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REVIEW

Safety of the newer antiepileptic drug oxcarbazepine during pregnancy

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ABSTRACT

Objective: Seizure control in pregnant women with epilepsy is vital, as maternal seizures may have deleterious consequences. The treatment of pregnant women with epilepsy is, however, complicated by the teratogenicity of older antiepileptic drugs (AEDs). In this review, the safety of the newer AED oxcarbazepine during pregnancy is assessed based on published pregnancy outcome data. Other relevant safety issues, such as oxcarbazepine pharmacokinetics during pregnancy and the compatibility of oxcarbazepine treatment with breastfeeding, are also discussed.

Methods: Literature searches of the following databases were performed: MEDLINE, EMBASE, eNova, NOWIMA (an internal Novartis Germany database), Derwent Drug File, SciSearch and BIOSIS. Identified publications were examined for original data reporting rates of foetal malformation following maternal exposure to oxcarbazepine as monotherapy or adjunctive therapy.

Results: Relevant publications reporting data from the worldwide Novartis safety database and pregnancy registries or study centres in six countries were identified. A total of 248 pregnancies involving maternal exposure to oxcarbazepine monotherapy and 61 involving adjunctive therapy were reported. There were six malformations among the monotherapy group, equating to a malformation rate of 2.4% (6/248). The malformation rate reported in the general population is 2–4%. There were four malformations associated with oxcarbazepine adjunctive therapy, equating to a malformation rate of 6.6% (4/61).

Conclusions: This literature review suggests that, compared with newborns in the general population, the newborns of women receiving oxcarbazepine monotherapy during pregnancy do not appear to show an increased risk for malformations. However, the number of pregnancies involving maternal exposure to oxcarbazepine identified by this review is not sufficient to draw definitive conclusions. Additional information from large-scale pregnancy registries is required to confirm the safety profile of oxcarbazepine as monotherapy or adjunctive therapy during pregnancy.

Introduction

There are over 1.1 million women of childbearing age with epilepsy in the United States, and an estimated 20 000 infants are born to women with epilepsy each year[1,2]. Adequate seizure control in pregnant women with epilepsy is vital, as frequent and prolonged maternal seizures may have deleterious consequences, including miscarriage, foetal intracranial haemorrhage and premature birth[3]. However, the treatment of epilepsy during pregnancy is complicated by the teratogenicity of some antiepileptic drugs (AEDs) and by potential

pregnancy-induced changes in the pharmacokinetics of AEDs[4–6]. After pregnancy, the compatibility of the mother's AED regimen with breastfeeding and the possibility of post-partum changes in AED plasma levels must also be considered[7–9].

Oxcarbazepine is a newer AED indicated for the treatment of partial seizures (with or without secondarily generalized seizures) as both monotherapy and adjunctive therapy in adults and children (US ≥ 4 years old, Europe ≥ 6 years old) with epilepsy. Following oral administration, oxcarbazepine is rapidly absorbed and extensively metabolized to its pharmacologically active metabolite, the 10-monohydroxy derivative (MHD). The pharmacological effects of oxcarbazepine are largely mediated by MHD, primarily via modulation of voltage-gated sodium and calcium ion channels[10,11].

Oxcarbazepine is approved for the treatment of partial seizures in more than 70 countries worldwide and is the only newer AED approved by the US Food and Drug Administration for use as monotherapy in newly diagnosed patients[12]. Therefore, establishing the safety of oxcarbazepine in pregnant women with epilepsy is vital. This article presents a comprehensive review of published pregnancy outcome data for oxcarbazepine. Other relevant safety issues, such as oxcarbazepine pharmaco-kinetics during pregnancy and the compatibility of oxcarbazepine treatment with breastfeeding, are also discussed.

Literature searches

In order to identify relevant publications, literature searches of the following databases were performed: MEDLINE, EMBASE, eNova, NOWIMA (an internal Novartis Germany database), Derwent Drug File, SciSearch and BIOSIS.

Publications reporting pregnancy outcome data from pregnancy registries, the Novartis safety database, case reports and single- and multicentre studies were identified. To avoid potential duplication of patient numbers, data were stratified by country of origin and, in the event of multiple publications by a single research group, only data from the most recent publication were analyzed. Publications not reporting the origins of the presented data were excluded. Where possible, results were summarized according to whether maternal exposure to oxcarbazepine was as monotherapy or adjunctive therapy. From these data, overall malformation rates following oxcarbazepine monotherapy or adjunctive therapy were calculated. As it was considered beyond the scope of this review to present data for AEDs other than oxcarbazepine, only details of overall malformation rates following maternal AED exposure are provided. Definitions of malformations varied between publications; where available, these definitions have been provided. Details of malformations and information regarding maternal folic acid supplementation are also provided where available.

