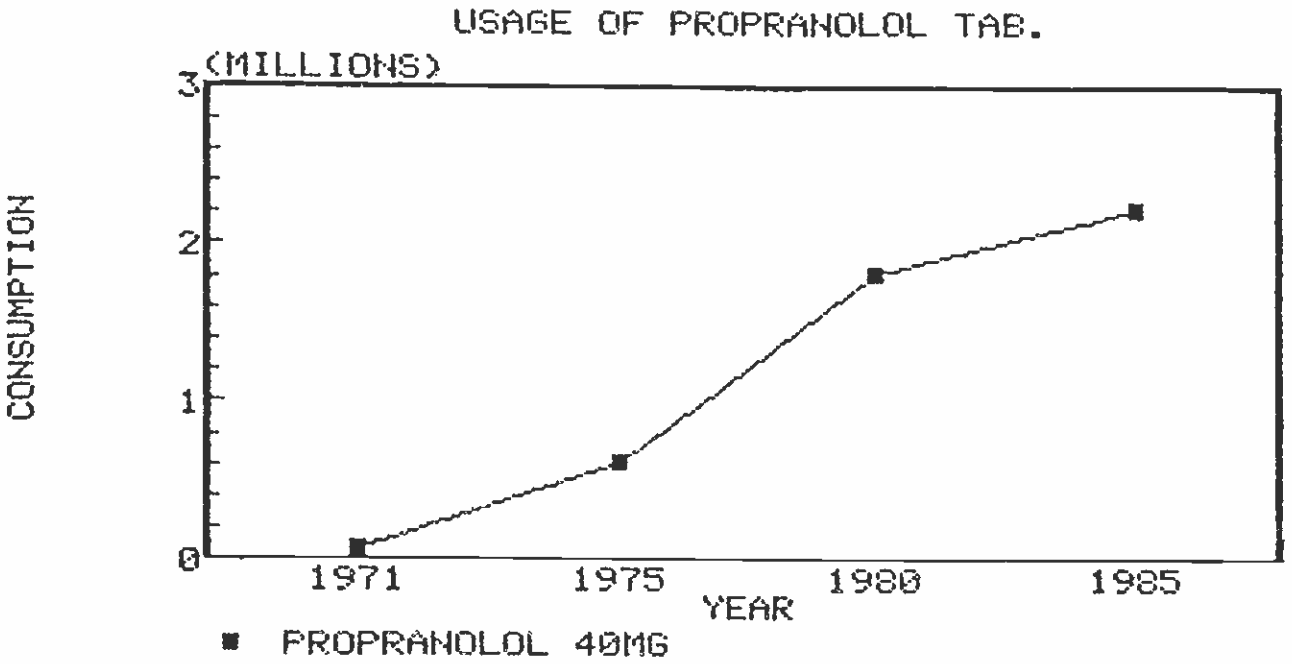

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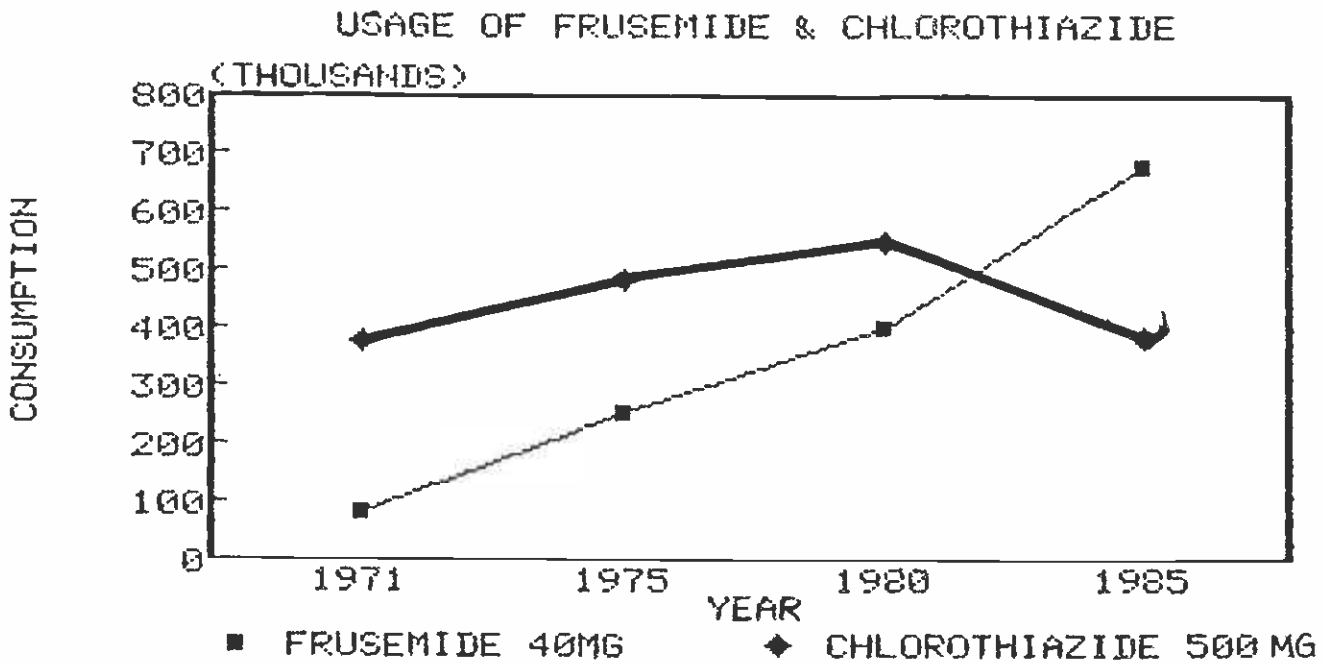

