Hypertension a physician perspective in 2015

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Hypertension remains a leading risk factor for cardiovascular morbidity and mortality. It is incidence is rising in both an ageing and increasingly obese population, but its control remains inadequate worldwide. More than a quarter of the world adult population is already hypertensive and this number is projected to increase to 29%, 1.56 billion, by 2025[1]. Three quarter of the worldwide population with hypertension will be in developing countries. Attention should be directed to possible ways to slow this occurrence through population wide manoeuvres.

Population based hypertension preventative policies are clearly different to treatment tailored to an individual. A reduction of the blood pressure of the whole population by 2 mm Hg will give more overall benefit than much larger individual reduction focussed on only a few people. Therefore, notwithstanding the importance of appropriate pharmacological treatments in many, the global aim should continue to focus on the implementation life style and dietary changes. Comprehensive modification of life style including diet, increased exercise, and decreased sodium intake does reduce blood pressure, but need substantial personal effort to sustain. Although there may be debate around the issue of salt sensitivity within individuals, this author takes the view that where the sodium content of food is clearly labelled, sodium restriction is the simplest measure to apply[2].

The last two decade has seen significant advances in hypertension management. Firstly large trial evidence has clearly shown the benefit of lower target blood pressure levels in all patients (HOT trial), furthermore the majority of trial patients achieve these targets albeit often at the expense of having to take multiple medications (table 1). Secondly, newer medications with clean side effect profiles have become available. Thirdly difficulties around the accuracy of blood pressure measurement and robust evidence of control and risk stratification have been improved by an increase in the use of ambulatory blood pressure monitors. Finally the concept of measuring overall cardiovascular risk rather than focussing on the blood pressure in isolation has assumed prominence.

The threshold at which a treatment should be started depends mostly on the accurate measuring of blood pressure and the calculated cardiovascular risk of each patient[3]. In most individuals with hypertension, blood pressure does not remain static during the

day, but is dynamic and rises and falls, in relation to time of day and activity. The early morning hours show a rise in blood pressure associated with alterations both in neurohormones and autonomic tone associated with awakening. The onset of cardiovascular events such as sudden death, myocardial infarction and stroke, follows a similar daily rhythm that maps the peaks and troughs of blood pressure with the highest incidence during the early morning hours[4]. Furthermore the increase in blood pressure variability has been independently linked with increase target organ damage and cardiovascular events. Therefore achieving consistent blood pressure control is an important goal. In this respect the advent and increasingly widespread use of validated ambulatory blood pressure monitoring has been a major advance. With this investigation hypertension can be confirmed, and prognostic information can be obtained by analysing the diurnal variation, the average pulse pressure and blood pressure variability. Furthermore ambulatory monitoring facilitates both the exclusion of white coat hypertension and also the measurement of the superadded white coat effect in hypertensives.

As part of any assessment in this area is a detailed history in relation to premature family history of cardiovascular disease, cigarette smoking history, alcohol consumption, BMI calculation, medication history e.g. NSAIDS, cold cures containing sympathomimetic amines etc. and detailed lipid and sugar profile check. Examination for evidence of hypertension related cardiovascular damage is important and it stands to reason that the result of this will depend on the thoroughness of checking. Whether all patients should have ultrasound imaging of heart and carotids is clearly contentious but this author would feel that left ventricular hypertrophy should be identified as it confirms such an ominous prognosis in the progression of cardiovascular disease. At the very least ophthalmic review, urinalysis, and electrocardiography should be performed. Further investigations in the case of suspected secondary hypertension are relevant in some patients but this assessment is beyond the scope of this article.

Once hypertension is confirmed and non pharmacological measures have been explored if possible, the issue of pharmacological therapy arises. What drug to use? Does it make any difference what drug is used if the blood pressure is lowered satisfactorily?
With the possible exception of the Antihypertensive and Lipid Lowering to Prevent Heart Attack Trial (ALLHAT) recent clinical trials have emphasized the overriding importance of lowering blood pressure rather than the specific agent chosen to begin therapy[5]. Therefore reduction of blood pressure by any agent reduces the cardiovascular morbidity and mortality. There is some evidence that different classes provided differing degrees of protection against individual cardiovascular morbidities.