Pregnancy outcomes in women treated with oxcarbazepine – worldwide experience

The rate of major malformations in newborns is estimated at 2–4% in the general population, rising to 4–8% in the newborns of women with epilepsy[4,5,9]. Several older generation AEDs are established human teratogens, and an increased risk of major malformations, including cardiac defects and lip and palatal malformations, is associated with maternal exposure to these drugs[13]. The incidence of the neural tube defect spina bifida is 1–2% following exposure to valproate and 0.5–1% following exposure to carbamazepine[14,15]. Minor malformations, including facial dysmorphism and digital malformations, are approximately twice as frequent in newborns exposed to AEDs *in utero* compared with newborns in the general population[13]. The foetus is at greatest risk for malformations upon exposure to AEDs during the first trimester, as this is when organogenesis occurs, and following exposure to multiple AEDs[3,16,17].

In this section, the reported incidence of malformations following maternal exposure to oxcarbazepine during pregnancy is reviewed.

Pregnancy registries

A significant challenge in evaluating the potential teratogenicity of newer AEDs is the need to examine a large number of pregnancies. In an effort to collect these data, several national and international pregnancy registries, such as the North American Antiepileptic Drug Pregnancy Registry and the Central Registry of Antiepileptic Drugs and Pregnancy (EURAP), have been established[18–20]. EURAP was originally founded in Europe, but now contains data from over 30 countries, including countries in Asia, Oceania and South America[20]. The UK Epilepsy and Pregnancy Register and the Australian Pregnancy Registry are also well established, with both registries actively involved in collaboration with EURAP[21,22]. To date, no data specifically relating to pregnancy outcomes following oxcarbazepine treatment has been released from EURAP or the North American, UK or Australian pregnancy registries. However, oxcarbazepine data have been published from other national pregnancy registries, and these data are summarized below by country.

Argentina

Meischenguiser *et al*. reported on pregnancy outcomes collected by an epilepsy pregnancy registry in Argentina[23]. A total of 114 pregnancies involving maternal exposure to AEDs were registered between January 1995 and September 2002 in 10 national centres and hospitals. Malformations observed during the first month after birth and that either required surgery or were likely to cause serious impairment or death were classified as major malformations; all other malformations were classified as minor. Sixteen (14.0%) pregnancies resulted in newborns with malformations (eight major, eight minor). All 16 newborns with malformations were exposed to older AEDs *in utero*. In total, 35 pregnant women with epilepsy received oxcarbazepine as monotherapy, all of whom delivered healthy newborns with no malformations. Of 20 women who were exposed to oxcarbazepine adjunctive therapy during pregnancy, one gave birth to a newborn with a major cardiac malformation. This woman received oxcarbazepine in combination with phenobarbital during pregnancy.

Denmark

Prospective pregnancy outcome data collected from six centres in Denmark has recently been published[24]. Pregnant women with epilepsy were recruited for the study between September 1996 and May 2000. Data for 128 newborns exposed to AEDs during the first trimester of pregnancy were available. Malformations were defined as abnormalities of an essential embryonic structure present at birth or discovered during the neonatal period. Four (3.1%) newborns with malformations were reported among this group. A total of 37 women received oxcarbazepine during pregnancy as either monotherapy or adjunctive therapy. The relative numbers of women receiving oxcarbazepine monotherapy and adjunctive therapy were not reported. There were two newborns with malformations (both ventricular septal defects) following maternal oxcarbazepine treatment, one following oxcarbazepine monotherapy and one following adjunctive therapy with lamotrigine. The mothers of both newborns with malformations received 5 mg/day folic acid before pregnancy and during the first trimester.

Finland

In a retrospective review, Artama *et al*. identified 20 101 patients with epilepsy eligible for AED reimbursement by the Social Insurance Institution of Finland for the first time between 1985 and 1994[25]. Data were collected from this national epilepsy cohort for a total of 2516 pregnancies from 1991–2000. Malformations occurred in 65/1453 (4.5%) newborns of women with epilepsy who received AEDs during pregnancy. There were no malformations in the newborns of 101 women who received oxcarbazepine as monotherapy. A total of 32 women received oxcarbazepine as adjunctive therapy during pregnancy. Two newborns with malformations were reported among this group; both mothers of these newborns received oxcarbazepine as adjunctive therapy with valproate.