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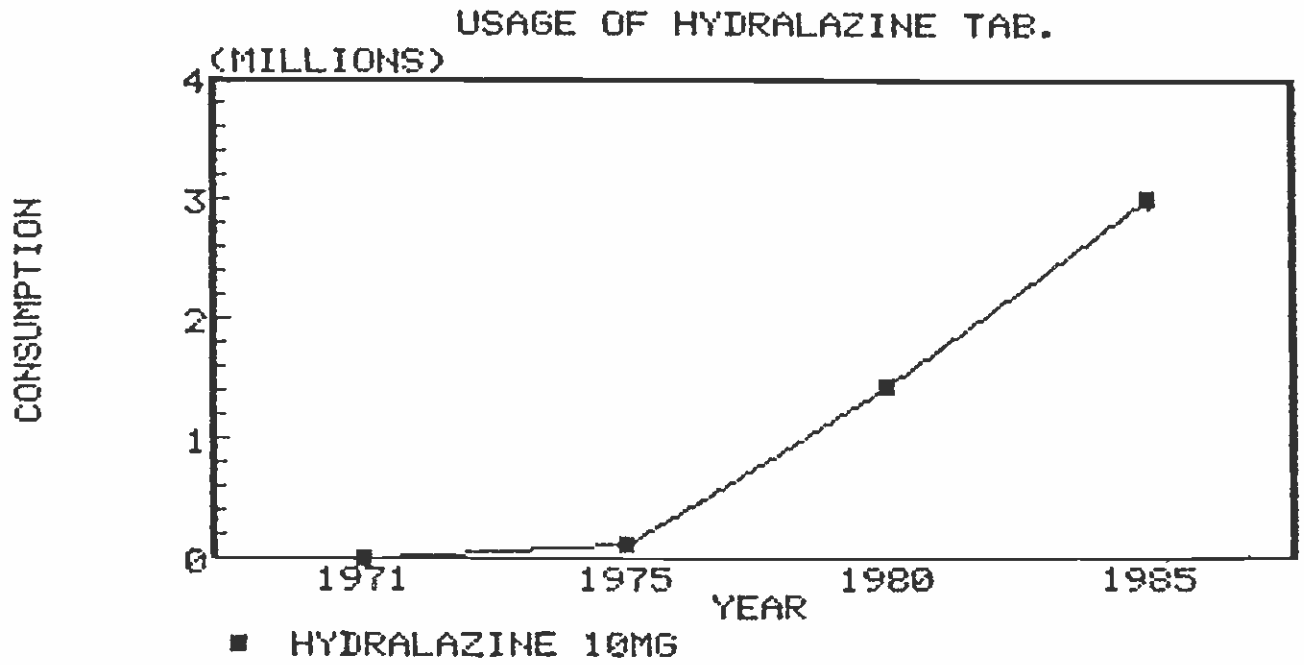