Although the majority of antihypertensive drugs administered as monotherapy have similar overall efficacy, there is considerable variation in individual response, which may require a dosage increase or switch to another agent. The recognition in recent years of a down ward trend in what we consider optimal blood pressure values frequently requires combination therapy in order to achieve the goals set[6]. An alternative strategy

for monotherapy therefore to prescribe two drugs with two different mode of action, which act synergistically to reduce the blood pressure. Low dose combination therapy is attractive in that efficacy is increased with a reduction in the potential for side effects. In addition it allows administration as single tablet which simplifies the treatment regimen and improves patient compliance.

The combination of diuretic and an ACE inhibitor appears to be especially attractive; the compensatory activation of the renin-angiotensin system in response to diuresis is inhibited by the activity of the ACE inhibitor, thereby counteracting the potential consequences of the renin increase and the potassium retention produces by the ACE inhibitor will limit the potassium loss seen with the diuretic[7]. This combination of diuretic and ACE inhibitor was used in clinical trails such as the PROGRESS Trail for the secondary prevention of stroke. It is also of known benefit in treatment of obese patients with high blood pressure. Of note this is the first combination licensed as first line treatment for hypertension.

The release of the Anglo-Scandinavian Cardiac Outcome Trial (ASCOT) – Blood Pressure Lowering Arm which compared the effectiveness of newer combination of antihypertensive drugs – Amilodipine and Prenidopril – with the widely use combination of Atenolol and Bendroflumethiazide (Figure 1&2). The types of patients included in this trial were fairly typical of the sort of patients that most doctors look after most of the time. Men and women aged 40 – 79 years coming from all over the UK, Ireland and the Nordic countries. ASCOT showed that the combination of newer blood pressure lowering drug reduce the risk of stroke, myocardial infarction, all cause of mortality and other related diseases such as diabetes compared with the traditional beta-blocker/ diuretic treatment[8].

Low dose combination therapy could include other agents than those mentioned earlier such as Angiotensin Receptor Blockers and Diuretics or even combination of loop diuretic and potassium sparing diuretics. Not infrequently several agents are required to achieve target blood pressure control. Of note most agents need four to eight weeks to produce their maximum effect increasingly it is difficult to assess efficacy on the basis of single clinic blood pressure measurement. We have a very low threshold to use ambulatory monitoring to assess adequacy of control in our unit.
Many factors will affect the choice of the antihypertensive agent and these include age, sex, race and co-morbidities as diabetes, renal diseases, obesity and cardiovascular diseases including stroke and myocardial infarction. All these are well outlined in various hypertension society guidelines (ASH, ISH and BHS).

There are some data confirming specific drug class effects in relation to protection against certain cardiovascular morbidities. ACE inhibitors and ARBs are reno-protective in patient with diabetes. The combination of these two classes provides a great reduction of proteinurea but little additive effect on blood pressure[9]. Calcium Channel

Blockers have an additive protective effect for the prevention of stroke (Value Trial) while a combination of ACE inhibitors and diuretics showed proven benefit for secondary prevention of stroke (Figure 3). ACE inhibitors of proven benefit on hypertensive patients with left ventricular dysfunction or having myocardial infarction (Figure 4). Alpha blockers are a good option for hypertensive males suffering from prostate symptoms.

The patient with white coat hypertension merits some discussion. This is a relatively common situation. Patients with white coat hypertension (Figure 5) should not be treated aggressively. Although not completely a benign condition our practice is to assess aggressively for end organ damage including echocardiography and, rather than completely reassure these patients repeat ambulatory monitoring on an annual basis. Some patients with clear hypertension have a superimposed white coat effect where control is only adequately confirmed with ambulatory monitoring. Patients with isolated systolic hypertension and a wide pulse pressure (Figure 6) represent a very high risk group who often require multiple medications in combination including a long acting calcium channel blocker. Those confirmed to be nocturnal dippers should be treated with shorter acting agents as perhaps diuretics (figure 7). Where hypertensive patients have high predicted ten year cardiovascular risk scores diseases, daily aspirin therapy as well as pharmacologic intervention to achieve normal lipid values based on current guidelines is appropriate.

Average Number of Anti-Hypertensive Agents Used to Achieve Target BP

	MDRD	ABCD	HOT	UKPDS
Goal BP	<92 mmHg MAP*	<75 mmHg DBP	<80 mmHg DBP	<85 mmHg DBP
Achieved BP	93	~75	81	82
Avg # of drugs per patient	3.6	2.7	3.3	2.8

*The goal mean arterial pressure (MAP) of <92 mmHg specified in the MDRD trial corresponds to a systolic/diastolic blood pressure of approximately 125/75 mmHg.

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Table 1: Showed number of Anti-Hypertensive agents used to achieve target BP in some of the major Trials.

