Valsartan exposure in pregnancy with resultant anhydramnios and chronic kidney disease in a late preterm infant

Sarah Petch,[1] Emily O'Connor,[1] Ailbhe McGrath ,[2,3] Sean Daly[4]

[1]Obstetrics and Gynaecology, Coombe Women and Infants University Hospital, Dublin, Ireland
[2]Molecular, Genetic and Population Health Science, The University of Edinburgh Edinburgh Medical School, Edinburgh, UK
[3]General Paediatrics, Children's Health Ireland at Crumlin, Dublin, Ireland
[4]Maternal Fetal Medicine, Coombe Women and Infants University Hospital, Dublin, Ireland

Correspondence to
Dr Ailbhe McGrath;
ailbhemcgrath@gmail.com

Accepted 7 April 2021

To cite: Petch S, O'Connor E, McGrath A, *et al*. *BMJ Case Rep* 2021;**14**:e240810. doi:10.1136/bcr-2020-240810

SUMMARY

In utero exposure to angiotensin II receptor blockers (ARBs) has fetotoxic effects including renal failure, oligohydramnios and lung hypoplasia. We present the case of a 24-year-old woman who presented to the maternity services in the 34th week of her first pregnancy. She was taking valsartan for hypertension. Ultrasound showed a structurally normal fetus with anhydramnios. The patient was admitted and valsartan was discontinued. She had spontaneous preterm delivery at 35 weeks' gestation of a baby girl. The baby's urine output was minimal in the first week of life and she was transferred to a paediatric hospital for specialist nephrology input. At 6 months of age, she requires ongoing nephrology follow-up and she remains on treatment for hypertension and anaemia. This case demonstrates the serious adverse effects resulting from ARB exposure in utero, and highlights the importance of avoiding fetotoxic medications in women of childbearing age.

BACKGROUND

Hypertension is the most prevalent diagnosis among young women of childbearing age.[1] The prevalence is about 8%, and approximately 4% of women of childbearing age take antihypertensive pharmacological therapy.[2] The possible teratogenic and fetotoxic effects of antihypertensive medications should be considered when initiating treatment of high blood pressure in young women.

ACE inhibitors and angiotensin II receptor blockers (ARBs) are frequently used in women worldwide to control hypertension, cardiac failure and diabetic renal disease.[1] ARBs, such as candesartan, losartan and valsartan, are competitive antagonists of the angiotensin II receptor which effectively block the actions of angiotensin II.[3] Angiotensin causes vasoconstriction and stimulates the release of aldosterone leading to an increase in systemic blood pressure.

The potentially adverse effects of in utero exposure to ACE inhibitors and ARBs are well documented, including fetal and postnatal renal failure, oligohydramnios, lung hypoplasia, limb contractures and fetal skull bone hypoplasia.[4] These adverse effects seem to be particularly pronounced if exposure occurs in the second or third trimester and may be as a result of fetal hypoperfusion. Consequently, they are thought to be fetotoxic rather than teratogenic.[4] Studies on the teratogenic effects of ARBs have shown conflicting results, but first trimester exposure to ARBs does not appear to increase the likelihood of major congenital fetal malformations adding to the belief that the adverse effects are fetotoxic.[5] However, due to the severity of the fetotoxic effects of ARBs late in pregnancy, they should be avoided where possible and alternative antihypertensive medications should be considered in women of childbearing age.[4]

CASE PRESENTATION

We present the case of a 24-year-old woman who presented as a late booker to a tertiary referral maternity service for her booking visit in the 34th week of her first pregnancy. The gestational age was calculated to be 34+2 weeks' gestation based on her last menstrual period date and obstetric ultrasound biometry findings. She had a history of anxiety, depression and essential hypertension, which had been diagnosed by her general practitioner (GP) at the age of 20 when she presented with a history of recurrent headaches. At that time, she was started on 'Exforge 5 mg/80 mg', a combined antihypertensive tablet containing amlodipine 5 mg and valsartan 80 mg. She was also taking fluoxetine 60 mg for depression.

When she presented to the maternity hospital, it was noted that she had been taking the antihypertensive containing valsartan prior to conception and throughout her pregnancy. Her blood pressure at presentation was 110/70 mm Hg. She had no symptoms or clinical signs of pre-eclampsia. An ultrasound revealed anhydramnios with normal anatomy. She reported no history of spontaneous rupture of membranes and there was no evidence of membrane rupture on speculum examination, and the Amnisure ROM test was negative.