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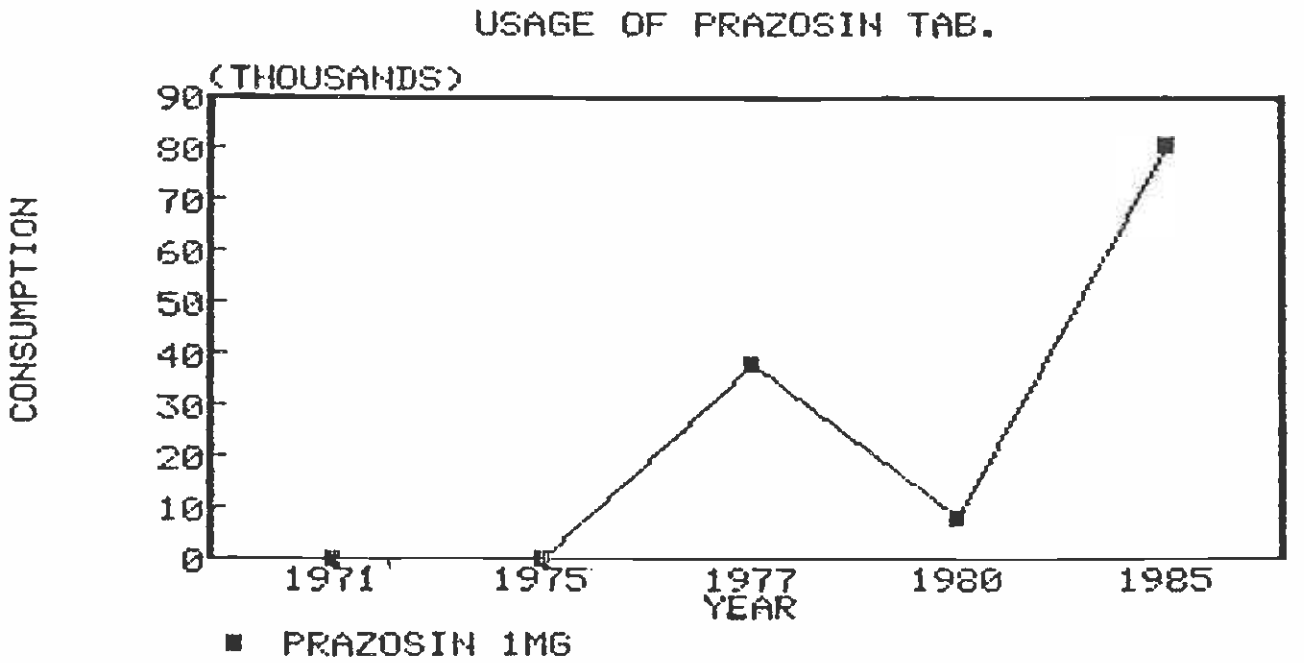