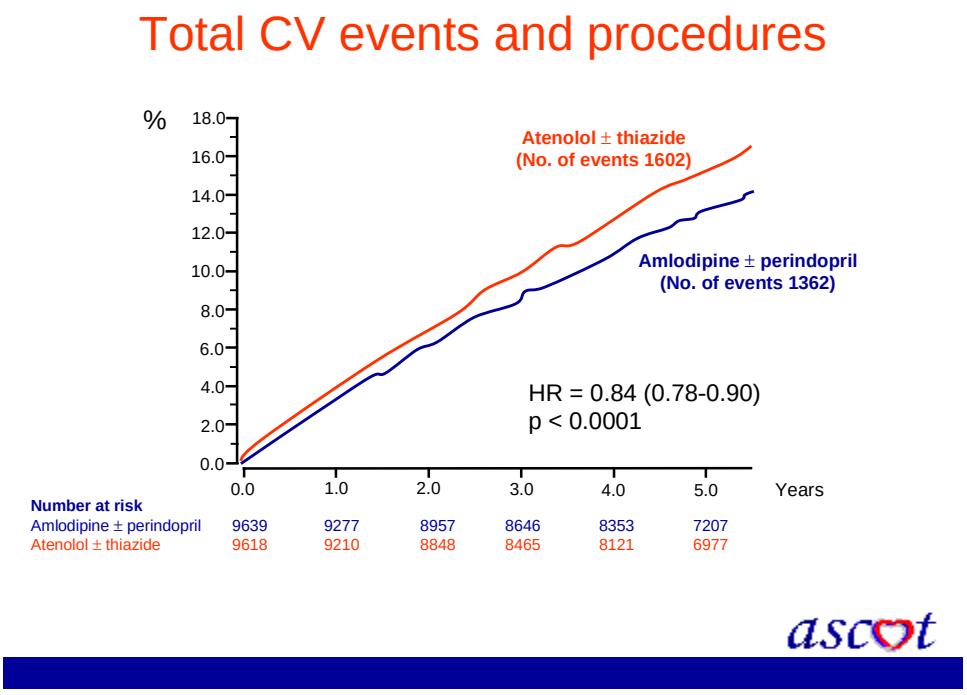

Figure 1: Total Cardiovascular events and procedure in ASCOT

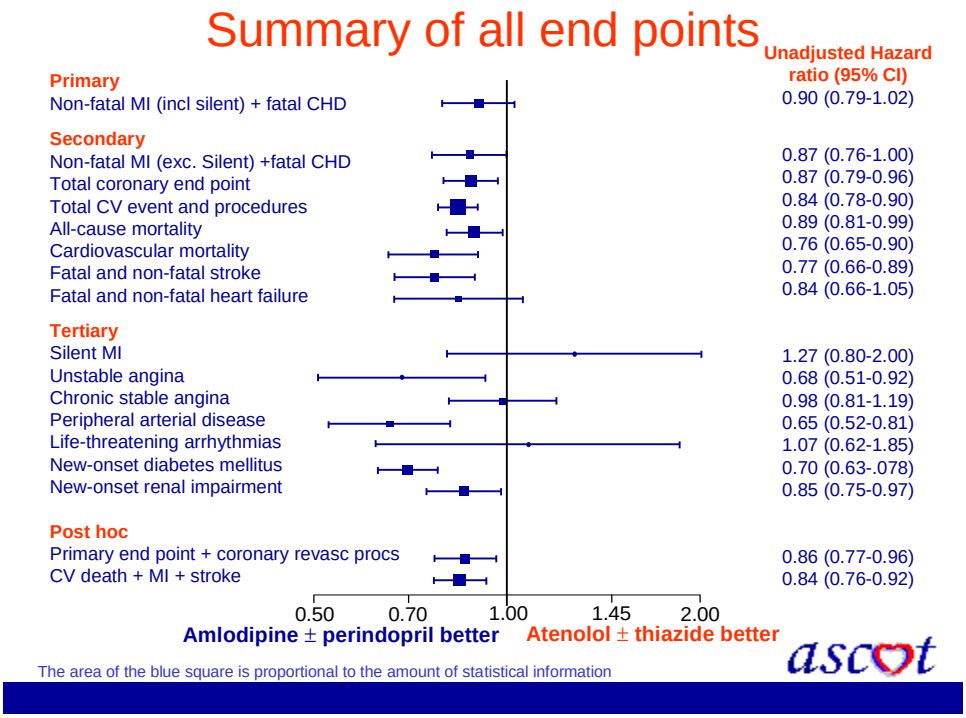

Figure 2: Summary of all end points in ASCOT

