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TREATMENT OF GLAUCOMA IN PREGNANCY

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SUMMARY: Glaucoma is a disorder of the eye characterised by loss of visual field with optic nerve damage. Usually glaucoma is associated with raised intra-ocular pressure, however it may occur when the intra-ocular pressure is within normal limits. Primary open-angle glaucoma (chronic simple glaucoma) is the most common form. The condition is asymptomatic and the patient may present with gradual loss of visual field. Primary angle-closure glaucoma (acute closed-angle glaucoma) is a medical emergency occurring where the flow of aqueous humour into the anterior chamber is blocked.

The condition is managed pharmacologically by using drugs which reduce the intraocular pressure. Treatments available include topical beta-adrenoceptor blocking drugs and prostaglandin analogues, considered the treatments of choice in the non-pregnant patient. Other medications such as miotics, sympathomimetics and carbonic anhydrase inhibitors may be required.

There are little or no data available on the use of any of these medications in pregnancy and this makes quantifying the risks to the developing fetus after maternal exposure very difficult.

Untreated or under-treated glaucoma could potentially lead to loss of vision and although risk assessment for a pregnant patient with glaucoma is difficult because of the lack of safety data, the potential benefits gained from the treatment are likely to outweigh any increase in risk. Optimum treatment for glaucoma in pregnancy must not be withheld.

Inadvertent exposure to medications used in the treatment of glaucoma would not usually be regarded as medical grounds for termination of pregnancy or any additional diagnostic tests.

If you require assistance in making a patient-specific risk assessment, please telephone UKTIS on 0844 892 0909 to discuss the case with a teratology specialist.

Please contact the service on 0844 892 0909 to inform us of any pregnancy where exposure to glaucoma medication has occurred.

Related Documents:

Use of timolol in pregnancy

Use of acetazolamide in pregnancy

Use of latanoprost in pregnancy

Use of pilocarpine in pregnancy

Human data
Often, data from observational sources or case reports, including data collected by UKTIS, may be confounded by maternal co-ingestion of a number of drugs, at varying doses, and for a range of indications. The severity of the underlying maternal condition, where relevant, is frequently unknown and information on other potential confounding variables may be incomplete. These factors should be considered when interpreting observational human pregnancy data.

Glaucoma is a disorder of the eye characterised by loss of visual field with optic nerve damage. Usually glaucoma is associated with raised intra-ocular pressure, however it may occur when the intra-ocular pressure is within normal limits. Primary open-angle glaucoma (chronic simple glaucoma) is the most common form. The condition is asymptomatic and the patient may present with gradual loss of visual field. Primary angle-closure glaucoma (acute closed-angle glaucoma) is a medical emergency occurring where the aqueous humour flow into the anterior chamber is blocked.[1]

The condition is managed pharmacologically by using drugs which reduce the intraocular pressure. Topical beta-adrenoceptor blocking drugs or prostaglandin analogues are the drugs of choice in the non-pregnant patient,[2] however there are no specific guidelines for the management of the pregnant patient. Other medications such as miotics, sympathomimetics and carbonic anhydrase inhibitors may be required. If considered clinically appropriate, then treatment with any of the medications listed above should not be withheld.

Pharmacological treatment used in the management of glaucoma

Beta-adrenoceptor blocking drugs
Topical beta-adrenoceptor blocking drugs such as timolol, betaxolol, carteolol, levobunol, and metipranol decrease the production of aqueous humour and subsequently lower the intraocular pressure.[1] Of the beta-adrenoceptor blocking drugs used in the treatment of glaucoma, timolol is the more commonly prescribed drug in the non-pregnant patient.

Studies have suggested a possible increased risk of congenital heart defects associated with systemic antihypertensive therapy in general, including beta-adrenoceptor blocking drugs,[3-5] however it is unclear whether these result from the underlying maternal condition or the use of medication.