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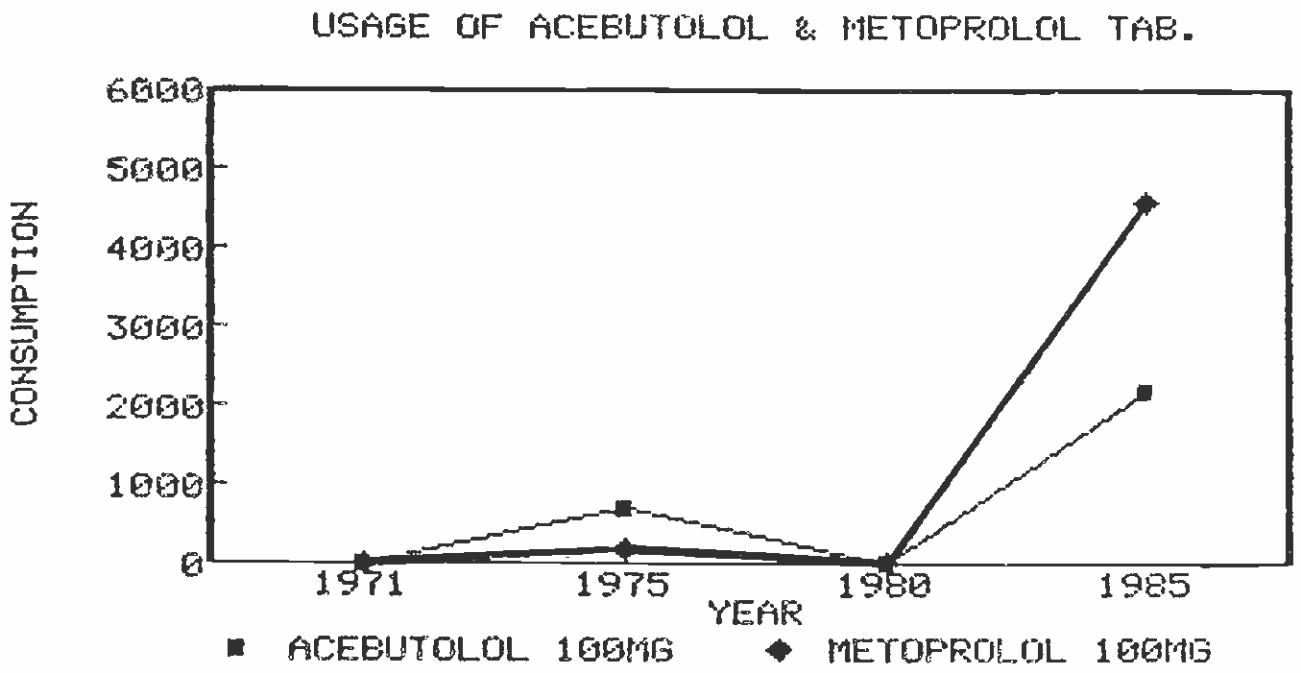

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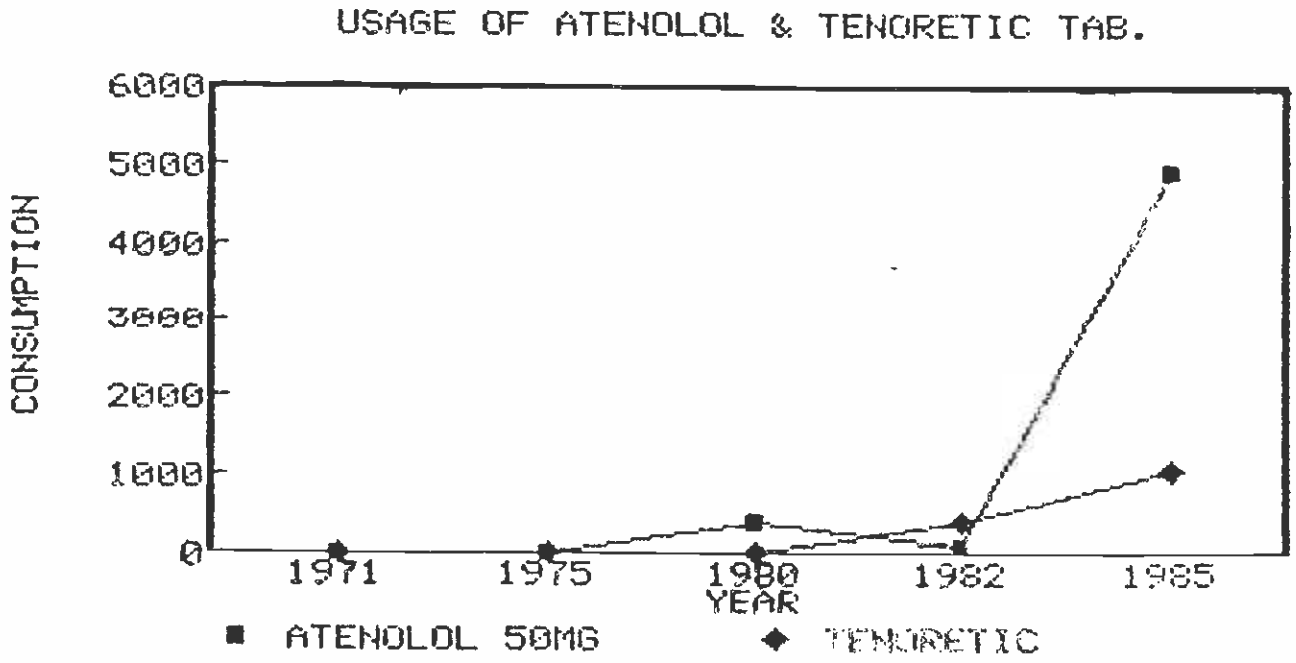