INVESTIGATIONS

1. Obstetric ultrasound scan at 34+2 weeks' gestation demonstrated a cephalic fetus with an estimated fetal weight of 2508 g, which was the 58th centile (Hadlock formula 1982). There was anhydramnios, with a single pool of amniotic fluid visualised, measuring less than 1 cm. The fetal bladder was not seen but normal kidneys were identified bilaterally. The fetus appeared otherwise structurally normal.
2. Cardiotocography on admission was normal.
3. Urine protein-creatinine ratio did not demonstrate proteinuria.
4. Blood tests demonstrated normal haemoglobin, platelets, urate, liver and renal function.

5. The Amnisure ROM test was negative.

TREATMENT

The woman was admitted to the maternity unit for further monitoring and investigation. Valsartan was stopped and labetalol 200 mg two times per day was started, which maintained her blood pressure below 140/90 mm Hg. A follow-up ultrasound with a maternal fetal medicine specialist confirmed the initial scan findings. She was planned for induction of labour at 37 weeks' gestation.

OUTCOME AND FOLLOW-UP

Maternal outcome

At 35+1 weeks' gestation, the woman went into spontaneous labour and delivered a baby girl weighing 2160 g via spontaneous vaginal delivery with meconium stained liquor. The woman had an uncomplicated postnatal course and was discharged home 3 days following delivery. She remained normotensive postnatally and all antihypertensive medications have been discontinued. She continues to take fluoxetine, at a reduced dose of 20 mg, for depression and esomeprazole 40 mg for gastro-oesophageal reflux.

Baby's outcome

Apgar scores were 6 at 1 min, 8 at 5 min and 9 at 10 min. She was intubated and ventilated at 16 min due to increasing FiO_2 requirement on continuous positive airway pressure (CPAP). One dose of endotracheal surfactant was administered.

She remained ventilated for 24 hours, weaned to CPAP and was breathing in air by day of life (DOL) 2. A small right-sided pneumothorax was noted and managed conservatively. She received benzylpenicillin and gentamicin as per hospital protocol due to preterm delivery. Blood culture was negative at 36 hours and antibiotics were stopped. On examination, she was non-dysmorphic but had contractures of upper and lower limbs bilaterally most likely due to longstanding anhydramnios. Birth weight was 2160 g (50th centile), occipitofrontal head circumference was 31 cm (50th centile) and length was 41 cm on (9th centile).

Cranial ultrasound on DOL 1 was normal. Abdominal ultrasound showed slightly echogenic kidneys and a bladder was not identified. Echocardiogram showed a small ventriculoseptal defect (VSD). Genetic testing by microarray CGH (comparative genomic hybridisation) was normal.

Initially, she was anuric. Renal function at 12 hours of age showed a urea of 7.1 mmol/L (range 1.4–4.3 mmol/L) and creatinine of 114 μmol/L (range 27–88 μmol/L) with normal electrolytes. She received two 20 mL/kg boluses of normal saline, a 1 mg/kg dose of furosemide and was then fluid restricted. She was started on enteral feeds with Kindergen (a feed low in potassium, chloride, calcium, phosphorus and vitamin A used in renal failure) and regular infant formula. By DOL 6, urine output was 0.6 mL/kg/day and renal function deteriorated (urea 12 mmol/L, creatinine 449 μmol/L, sodium 124 mmol/L, potassium 4.44 mmol/L and chloride 91 mmol/L). She was transferred to a tertiary paediatric hospital for specialist nephrology input.

On DOL 7 she was oedematous and hyponatraemic (sodium 121 mmol/L) and started 30% sodium chloride supplementation. Repeat renal ultrasound showed increased echogenicity and reduced corticomedullary differentiation bilaterally and the bladder could not be assessed.

On DOL 8, she had bilious vomiting. Upper gastrointestinal contrast study showed a malrotation which was managed conservatively. Furosemide was started on DOL 11. Urine output improved despite worsening renal function.