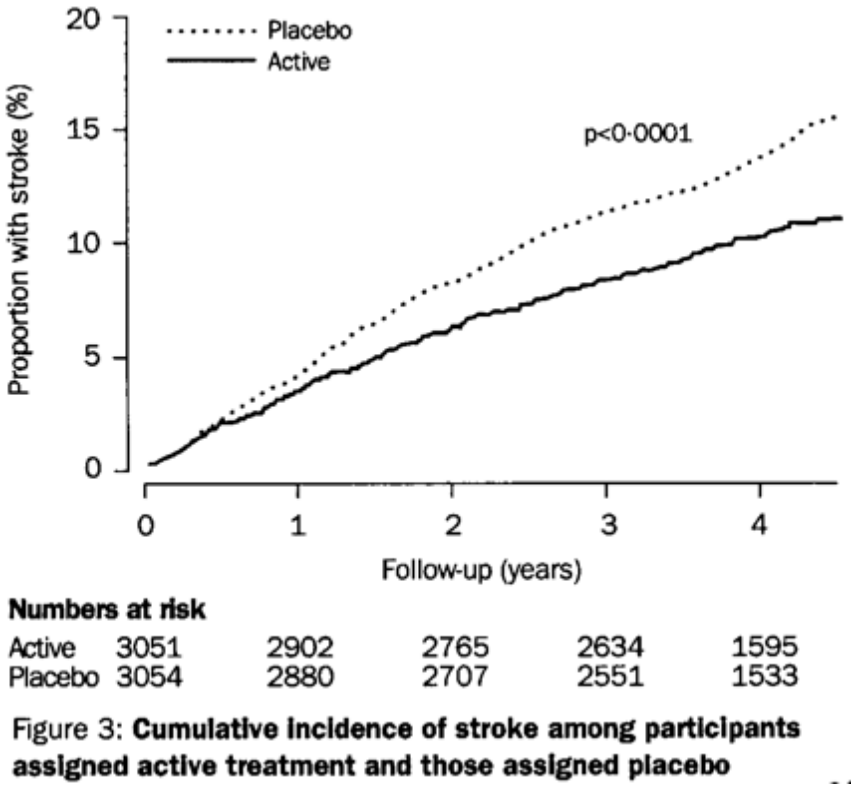

Figure 3: **Cumulative incidence of stroke among participants assigned active treatment and those assigned placebo**