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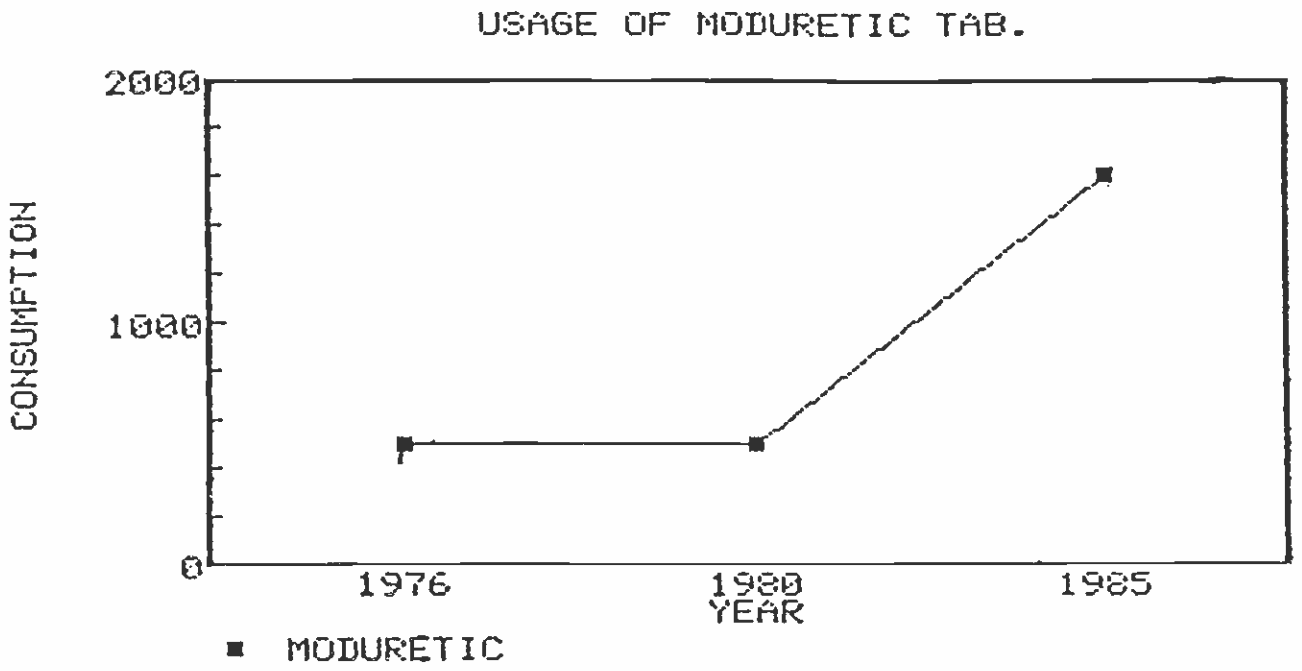