Novartis safety database

The Novartis safety database collects all safety reports related to oxcarbazepine use in patients worldwide, including pregnancy cases collected from post-marketing surveillance, clinical studies, named patient programs and literature reviews (providing patients can be identified). Most of these pregnancy cases consist of spontaneous reports of adverse events. In a recent study, Lassiter *et al*. reviewed all adverse event reports related to pregnancy or newborns in the Novartis safety database[26]. As of the end of 2002, post-marketing experience with oxcarbazepine was estimated at 774 000 patient-treatment years. From this exposure, the authors estimated that 360–600 pregnancies in women receiving oxcarbazepine could have occurred up to 31 December 2002. Safety data from approximately 3000 patients from clinical trials was held in the Novartis safety database at the time of analysis. Of 166 reports of oxcarbazepine exposure during pregnancy, 128 (92 post-marketing reports, 36 reports from clinical trials) pregnancies had a known outcome. Reports were identified for 88 pregnancies with a known outcome in women receiving oxcarbazepine monotherapy. These monotherapy reports identified 67 healthy newborns, five newborns with malformations, 13 abortions, two other adverse events and one newborn with a low birth weight. The five malformations were cleft soft palate, facial dysmorphism, terminal transverse defect (three fingers), disproportion of head and trunk and extrophia vesicae. The authors concluded that, with five reported malformations and 360 estimated pregnancies, no increased risk of malformation following maternal exposure to oxcarbazepine monotherapy was observed.

Other studies

As well as data obtained from pregnancy registries and the Novartis safety database, the literature searches identified other pregnancy outcome data for women with epilepsy exposed to oxcarbazepine. These additional data originate from single- and multicentre studies, case reports and review articles. The following section summarizes these data by country. Some studies

identified by the literature search were omitted from our analyses because the origins of the reported data were not provided[27–30].

Denmark

Fonager *et al*. searched the Danish North Jutland Pharmaco-Epidemiological Prescription Database in order to identify AED prescriptions for women in North Jutland County, Denmark, who gave birth between 1 January 1991 and 31 December 1998[31]. Malformation data were obtained from the Regional Hospital Discharge Registry. A total of 162 newborns were identified whose mothers received prescriptions for AEDs within the 30 days before pregnancy or during the first trimester. Malformations occurred in 15 (9.3%) of these newborns. Six newborns whose mothers received oxcarbazepine prescriptions (as monotherapy or adjunctive therapy) within the 30 days before pregnancy or during the first trimester were identified. One malformation (congenital hydronephrosis) was reported; according to prescription details, this newborn was exposed to oxcarbazepine in combination with vigabatrin.

In another Danish study, pregnant women with epilepsy who attended Aarhus University Hospital for antenatal care between July 1989 and January 1997 were identified[32]. Patients reported AED intake during the first trimester, and information about major malformations was collected. Major malformations occurred in 4/87 (4.6%) newborns following exposure to AEDs during the first trimester of pregnancy. There were no major malformations in seven newborns whose mothers were exposed to oxcarbazepine monotherapy during the first trimester.

In a retrospective survey of all patients treated with oxcarbazepine in eight epilepsy clinics in Denmark between 1981 and 1990[33], 12 women who received oxcarbazepine as either monotherapy or adjunctive therapy during the first trimester of pregnancy were identified. Of these 12 women, three had spontaneous abortions, and the remaining nine women gave birth to healthy newborns, with no malformations reported.

Finland

In the study of Kaaja *et al*., the pregnancy outcomes of women with epilepsy treated at a single maternity clinic in Helsinki, Finland were prospectively reviewed[34]. Major malformations were defined as those that were fatal, likely to cause a serious handicap, or requiring surgery, and were detected in 28/740 (3.8%) newborns following maternal exposure to AEDs during pregnancy. Of nine newborns exposed to oxcarbazepine monotherapy, one had a major malformation (urinary tract defect). The authors concluded that the occurrence of major malformations was independently associated with the use of oxcarbazepine. However, only nine pregnant women were exposed to oxcarbazepine monotherapy and the validity of the logistic regression analysis performed to determine this association has been questioned[35,36].