On DOL 13, she deteriorated clinically and was admitted to Paediatric Intensive Care (PICU) until DOL 20 due to cardiorespiratory decompensation. She received fluid resuscitation, sodium bicarbonate and antibiotics. Echocardiogram showed reduced biventricular function with multiple small VSDs, a moderate atrial septal defect (ASD), a patent ductus arteriosus and tricuspid regurgitation. She required carvedilol, metolazone and milrinone to improve cardiac function and blood pressure. She received one red cell transfusion following a haemoglobin of 81 g/L. Diuretic therapy was increased (spironolactone and furosemide) and she received 20% albumin due to ongoing oedema and hypoalbuminaemia. Alpha-calcidiol was started due to hypocalcaemia.

She was discharged back to the ward on DOL 20 with a urea of 16.8 mmol/L, creatinine 452 μmol/L, sodium 145 mmol/L, potassium 4 mmol/L and calcium 2.37 mmol/L. Urine output was 4.9 mL/kg/hour. On DOL 21, she became hypertensive requiring amlodipine. Carvedilol dosing was increased to control hypertension without amlodipine prior to discharge. Diuretic therapy was stopped and urine output remained stable. Total fluid intake was slowly increased and her renal function gradually improved. Haemoglobin was 79 g/L and she was started on ferrous fumarate followed by subcutaneous erythropoietin.

For the remainder of her inpatient stay, she received multidisciplinary input. A high-energy supplement was added as her weight dropped to the 0.4th centile. Her limb contractures resolved. Repeat echocardiogram on DOL 44 showed a moderate ASD, mild decrease in left ventricular systolic function and mild tricuspid regurgitation. From DOL 48 to 63 she received sodium bicarbonate supplementation due to metabolic acidosis. Renal function on DOL 61 showed a urea of 5.3 mmol/L and creatinine 188 μmol/L. She was discharged home on DOL 68 weighing 2.92 kg on carvedilol, erythropoeitin two times weekly, omeprazole, ferrous fumarate and alpha-calcidiol.

At 10 weeks corrected gestational age, the infant attended the cardiology outpatient clinic. Echocardiogram showed a moderate sized ASD, smaller than previously and an intact ventricular septum. Renal function showed a urea of 14 mmol/L and creatinine of 169 μmol/L and she was admitted for rehydration for four nights.

Outpatient nephrology review at 6 months corrected gestational age showed an improvement of renal function with a creatinine of 129 μmol/L. Her haemoglobin was 129 g/L and erythropoietin dosing was decreased to once weekly. Her blood pressure was stable on carvedilol. She is currently well with good interval growth, normal development and is scheduled for nephrology review again at 10 months corrected gestational age.

DISCUSSION

We report a case of accidental ARB exposure from conception to the third trimester of pregnancy and resultant anhydramnios, preterm birth and a complicated neonatal and infant course with transient limb contractures, initial failure to thrive, malrotation, cardiac defects, chronic kidney disease, hypertension and anaemia.

In 2001, Saji *et al* described a case of in utero exposure to losartan from weeks 20–31 of pregnancy with fetal toxic effects.[6] There was oligohydramnios, pulmonary hypoplasia and hypoplastic skull bones. Sadly, in this case there was fetal demise 2 days following presentation.

Since then, there have been several more case reports describing severe and sometimes fatal fetopathic effects of ARB exposure in utero.[7–9] The risk of fetotoxic effects is greatest in the second and third trimester and the severity seems to correlate with the duration and gestation of exposure.[4] Oppermann and colleagues prospectively studied 28 pregnancies with ARB exposure beyond week 13 and found a 30% risk of fetopathy if ARB exposure continued beyond the 20th week gestation.[10] They also described thrombosis of the inferior vena cava as a possible consequence of in utero ARB exposure.[10] Oligohydramnios and fetal renal insufficiency may persist even following discontinuation of the ARB, particularly if this occurs late in pregnancy.[11] Transient neonatal renal failure has also been reported following a short exposure (4 weeks) to an ARB in the third trimester in a woman with refractory hypertension.[12]