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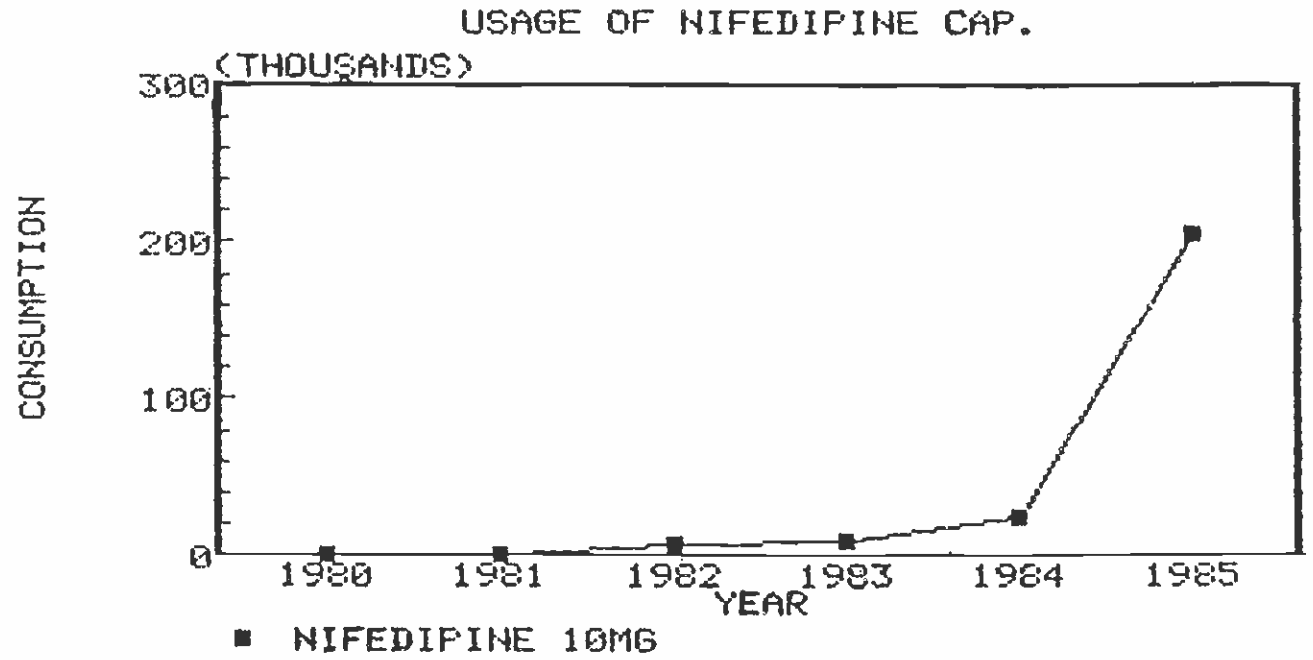

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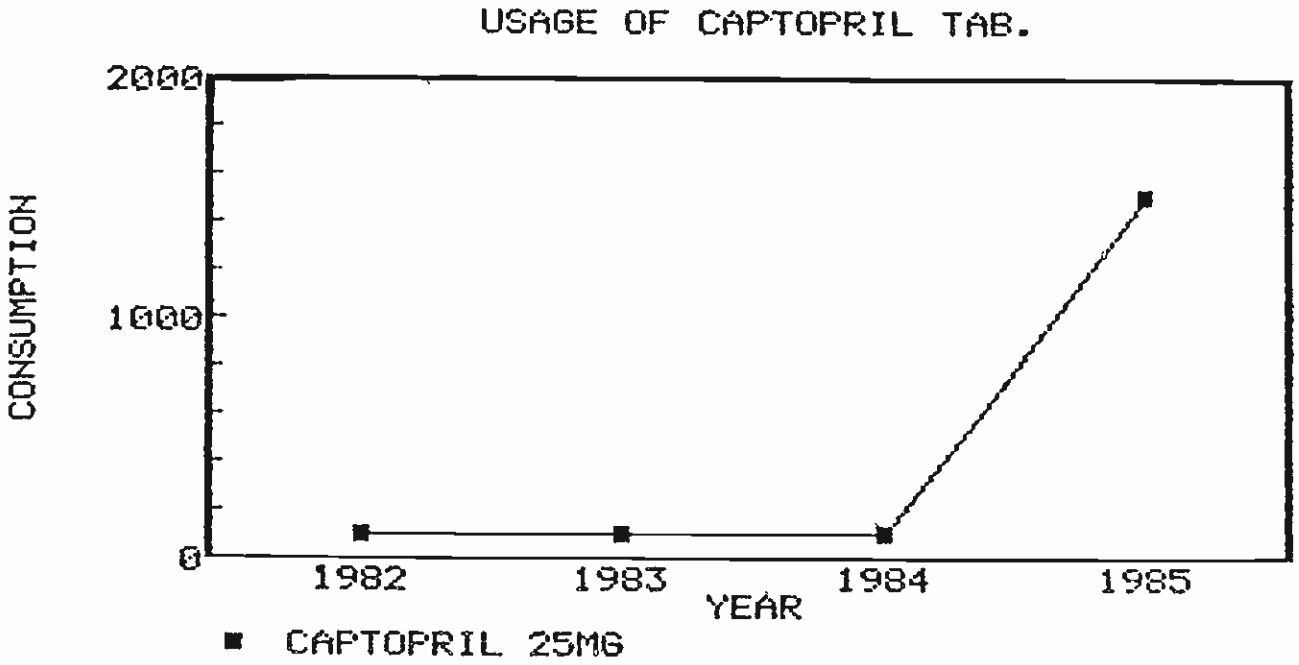