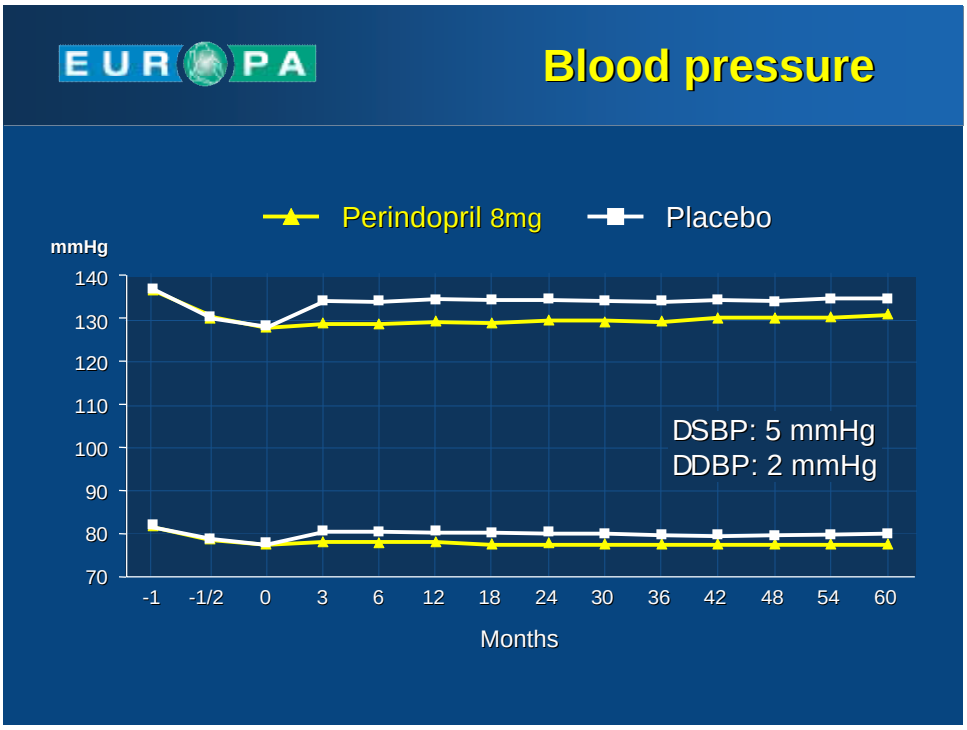

Figure 4: Effect of Prenidopril compare to placebo in the Europa Trial

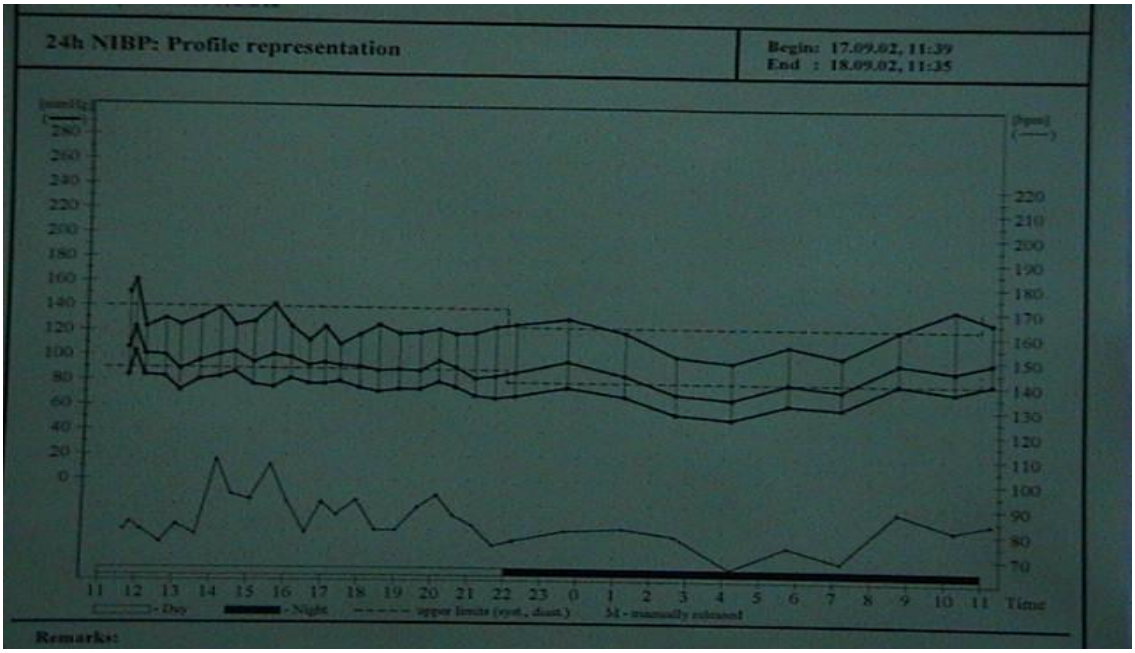

Figure 5: 24 hour profile representation in a patient with white coat hypertension.