One group proposed that the term 'fetal renin-angiotensin system (RAS) blockade syndrome' be applied to the clinical manifestations of in utero ACE inhibitor and ARB exposure: renal failure, oligohydramnios, death, arterial hypotension, intrauterine growth retardation, respiratory distress syndrome, pulmonary hypoplasia, hypocalvaria, limb defects, persistent patent ductus arteriosus or cerebral complications.[13] In this systematic review, they found that the likelihood of RAS blockade syndrome was higher with ARBs than ACE inhibitors.[13] The long-term consequences of ACE inhibitor and ARB exposure in infancy and childhood include end-stage renal failure, dialysis, failure to thrive and developmental delay.[13] A case of salt-losing nephrogenic diabetes insipidus was reported in a child 6 years following in utero exposure to an ARB.[14] For the majority of infants, the renal failure is transient and only 10% have long-term adverse outcomes such as end-stage kidney disease.[13 15]

Despite decades of publications on the adverse fetal effects of ACE inhibitors and ARBs, some physicians continue to prescribe these medications to women of childbearing age. The reasons for this are likely multifactorial. There may be a lack of knowledge among prescribers and healthcare professionals about teratogenic and fetotoxic medications. One survey, conducted in France, found that 22% of GPs and community pharmacists thought there was no fetal or neonatal risk to prescribing enalapril (an ACE inhibitor) in the third trimester of pregnancy and a further 35% were unsure of the risk.[16] Furthermore, the widespread prescribing of drugs by tradename may result in the accidental prescribing of teratogenic or fetotoxic medications in combination tablets. Additionally, women may not become aware that they are pregnant until late in the pregnancy, missing the opportunity for pharmacological therapy to be optimised.

The management of women with hypertensive disorders in pregnancy presents a challenge. Ideally, all women with pre-existing hypertension should have prepregnancy counselling with a specialist in hypertensive disorders in pregnancy.[17] The National Institute for Health and Care Excellence (NICE) in the UK recommends that alternative antihypertensive treatment should be discussed with women who are taking an ARB or ACE inhibitor if they are planning to become pregnant and that these medications should be switched to an alternative antihypertensive as soon as the woman becomes pregnant.[17] The American College of Cardiology recommends that ACE inhibitors and ARBs should be avoided during pregnancy and that women with hypertension who are pregnant or planning to become pregnant should be switched to labetalol, methyldopa or nifedipine.[18]

Women should be informed of the potential adverse fetal effects of ACE inhibitors and ARBs. The NICE guideline states that there may be an increased risk of congenital abnormalities if ACE inhibitors or ARBs are taken during pregnancy.[17] Whether ARB or ACE inhibitor exposure limited to the first trimester is associated with an increased risk of congenital abnormality is controversial. The literature suggests that ARBs are fetotoxic rather than teratogenic and that their adverse effect is more pronounced from the second and third trimester.[5 7] One retrospective cohort study found an increased risk of major cardiac and central nervous system anomalies in patients who had only first trimester ACE inhibitor exposure.[19] Subsequent studies do not support this finding, once confounders in women with hypertension were adjusted for, and it is suggested that first trimester hypertension itself is a risk factor for fetal anomalies.[20 21] First trimester exposure to ARBs does not appear to be associated with an increased risk of congenital malformation[5 7 21] but there may be an increased risk of miscarriage.[21] Thus, it is recommended that they are avoided in all trimesters of pregnancy.

The prevalence of hypertension in women of childbearing age and in pregnancy is rising[2 22] and the prescribing of ACE inhibitors and ARBs in this cohort is widespread in the primary care setting.[23] Prescription of these antihypertensives may be appropriate, for example, in women with chronic kidney disease (CKD); however, women should be informed of their potential fetotoxic effects and contraception should be discussed. Unfortunately, studies have shown that women are not consistently informed of these risks and are often not on reliable contraception.[23 24] International best-practice guidelines recommend avoiding ACE inhibitors and ARBs in pregnancy, and if possible

Patient's perspective

The experience of being pregnant and having a baby, especially your first, is supposed to be a magical time but for me it was absolutely terrifying due to the threat to my baby's life from medications prescribed to me. Some doctors even made me feel as though it was my fault even though I had been prescribed those medication by a medical professional how was I to know any different? I trusted them.

However once my baby was delivered she received the best care available to her as did I during my recovery post-delivery for which I am eternally grateful. I don't doubt for a second that without it I wouldn't have my baby girl with me today.

It was a truly terrifying experience and I hope my case can help to prevent this from happening to anyone else.