TABLE 14

DISCUSSION

From the studies it is seen that the Singapore General Hospital no longer uses reserpine and guanethidine because of suicidal tendencies with reserpine and paralytic ileus with guanethidine. This is in keeping with world trends. Use of clonidine was negligible. The drop in use was due partly to it not being included in the standard drug list, its cost and side effects of sedation, depression and hypertensive crises on wthdrawal.

The predominant centrally-acting anti-hypertensive agent used was methyldopa. Generally the use of centrally-acting anti-hypertensive agents showed a decline from 1975. Usage of methyldopa however is still high, ranking 3rd after B-blocker and diuretics. This is surprising as side effects of orthostatic hypotension and sexual impotence are quite common. It could be due to the fact that many patients are already stabilized with this drug and doctors are reluctant to change. It also has the advantage of being safe in asthmatics, heart failure and in pregnancy.

Thiazide diuretics, a first line treatment in hypertension previously is now overtaken by B-blockers. Chlorothiazide is definitely showing a decline. There is much concern of the effect of thiazide diuretics to changes in body chemistry such as blood glucose and potassium levels. More significantly it also raises low density lipoproteins (LDL) cholesterol and triglyceride levels.

Until recently, propranolol was used almost exclusively as the only B-blocker. It has reached its peaks and usage is now levelling off due perhaps to reports of disturbances in cholesterol and triglyceride levels. Use of selective B-blockers like atenolol, acebutolol, metoprolol and combination drugs like Moduretic, Secadrex Tenoretic are not in the standard drug list. This reason and their higher cost will therefore curtail widespread use, although many reports have supported their usefulness and effectiveness in the management of hypertension.

Vasodilator anti-hypertensive drugs serve useful combinations with B-blockers. It is therefore not surprising that the use of hydralazine increases in use synonymously with propranolol. Although usage of propranolol is showing a levelling off the usage of hydralazine however is still showing a steep increase.

Prazosin usage increased since its first launching in 1975 but tailed off from 1977 due to inexperienced use and reports of drastic fall of BP after the first dose. The inclusion of this drug in the standard drug list in 1984 is the explanation for its interest in use again. It has been reported that prazosin reduces cholesterol and triglyceride levels and increases high density lipoproteins (HDL). Because of this advantage, consumption of this drug is expected to continue to rise.

The use of calcium antagonists was kept to a minimum since its introduction in 1981. High cost was the controlling factor. It was made a standard drug in 1984, hence the meteoric rise of over 205,000 times in 1985. Nifedipine had become the drug of choice in combination therapy in the treatment of refractory hypertension. Renal physicians even used it as a single drug therapy when other anti-hypertensive agents had failed. Calcium antagonists are an important, promising additional armament in the treatment of severe hypertension.

Captopril, an ACE inhibitor and potent vasodilator is an exciting drug to watch in the treatment of refractory hypertension. The high cost will be its limiting factor. Earlier reports of adverse reactions of steep but not always readily predictable fall in BP were somewhat alarming and doctors were cautious.

B-blockers and vasodilator anti-hypertensive drugs will remain the mainstay management of hypertension in the next few years.

We expect further increases in the use of calcium antagonists, selective B-blockers and ACE inhibitors in the treatment of hypertension. Among the selective B-blockers, those with ISA will probably be favoured as it is believed that this property reduces the risk of plasma lipid disturbances. Combination drugs because of their limitations in tailoring individual dosages have yet to prove popular with our doctors.

CONCLUSION

Expenditure on cardiac drugs and anti-hypertensive agents were more or less steady until 1982 when newer drugs like calcium antagonists, prazosin and selective B-blockers began to be used in greater quantities. The introduction of captopril in 1984 also escalated costs partly the reason for resulting in a 128% increase in expenditure from 1982 to 1985. Expenditure is expected to increase further in the coming years.