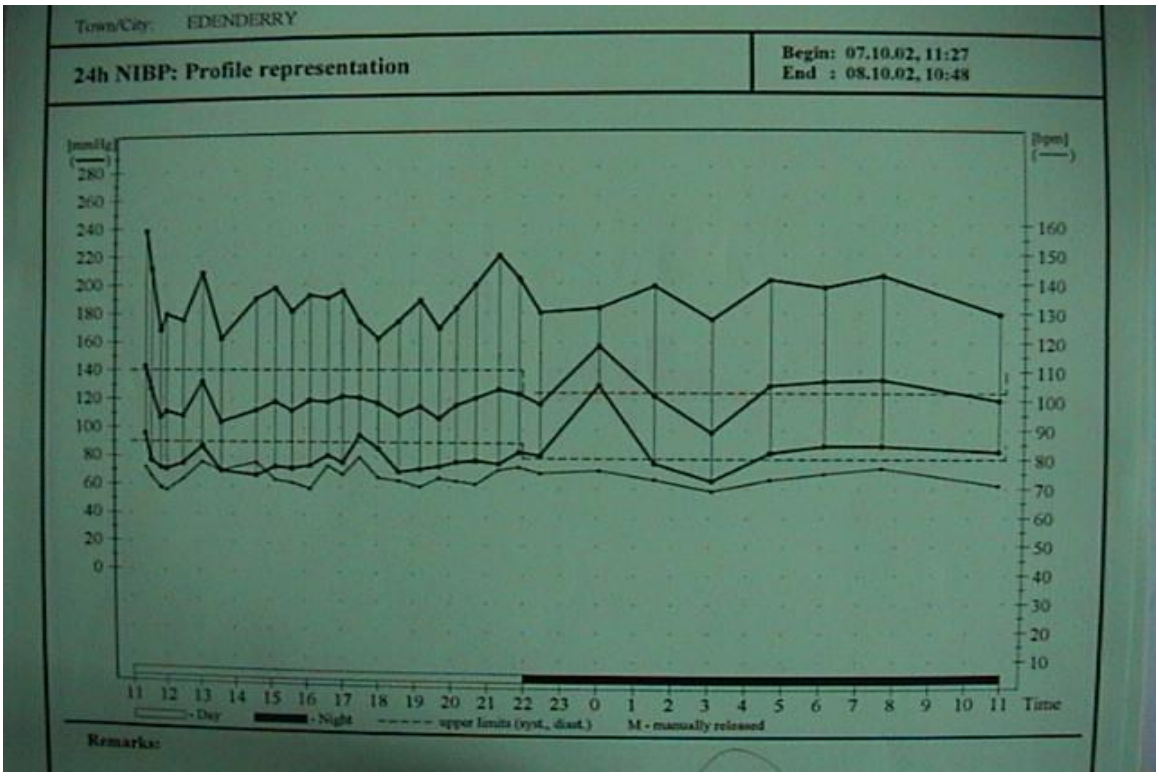

Figure 6: 24 hour profile representation in a patient with isolated systolic hypertension with super added white coat hypertension.

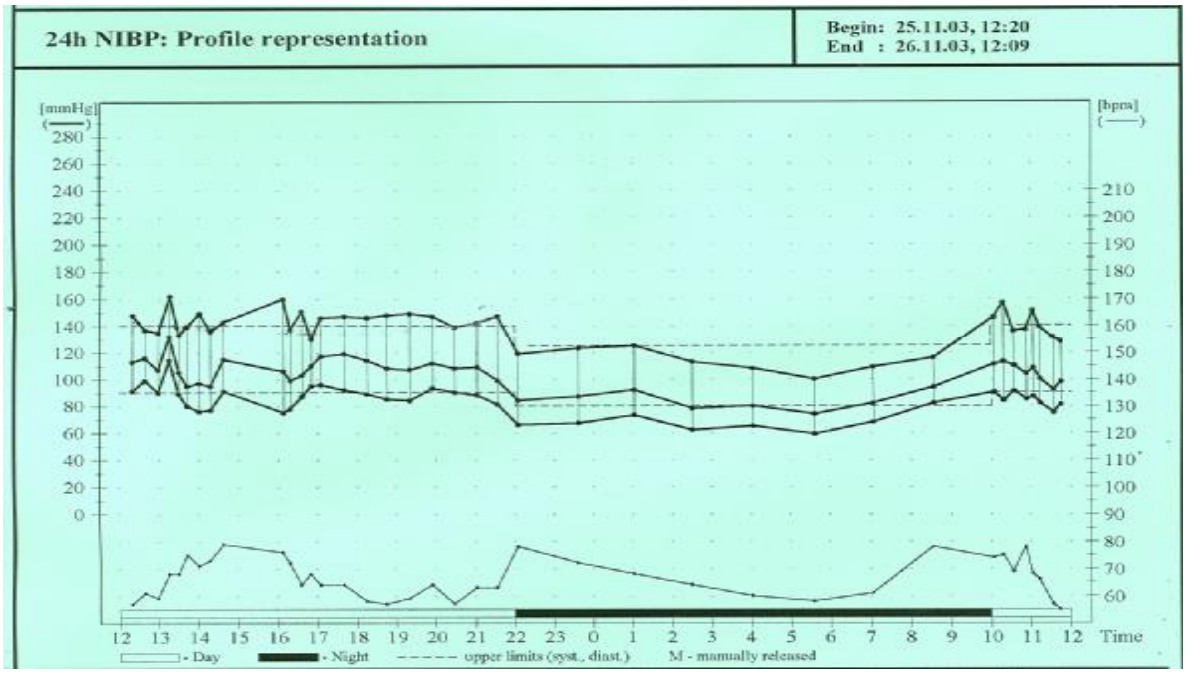

Figure 7: Showing Nocturnal dipping of blood pressure by nearly 20%

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