The literature search identified two additional reports of pregnancy outcome data from Finland[37,38]. Although these reports were authored by research groups different to Artama and colleagues, it is possible that the presented data may be included in the 2004 publication of Artama *et al*.[25]. Kalviainen *et al*. reviewed the pregnancy registry of a single Finnish hospital and identified 117 singleton pregnancies of women with epilepsy that were registered between January 1989 and October 2000[37]. Of two pregnancies during which mothers received oxcarbazepine as monotherapy, neither resulted in newborns with malformations. In the retrospective, single-centre study of Peltola *et al*., a hospital registry was searched for pregnant women diagnosed with epilepsy since 1995[38]. The patient files of 17 pregnant women receiving oxcarbazepine were reviewed. A total of 23 pregnancies involving maternal exposure to oxcarbazepine were identified, 20 as monotherapy and three as adjunctive therapy. Folic acid was used during 17/23 pregnancies and was not used during 1/23 pregnancies; information regarding folic acid use was not available for the remaining five pregnancies. There were no malformations in newborns for 22/23 pregnancies. One newborn, whose mother received oxcarbazepine monotherapy during pregnancy, had a minor oro-facial cleft malformation. This woman had mild mental retardation, which is associated with an increased risk of developmental abnormalities.

Germany

Bilic and Steinhoff presented a case report of a pregnant woman who received oxcarbazepine as adjunctive therapy with levetiracetam and lamotrigine[39]. The woman gave birth to a newborn with no malformations and with normal psychomotor development measured up to 12 months post-partum.

The Netherlands

Samren *et al*. retrospectively studied pregnancy outcomes in women with epilepsy who gave birth between 1972 and 1994 in the Netherlands[17]. Data from 28 hospitals in four provinces were reviewed. Of 1411 newborns (96% of whose mothers were exposed to ≥ 1 AED during pregnancy), 52 (3.7%) were reported to have major malformations. Malformations observed at birth or during the 6 weeks after birth and requiring significant therapy or involving abnormality of an essential embryonic structure were considered

major. Five newborns were identified whose mothers were exposed to oxcarbazepine (two monotherapy, three adjunctive therapy) during pregnancy. A major malformation (spina bifida cystica with clubfoot) was reported in one newborn whose mother received oxcarbazepine in combination with valproate and clobazam during pregnancy. The authors calculated the relative risk (95% confidence interval) of major malformations for oxcarbazepine adjunctive therapy to be 34.0 (3.0–386.0).

Poland

Jedrzejczak and Greese-Lyko retrospectively reviewed pregnancy outcomes in women admitted to a centre for women with epilepsy in Warsaw, Poland[40]. Women included in the study were exposed to AEDs before the sixteenth week of pregnancy. In total, 19 and six women received oxcarbazepine as monotherapy and adjunctive therapy, respectively. The authors reported no teratogenic effects directly connected with any of the newer AEDs, including oxcarbazepine.

Sweden

In a retrospective study by Wide *et al*., women who reported AED use during pregnancy and who gave birth between 1 July 1995 and 31 December 2001 were identified from the Swedish Medical Birth Registry[41]. Of 1398 newborns whose mothers were exposed to AEDs during pregnancy, 121 (8.7%) had a malformation identified. There were no malformations in four newborns of women exposed to oxcarbazepine. The number of patients receiving oxcarbazepine as monotherapy or adjunctive therapy was not provided.

United States

Included in a report of a prospective clinical trial by Beydoun *et al*. (2003) are details of a woman with epilepsy who received oxcarbazepine throughout her pregnancy and delivered a full-term, healthy male infant[42].

Overall malformation rates

Table 1 summarizes reported malformation rates in newborns following maternal exposure to oxcarbazepine monotherapy or adjunctive therapy. Data from case reports and those studies[37,38] that potentially included data reported by Artama *et al*.[25] were not used in the calculation of malformation rates. In the case of the Novartis safety database study[26], the number of newborns exposed to oxcarbazepine *in utero* (75), and not the estimated number of exposed pregnancies (360–600), was used in the calculation of the malformation rate. This approach would tend to lead to an overestimation of the malformation rate following oxcarbazepine monotherapy, as Lassiter *et al*. used the estimated number of exposed pregnancies in their calculation of the malformation rate following maternal exposure to oxcarbazepine.

