CHAPTER - 1

INTRODUCTION
Hypertensive disorders of pregnancy are the common medical disorders in pregnancy. It has effects both on expectant mother and foetus (Yucesoy et al., 2005; Duley, 2009; Steegers et al., 2010). The impact due to hypertensive disorders in pregnancy on maternal and neonatal mortality and morbidity is very high in India and other developing countries (Xiong et al., 2007; Moodley, 2011). The incidence of pregnancy induced hypertension in India is about 7-10% of all antenatal admission (Shruti et al., 2008). Severe forms of hypertensive disorders of pregnancy like eclampsia is a major cause of maternal mortality (Huang, 2001; Soares et al., 2009; Bell, 2010).

There are various categories of hypertensive disorders in pregnancy like pregnancy induced hypertension (gestational hypertension), preeclampsia, eclampsia and chronic hypertension. Pregnancy induced hypertension is the appearance of hypertension of more than 140/90 mm of Hg after 20 weeks of gestation. When hypertension is associated with significant proteinuria it is called preeclampsia. Preeclampsia complicated by seizures is called eclampsia. Hypertension antecedent before pregnancy is known as chronic hypertension. Chronic hypertension can be superimposed with preeclampsia or eclampsia.

Pregnancy induced hypertension is a disease of multiple organ system that is unique to pregnancy can cause maternal complications like eclampsia, HELLP syndrome, acute renal failure, cerebrovascular accidents etc. It has effect on the foetus like foetal growth restriction, oligohydramnios, foetal distress etc. During pregnancy the priority regarding hypertension is in making the correct diagnosis as to distinguish pre-existing (chronic) from pregnancy induced (gestational hypertension). Then is to distinguish blood pressure levels as either mild (140/90 to 159/109 mm of Hg) or severe (≥ 160/110 mm of Hg) rather than as stages.

The management of pregnancy induced hypertension is aimed at termination of pregnancy, but this cannot be done in all cases, as most cases are preterm or very preterm. The pregnancy can be prolonged by using antihypertensive agents by till a period where in foetal survival is good, there by maximizing the gestational age of infant and minimizing the foetal exposure to medication that may have adverse effects. The focus of treatment is the 9 months of pregnancy during which, untreated
Introduction

mild to moderate hypertension generally have maternal and foetal outcome as comparable to normotensive women. In this regard antihypertensive agents are mainly used to prevent and treat severe hypertension. There is no consensus regarding the use of antihypertensive agents in mild hypertension, but in view of unpredictable transition to severe variety, it is suggested to start antihypertensive therapy to maintain the blood pressure in mild variety itself (Podymow and August, 2008).

The antihypertensive agents have a role in controlling hypertension and thereby maternal and foetal complications can be avoided (Naden and Redman, 1985; Ferrao et al., 2006; Fabry et al., 2010). The choice of antihypertensive agents is less complex, since only a small proportion of currently available drugs have been adequately evaluated in pregnant women and many others are contraindicated.

The commonly used antihypertensive drugs in pregnancy induced hypertension are methyldopa, labetalol, other beta blockers (acebutolol, metoprolol, pindolol and propranolol) and calcium channel blockers nifedipine. The society of Obstetrician and Gynaecologists of Canada has recommended labetalol, nifedipine and hydralazine as initial antihypertensive therapy for severe hypertension (Magee et al., 2008). Most antihypertensive agents used in pregnancy are designated as “category C,” which states that human studies are lacking, animal studies are either positive for foetal risk or are lacking, and the drug should be given only if the potential benefits justify potential risk to foetus. This category cannot be interpreted as any evidence of risk and is so broad to preclude usefulness in practice. Information is thus based on clinical cases, small studies and meta-analyses (Podymow and August, 2008). A meta-analysis of 24 trials (2949 women) in which different antihypertensive drugs were compared for treatment of severe hypertension in pregnancy concluded that there is insufficient data to favour one agent over other (Duley, 2006). Also these studies were done by comparing two drugs or in same drug with two different dosage forms or different route of administration, either with respect to efficacy or maternal outcome or foetal outcome etc. There are no studies available in which more than two different class of antihypertensive drugs were compared in the same setting with respect to control of blood pressure, maternal outcome, foetal outcome and side effects in mild and severe hypertension in pregnancy.
There are few studies evaluating the efficacy of antihypertensive agents in pregnancy. The efficacy of the drug in controlling the high blood pressure is important in preventing complications both to women and foetus (Ferrao et al., 2006). At the same time the adverse effect of antihypertensive agents on mother and foetus is also important. Many a time these drugs affect the uterine contraction there by causing labour dysfunction resulting in operative deliveries. The effects of maternal antihypertensive drug use during pregnancy on foetal growth and wellbeing remains uncertain. Meta-analysis of randomized clinical trials has highlighted the possible association between antihypertensive therapy and both intrauterine growth restriction (IUGR) and small for gestational age (SGA) birth weight. Multiple drug therapy had the strongest association with these events (Ray et al., 2001). Gestational use of antihypertensive, especially beta-blockers, alpha beta blockers, or centrally acting adrenergic agents may increase the risk of SGA births (Nakhai-Pour et al., 2010).

Thus there is a need to study in detail the antihypertensive efficacy and its effect on maternal and foetal outcome. In the present study the drugs chosen were methyldopa, nifedipine and labetalol as they belong to different class based on their mode of action and are most recommended agents internationally. Hence the present study was undertaken to compare these drugs with respect to efficacy in control of blood pressure, maternal outcome, perinatal outcome, and adverse effects in mild and severe hypertension in pregnancy. Outcome of this study may be useful to the practicing obstetricians in choosing the appropriate antihypertensive agent in pregnancy as well as in developing the guidelines for diagnosis, evaluation and treatment of hypertensive disorders in pregnancy for India.