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CASE REPORT

Paternal exposure to irbesartan coadministered with multiple antihypertensive and antidiabetic drugs: a case report of a baby born healthy

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ABSTRACT

Objective: To report the fetal outcome of a baby with paternal exposure to irbesartan and other antihypertensive and antidiabetic drugs. **Case:** The baby was conceived by *in vitro* fertilization with an egg obtained from a woman with untreated diabetes and hypertension and the sperm from a male with type-2 diabetes and hypertension. At the time of sperm donation, he was taking irbesartan 150 mg d⁻¹ in addition to amlodipine, aspirin, carvedilol, glibenclamide, hydrochlorothiazide, metformin, ramipril, and triazolam. At 38 weeks gestation, a 3,090 g female baby was delivered by cesarean section due to placenta previa. At 40 months postnatal age, the baby was 18 kg with normal growth and development. **Conclusion:** This case suggests that paternal exposure to irbesartan as part of a combination therapy with other antihypertensive drugs and antidiabetics, does not alter sperm cells or increase the risk for fetal malformations.

Key words

Angiotensin II type 1 receptor blockers; Antihypertensive agents; Paternal exposure; Sartans

RÉSUMÉ

Objectif: Rapport du cas d'un enfant après exposition paternelle à l'irbesartan et d'autres médicaments antihypertenseurs et à des antidiabétiques. **Rapport du cas:** L'enfant a été conçu par fertilisation *in vitro* à partir d'un œuf obtenu chez une femme souffrant de diabète et d'hypertension non traités, et du sperme d'un homme souffrant de diabète de type-2 et d'hypertension. Lors du don de sperme l'homme prenait 150 mg/jour d'irbesartan, ainsi que de l'amlodipine, de l'aspirine, du carvedilol, du glibenclamide, de l'hydrochlorothiazide, de la metformine, du ramipril et du triazolam. À 38 semaines de grossesse une fillette de 3,090 g est née par césarienne suite à un placenta praevia. À l'âge de 40 mois l'enfant pesait 18 kg et présentait une croissance et un développement normaux. **Conclusion:** Ce cas suggère que l'exposition paternelle à l'irbesartan associée à d'autres antihypertenseurs et à des antidiabétiques n'a aucun effet défavorable sur ses cellules spermatiques et n'augmente pas le risque des malformations fœtales.

Mots clés

Antagonistes des récepteurs de l'angiotensine II; Agents antihypertenseurs; Exposition paternelle; Sartans

RESUMEN

Objetivo: Reportar el caso de un bebé con exposición paterna a irbesartan y otros medicamentos. **Caso:** El bebé fue concebido por fertilización in vitro de un huevo proveniente de una mujer con diabetes e hipertensión sin tratamiento farmacológico, y del esperma de un sujeto con diabetes tipo 2 e hipertensión. Al momento de la donación del esperma, el papá estaba tomando irbesartan 150 mg d⁻¹ además de amlodipina, aspirina, carvedilol, glibenclamida, hydrochlorothiazida, metformin, ramipril, and triazolam. En la semana 38 de gestación nació una niña de 3,090 g por cesárea debido a placenta previa. A los 40 meses de edad postnatal, el bebé pesaba 18 kg y tenía un crecimiento y desarrollo normales. **Conclusión:** Este caso sugiere que la exposición paterna a irbesartan como parte de un tratamiento combinado con otros antihipertensivos e hipoglucemiantes, no altera los espermatozoides ni tampoco incrementa el riesgo de malformaciones fetales.

Palabras clave

Bloqueadores de los receptores de angiotensina II tipo 1; Agentes antihipertensivos; Exposición paterna; Sartanes

INTRODUCTION

A recent systematic review of the published literature on exposure to angiotensin II receptor blockers (ARBs) in pregnancy showed that, of the 65 cases currently available, approximately 40% had unfavorable outcomes [1]. However, there is no information on whether paternal exposure to ARBs may also be associated with a similar high risk of adverse pregnancy outcome in their partner. In this context, the present case report provides anecdotal but relevant information on the lack of adverse reproductive outcomes when paternal exposure to irbesartan occurs.

CASE

A 31 year-old woman (gravida 2, para 0, and therapeutic abortion 1) with untreated type-2 diabetic and untreated arterial hypertension came to the Korean Motherisk Program with her partner to receive teratogen-risk counseling. She had a history of secondary infertility with retrograde ejaculations in her partner. Therefore, she conceived by in vitro fertilization with her egg fertilized by the sperm obtained from her partner. She decided not to take any medication for treating her metabolic disorder and hypertension during pregnancy. Her partner was 29 years of age and had type-2 diabetes and hypertension. Since the age of 26, he had been taking irbesartan 150 mg d⁻¹ in addition to amlodipine besylate 5 mg d⁻¹, aspirin 100 mg d⁻¹, carvedilol 25 mg d⁻¹, glibenclamida 15 mg d⁻¹,

hydrochlorothiazide 12.5 mg d⁻¹, metformin 2,400 mg d⁻¹, ramipril 10 mg d⁻¹, and triazolam 5 mg d⁻¹.

The woman underwent a high-resolution ultrasound examination at 20 weeks of pregnancy that reported a single fetus without any evidence of major congenital malformations and normal development (estimated fetal weight: 342 g). At 38 weeks gestation, a 3,090 g female baby was delivered by cesarean section due to placenta previa. At 40 months postnatal age, the baby weighed 18 kg and a detailed pediatric examination found her healthy, with normal growth and proper development of all milestones.

DISCUSSION

Paternal exposure to irbesartan may be of relevant concern especially when ARB exposure in pregnant women has been related to a rate of adverse fetal outcomes in more than 40% of cases [1]. This is a case of a baby born by in vitro fertilization with an egg obtained from a type-II diabetic woman and the sperm of a male chronically exposed to irbesartan and other multiple medications as part of his antihypertensive and antidiabetic treatment.

A study in insulin-dependent and non-insulin-dependent diabetic men either with or without neuropathy found sperm motility and semen volume to be approximately 30% and 60% less, respectively [2]; however, sperm morphology and quality of sperm motility remained unaffected. Of the treatment received by the male parent, angiotensin converting enzyme lisinopril has shown to improve sperm count and motility in both experimental animal models [3] and humans [4]. In contrast, amlodipine and aspirin may exhibit deleterious effects on the reproductive function of males [5] [6].

In addition to the paternal morbidities and multiple drug therapy, the mother had untreated hypertension. Fetal growth is regulated by complex mechanism in which hormonal and vascular changes simultaneously play a critical role [7] [8] [9] [10]. Hypertension may adversely alter the placental blood flow subsequently negatively affecting the normal fetal growth and development.

Although anecdotal, this case suggests that paternal exposure to irbesartan as part of combination therapy with other antihypertensive drugs and antidiabetics, does not appear to alter sperm cells or increases the baseline risk for fetal malformations.

AUTHORS' PARTICIPATION

SC H, JY H, JS C, and HK A identified the case, provided prenatal teratogen-risk counseling and medical and obstetric follow-up. JY H, EY V-A & AA N-O conceived the idea to report the case, drafted the manuscript, discussed the findings, and researched the literature.

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None to declare.

CONFLICT OF INTERESTS/DISCLAIMERS

Y H, EY V-A & AA N-O are members of the Editorial Board of the journal.

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