Table 1. *Malformation rates following maternal exposure to oxcarbazepine monotherapy or adjunctive therapy. Rates of malformation are also shown for those publications where the overall numbers of patients receiving monotherapy or adjunctive therapy is not stated. Details of malformations are provided where available*

Reference	Malformations/total number of newborns		
	Monotherapy	Adjunctive therapy	Not stated
Meischenguiser *et al*. 2004[23]	0/35	1/20[a]	–
Sabers *et al*. 2004[24]	–	–	2/37[b]
Artama *et al*. 2004[25]	0/101	2/32	–
Lassiter *et al*. 2004[26]	5/75[c]	–	–
Fonager *et al*. 2000[31]	–	–	1/6[d]
Hvas *et al*. 2000[32]	0/7	–	–
Friis *et al*. 1993[33]	–	–	0/9
Kaaja *et al*. 2003[34]	1/9[e]	–	–
Samren *et al*. 1999[17]	0/2	1/3[f]	–
Jedrzejczak and Greese-Lyko 2002[40]	0/19	0/6	–
Wide *et al*. 2004[41]	–	–	0/4
Total (overall malformation rate)	6/248 (2.4%)	4/61 (6.6%)	–

[a]Major cardiac malformation (adjunctive therapy with phenobarbital)
[b]Both ventricular septal defects (one monotherapy, one adjunctive therapy with lamotrigine)
[c]Cleft soft palate, facial dysmorphism, terminal transverse defect (three fingers), disproportion of head and trunk, and extrophia vesicae
[d]Congenital hydronephrosis (adjunctive therapy with vigabatrin)
[e]Major urinary tract defect
[f]Spina bifida cystica and clubfoot (adjunctive therapy with valproate and clobazam)

A total of 248 pregnancies involving maternal exposure to oxcarbazepine monotherapy were identified. Six malformations were reported among this group, representing a malformation rate following oxcarbazepine monotherapy of 2.4%. So far, data from only 61 pregnancies during which women received oxcarbazepine adjunctive therapy are available. Four newborns with malformations were identified from this group, representing a malformation rate of 6.6% following oxcarbazepine adjunctive therapy.

Breastfeeding and oxcarbazepine

The health benefits of breastfeeding newborns are well documented. These benefits include greater resistance to infectious and noninfectious diseases, improved nutrition and enhanced antibody response to vaccination[8,43–45]. Mother-child interactions may also be positively influenced by breastfeeding. The compatibility of breastfeeding with the mother's AED regimen is an important issue for women with epilepsy. Indeed, women receiving AEDs appear less likely than those not receiving AEDs to choose breastfeeding as the initial method of providing nutrition to their newborns[46]. The older generation AEDs carbamazepine, valproate and phenytoin are considered compatible with breastfeeding[7,8,47].

The milk/maternal plasma concentration ratio is the most commonly used measure of drug transfer into breast milk. Although only limited data are available, the milk/maternal plasma concentration ratio for oxcarbazepine is estimated to be 0.5[48,49] and 0.5–0.8 for MHD[48–50]. This is broadly comparable with the milk/maternal plasma concentration ratio of 0.2–0.7 reported for carbamazepine[7].

Bulau *et al*. measured plasma oxcarbazepine and MHD concentrations in a mother and her newborn child[48]. At delivery, mean newborn plasma concentrations were apparently equal to the maternal plasma concentrations (oxcarbazepine 0.38 ± 0.11 µg/mL, MHD 5.70 ± 1.68 µg/mL), consistent with the significant placental transfer of oxcarbazepine and MHD reported elsewhere[51]. Although the newborn was breastfed from the third day after delivery, neonatal oxcarbazepine and MHD plasma concentrations on the fifth postpartum day were 12% and 7% of those on the first day after delivery. Therefore neither oxcarbazepine nor MHD appear to accumulate in newborns despite ingestion via breast milk. Pienimaki *et al*. showed that oxcarbazepine is metabolized to MHD in the placenta to some extent *in vitro* and suggested that the placenta may contribute to oxcarbazepine metabolism *in vivo*[52].

Case reports published to date show no effects on the development of infants breastfed by a mother receiving oxcarbazepine[28,48,50]. The literature searches did not reveal any reports of adverse events or developmental effects in newborns as a consequence of oxcarbazepine exposure via breast milk.