Although systemic use of beta-adrenoceptor blocker therapy during the first and second trimesters of pregnancy has been associated with intrauterine growth retardation (IUGR) and low birth weight, no significant difference in the risk of having a low birth weight (LBW) infant was observed between mothers prescribed topical beta-adrenoceptor blocking drugs (n=189) for the treatment of glaucoma during pregnancy and a non-exposed group (n=1952) [OR 1.48; 95% CI 0.86 to 2.56], although there was a significantly higher risk for LBW infants in the mothers who had used other topical glaucoma medications (n=55) during pregnancy (OR 2.15; 95% CI 1.05 to 5.00, $p<0.05$).[8]

Systemic use of beta-adrenoceptor blocking drugs near term may result in neonatal bradycardia, hypotension and hypoglycaemia. Respiratory distress and apnoea have also been reported following *in utero* exposure. The data on the safety of discontinuing treatment 24-48 hours before delivery are conflicting.[6] When reported, neonatal symptoms due to beta blockade are usually mild and resolve within 48 hours. Fetal bradycardia has been reported following topical use.[7]

Parasympathomimetic agents (Miotics)
Parasympathomimetic agents such as pilocarpine reduce intraocular pressure by contracting the ciliary muscle which in turn tightens the trabecular meshwork and allows increased outflow of the aqueous humour.[1]

There are no published epidemiological data on the potential effects of pilocarpine in human pregnancy. Preclinical data has not demonstrated teratogenicity, however abnormal tooth development has been observed in some animal species.[9] The use of pilocarpine should be reserved for appropriate indications where no suitable alternative treatment is available. Exposure to pilocarpine at any stage of pregnancy would not usually be regarded as medical grounds for termination of pregnancy or any additional fetal monitoring.

Carbonic anhydrase inhibitors

Carbonic anhydrase inhibitors such as acetazolamide, brinzolamide and dorzolamide lower intraocular pressure by reducing the secretion of aqueous humour thereby blocking the enzyme carbonic anhydrase in the cilliary body.[1]

There are limited data on which to base an assessment of the safety of acetazolamide in human pregnancy. Preclinical studies have demonstrated teratogenic risk, however available data from human pregnancies do not suggest a significantly increased risk of congenital malformations or spontaneous abortion following exposure. As yet it is difficult to draw conclusions from the available data as they are currently too limited to exclude any increase in risk. Use of acetazolamide in late pregnancy has been associated with neonatal electrolyte imbalance and metabolic acidosis.[10, 11] Following exposure, monitoring of the neonatal electrolytes is recommended.

There are no published data regarding the use of brinzolamide or dorzolamide in pregnancy.

Prostaglandin analogues

Prostaglandin analogues such as latanoprost, bematoprost and travoprost reduce intraocular pressure by increasing the uveoscleral outflow of aqueous humour.[1] Because the prostaglandin analogues can increase uterine tone and may act as an abortifacient, there are concerns regarding their use in pregnancy. Latanoprost exposure in pregnancy has not been associated with an increased risk of congenital malformations or spontaneous abortion in 15 exposed infants.[12, 13] Low birth weight was found to be more common in latanoprost-exposed babies (n=5) than in the non-exposed controls (n=24), however no other differences were observed between groups.[13] There are no published data regarding the use of bematoprost or travoprost in pregnancy.

Alpha 2-adrenergic agonists

Alpha-2 adrenergic agonists such as brimonidine and apraclonidine reduce intraocular pressure by decreasing the production of the aqueous humour and increasing the trabecular outflow.[1]

No adverse effects were reported in a fetus exposed to topical brimonidine in the first or third trimester of pregnancy.[14] There are no data on the use of apraclonidine in human pregnancy.

Conclusions

There are no guidelines regarding the treatment of choice for glaucoma during pregnancy. There are no data suggesting that the agents commonly used in the treatment of glaucoma are associated with an increased incidence of congenital malformations or other adverse fetal effects, however the data is insufficient to state no risk. Because untreated or under-treated glaucoma could potentially lead to loss of maternal vision it is important that the pregnant woman receives optimum treatment.

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