Learning points

- ACE inhibitors and angiotensin II receptor blockers (ARBs) are widely used to treat hypertension but their use should be avoided in women of childbearing age unless absolutely necessary due to their fetotoxic effects and women should be made aware of these potential adverse effects.
- ARB exposure in utero, particularly in the second and third trimester, can result in severe fetotoxicity including anhydramnios, lung hypoplasia, limb contractures and hypoplasia of the skull bones.
- There may be long-term consequences in childhood including end-stage kidney disease.
- All women who become pregnant, particularly those with pre-existing medical conditions, should be referred immediately to a maternity unit.
- The 'booking visit' can be an opportunity to review medications and make changes to prescriptions if necessary.

in women of childbearing age but they do not specifically mention contraceptive options for women on ACE inhibitors or ARBs.[17 18 25 26] Combined hormonal contraception should be avoided or used with extreme caution in women with hypertension due to their cardiovascular and thrombotic risks and physicians should refer to the UK Medical Eligibility Criteria for Contraceptive Use (UKMEC) guidelines when prescribing contraception.[27] A recently published best-practice position statement from the Kidney and Pregnancy Group of the Italian Society of Nephrology on contraception in women with CKD provides a useful summary of contraceptive options and emphasises that careful planning of pregnancy is important in this cohort to avoid adverse effects for the woman and fetus.[28]

ACE inhibitors and ARBs are best avoided in women of childbearing age unless absolutely necessary and women should be informed of their fetotoxic effects. In pregnant women where inadvertent exposure to ACE inhibitors or ARBs occurs, they should be switched to an alternative safe antihypertensive as soon as possible. Follow-up ultrasound should be offered to monitor for features of RAS blockade syndrome and referral to a fetal medicine specialist should be arranged if appropriate. Women should be monitored for signs of pre-eclampsia and a plan for delivery should be made on a case-by-case basis with senior obstetric and neonatal input.

Our case illustrates the adverse fetal effects of accidental ARB exposure in utero with resulting chronic kidney disease. Long-term renal and developmental outcomes for this infant are currently unknown. Approximately 0.9%–1.5% of pregnant women have chronic hypertension and the prevalence is increasing.[22] Thus, improved awareness of the potential fetotoxic effects of antihypertensive drugs, along with appropriate counselling of women of childbearing age with hypertension, is needed in order to prevent future cases like this.

Acknowledgements Thank you to Dr Anne Doolan, consultant neonatologist, Coombe Women and Infants University Hospital, Dublin 8, Ireland. The baby was under Dr Doolan's care while in the Coombe and Dr Doolan assisted with editing the case report. Thank you to Dr Niamh Dolan, consultant paediatric nephrologist, Children's Health Ireland, Crumlin, Dublin 8, Ireland. The baby remains under Dr Dolan's care for ongoing nephrology follow-up. Dr Dolan approved the submitted draft.

Contributors SP and EO'C, Specialist Registrars in Obstetrics and Gynaecology, were involved in planning and data collection. SP wrote the background and discussion. EO'C collected the information needed for the maternal outcome. AM, Specialist Registrar in Paediatrics, was involved in planning of the article and contributed to the paediatric outcome section. SD was involved in the planning and reporting of the paper and approved the final draft.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD
Ailbhe McGrath http://orcid.org/0000-0003-1653-9556