Discussion

The efficacy and favourable tolerability profiles of oxcarbazepine as monotherapy and adjunctive therapy in adults with epilepsy are well established[53–59]. Oxcarbazepine as monotherapy and adjunctive therapy is also well tolerated and effective in children ≤ 16 years old with epilepsy[60–66]. In addition, good safety and tolerability profiles of oxcarbazepine have been demonstrated in younger children and infants 1 month to < 4 years old[67,68]. Oxcarbazepine is approved for the treatment of partial seizures (with or without secondarily generalized seizures) in more than 70 countries worldwide and is the only newer AED approved for use in the US as monotherapy in newly diagnosed patients[12]. Therefore, determining the safety of oxcarbazepine in pregnant women with epilepsy is vital. The teratogenicity of older AEDs is well established[4–6], and it is possible that newer AEDs such as oxcarbazepine may offer a preferable alternative to the use of older AEDs in pregnant women with epilepsy.

Although this retrospective analysis was limited by the different design of the various studies and, in some cases, by a lack of information relating to study design or the overall numbers of patients exposed to oxcarbazepine monotherapy or adjunctive therapy, 248 and 61 pregnancies were identified during which women received oxcarbazepine monotherapy and adjunctive therapy, respectively. Following this comprehensive review of the literature, the malformation rate following maternal exposure to oxcarbazepine monotherapy was calculated to be 2.4%. This figure lies within the 2–4% malformation rate seen in the general population[4,9] and is lower than the rates of malformation reported by the North American Antiepileptic Drug Pregnancy Registry for phenobarbital and valproate monotherapy of 6.5% and 8.9%, respectively[69,70]. Although preliminary data for monotherapy with the newer AEDs gabapentin and lamotrigine do not suggest an increased risk of malformation[24,71], increased numbers of exposures are required to confirm these observations. In a report from the UK pregnancy registry, Barret and Richens reported the risk of a major malformation following lamotrigine and valproate combination therapy to be 11.9%; however, patient numbers were small[72].

From a total of 61 pregnancies involving maternal exposure to oxcarbazepine adjunctive therapy, 4 (6.6%) resulted in newborns with malformations. All four of these malformations were associated with oxcarbazepine adjunctive therapy with older AEDs (two valproate, one phenobarbital, one clobazam and valproate). A further three malformations associated with maternal exposure to oxcarbazepine were identified, however, these were not included in the calculation of the overall malformation rates as the total numbers of women exposed to oxcarbazepine as monotherapy or adjunctive therapy were not reported. In these studies, details of oxcarbazepine treatment were provided for the malformation cases only; of the three malformations, two were associated with oxcarbazepine adjunctive therapy (one lamotrigine, one vigabatrin) and one with oxcarbazepine monotherapy.

Several studies have demonstrated a decrease in the plasma concentration of older AEDs during pregnancy[9]. In some cases, reduced AED plasma concentrations may be associated with increased maternal seizure frequency[5,9]. Decreased plasma concentrations of AEDs may be a result of reduced compliance or pharmacokinetic changes[4–6,9]. Possible causes of pharmacokinetic changes during pregnancy include increased plasma volume, decreased protein binding and increased renal clearance[4,6]. Oxcarbazepine is predominately excreted in the form of MHD and its metabolites by renal clearance[73]. At the time of this review, no published pharmacokinetic data on oxcarbazepine during pregnancy are available. Women with epilepsy receiving oxcarbazepine should be monitored both during pregnancy, to ensure that adequate seizure control is maintained, and following delivery, to ensure that any potential post-partum changes in pharmacokinetics do not affect tolerability.

As with most other AEDs[7], oxcarbazepine and its active metabolite MHD are excreted into breast milk. Although a small number of case reports showing no effects of oxcarbazepine exposure via breast milk on infant development were identified[28,48,50], further study is required to determine the compatibility of oxcarbazepine with breastfeeding. The relative importance of adequate maternal seizure control, the benefits of breastfeeding and the perceived risk to the newborn should be assessed on an individual basis for nursing mothers with epilepsy receiving AEDs. The health and well-being of newborns of nursing mothers who continue oxcarbazepine treatment should be monitored.

Conclusions

Due to the potential risk to the developing foetus during maternal seizures, it is important that optimum seizure control is maintained in pregnant women with epilepsy. Many of the older AEDs used to control maternal seizures are, however, associated with an increased risk for foetal malformation. This analysis of the literature suggests that the newborns of women receiving oxcarbazepine monotherapy during pregnancy do not appear to show an increased risk for malformations. However, the number of identified pregnancies involving maternal exposure to oxcarbazepine identified by this review is too small to draw definitive conclusions. Additional information from large-scale national and international pregnancy registries is required to confirm the safety profile of oxcarbazepine monotherapy and adjunctive therapy during pregnancy.

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