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SAFETY OF DOXAZOSIN IN EARLY PREGNANCY

Question:
What is the safety of doxazosin in early pregnancy?

Answer:
First-trimester
There are very little human data describing outcomes following exposure to the peripherally acting alpha(1)-blockers (bunazosin, doxazosin, prazosin, terazosin) in the first-trimester of pregnancy[1-4].

Doxazosin: We are not aware of any reports describing the use of doxazosin in the first-trimester of human pregnancy[1-4]. No adverse effects have been observed when doxazosin was administered in doses of 75 and 150 times the maximum recommended human doses to pregnant rats and rabbits, respectively[1]. Care must be taken when extrapolating data from animals to humans.

Other alpha(1)-blockers: One case report has associated prazosin with multiple foetal abnormalities (transverse limb defects, bilateral cleft lip and palate, renal hypoxia)[5]. This was postulated to be due to drug-associated maternal hypotension and the resultant reduced placental blood flow.

Another case report[6] described a six week pregnant woman with a diagnosis of phaeochromocytoma. She was initially on terazosin 6mg/day (assumed to be throughout most of the first six weeks of pregnancy) but was changed to prazosin 2mg three times daily (because of hospital formulary requirements) plus propranolol 40mg twice daily. She underwent surgery for phaeochromocytoma in the first trimester and received an extensive array of anaesthetic agents. She was described as having made an uneventful post operative recovery. Pregnancy was induced at 37 weeks because of signs of intrauterine growth retardation which had occurred with her previous pregnancy. She delivered a 3 kg baby by Caesarean section. No abnormalities were reported and the baby was thriving at more than one year of age at the time of publication[6].

Third trimester
There is more experience with the use of alpha(1)-blockers (primarily prazosin) in the latter stages of pregnancy where it has been used in combination with other agents for hypertension and for phaeochromocytoma[7,8].

Other agents
Phenoxybenzamine antagonises alpha(1) and alpha(2) receptors[9] and has been used in the latter stages of pregnancy for the management of phaeochromocytoma[1]. Reports in the first trimeser are lacking [1].

Other information
Doxazosin is not considered to be a first-line antihypertensive, either in the pregnant or non-pregnant state. Preliminary results of the ALLHAT study[10] lead New Zealand's Medicine Adverse

Reactions Committee (MARC) to advise that alpha-blockers should probably not be used as a first line antihypertensive, if alternative options are available (eg. beta-blockers)[11].

Conclusions:

There is insufficient data with which to assess the safety of this class of agents in the early stages of pregnancy. Therefore, we would recommend the use of more established agents such as methyldopa and beta-blockers, unless contraindications to their use exist.

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