REFERENCES

1 Yoder SR, Thornburg LL, Bisognano JD. Hypertension in pregnancy and women of childbearing age. *Am J Med* 2009;122:890–5.
2 Bateman BT, Shaw KM, Kuklina EV, *et al*. Hypertension in women of reproductive age in the United States: NHANES 1999-2008. *PLoS One* 2012;7:e36171.
3 Barreras A, Gurk-Turner C. Angiotensin II receptor blockers. *Baylor University Medical Center Proceedings* 2003;16:123–6.
4 Quan A. Fetopathy associated with exposure to angiotensin converting enzyme inhibitors and angiotensin receptor antagonists. *Early Hum Dev* 2006;82:23–8.
5 Walfisch A, Al-maawali A, Moretti ME, *et al*. Teratogenicity of angiotensin converting enzyme inhibitors or receptor blockers. *J Obstet Gynaecol* 2011;31:465–72.
6 Saji H, Yamanaka M, Hagiwara A, *et al*. Losartan and fetal toxic effects. *The Lancet* 2001;357:363.
7 Schaefer C. Angiotensin II-receptor-antagonists: further evidence of fetotoxicity but not teratogenicity. *Birth Defects Res A Clin Mol Teratol* 2003;67:591–4.
8 Alwan S, Polifka JE, Friedman JM. Angiotensin II receptor antagonist treatment during pregnancy. *Birth Defects Res A Clin Mol Teratol* 2005;73:123–30.
9 Hünseler C, Paneitz A, Friedrich D, *et al*. Angiotensin II receptor blocker induced Fetopathy: 7 cases. *Klinische Pädiatrie* 2011;223:10–14.
10 Oppermann M, Padberg S, Kayser A, *et al*. Angiotensin-II receptor 1 antagonist fetopathy - risk assessment, critical time period and vena cava thrombosis as a possible new feature. *Br J Clin Pharmacol* 2013;75:822–30.
11 Spaggiari E, Heidet L, Grange G, *et al*. Prognosis and outcome of pregnancies exposed to renin-angiotensin system blockers. *Prenat Diagn* 2012;32:1071–6.
12 Marchetto L, Sordino D, De Bernardo G, *et al*. Postnatal acute renal failure after fetal exposure to angiotensin receptor blockers. *BMJ Case Rep* 2015:bcr2014207450.
13 Bullo M, Tschumi S, Bucher BS, *et al*. Pregnancy outcome following exposure to angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists. *Hypertension* 2012;60:444–50.
14 Miura K, Sekine T, Iida A, *et al*. Salt-Losing nephrogenic diabetes insipidus caused by fetal exposure to angiotensin receptor blocker. *Pediatr Nephrol* 2009;24:1235–8.
15 Celentano C, Prefumo F, di Vera E, *et al*. Reversible acute fetal renal failure due to maternal exposure to angiotensin receptor blocker. *Pediatr Nephrol* 2008;23:333–4.
16 Damase-Michel C, Pichereau J, Pathak A, *et al*. Perception of teratogenic and foetotoxic risk by health professionals: a survey in Midi-Pyrenees area. *Pharmacy Practice* 2008;6:15.
17 NICE Guideline. *Hypertension in pregnancy: diagnosis and management*, 2019.
18 Whelton P, Carey R, Aronow W, *et al*. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American heart association Task force on clinical practice guidelines. *Hypertension* 2018;71.
19 Cooper WO, Hernandez-Diaz S, Arbogast PG, *et al*. Major congenital malformations after first-trimester exposure to ACE inhibitors. *New England Journal of Medicine* 2006;354:2443–51.
20 Bateman BT, Patorno E, Desai RJ, *et al*. Angiotensin-Converting enzyme inhibitors and the risk of congenital malformations. *Obstetrics Gynecology* 2017;129:174–84.
21 Moretti ME, Caprara D, Drehuta I, *et al*. The fetal safety of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers. *Obstet Gynecol Int* 2012;2012:1–6.
22 Bateman BT, Bansil P, Hernandez-Diaz S, *et al*. Prevalence, trends, and outcomes of chronic hypertension: a nationwide sample of delivery admissions. *Am J Obstet Gynecol* 2012;206:134.e1–134.e8.
23 Martin U, Foreman MA, Travis JC, *et al*. Use of ACE inhibitors and Arbs in hypertensive women of childbearing age. *J Clin Pharm Ther* 2008;33:507–11.
24 Force RW, Keppel GA, Guirguis-Blake J, *et al*. Contraceptive methods and informed consent among women receiving medications with potential for adverse fetal effects: a Washington, Wyoming, Alaska, montana, Idaho (WWAMI) region study. *The Journal of the American Board of Family Medicine* 2012;25:661–8.
25 NICE Guideline. *Hypertension in adults: diagnosis and management*, 2019.
26 National Heart Foundation of Australia. *Guideline for the diagnosis and management of hypertension in adults*, 2016.
27 Faculty of Sexual & Reproductive Healthcare (FSRH). *Uk medical eligibility criteria for contraceptive use (UKMEC)*, 2016.
28 Attini R, Cabiddu G, Montersino B, *et al*. Contraception in chronic kidney disease: a best practice position statement by the kidney and pregnancy group of the Italian Society of nephrology. *J Nephrol* 2020;33:1343–59.