International Journal of Epilepsy xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Epilepsy

journal homepage: http://www.journals.elsevier.com/international-journal-of-epilepsy

Case report

Valproic acid during pregnancy: Case report of a child with congenital malformations due to fetal valproate syndrome, and a high unbound serum level of valproic acid at birth

Shirley Sparla [a,*], Paul Hogeman [b], Maarten van Gemert [c], Eleonora Swart [d], Mirte Malingre [a]

[a] Department of Clinical Pharmacy, Meander Medical Centre, Maatweg 3, 3813 TZ Amersfoort, The Netherlands
[b] Department of Pediatrics, Meander Medical Centre, Maatweg 3, 3813 TZ Amersfoort, The Netherlands
[c] Department of Neurology, Meander Medical Centre, Maatweg 3, 3813 TZ Amersfoort, The Netherlands
[d] Department of Clinical Pharmacology and Pharmacy, VU University Medical Centre, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands

ARTICLE INFO

Article history:
Received 1 July 2016
Accepted 11 November 2016
Available online xxx

Keywords:
Valproic acid
Congenital malformations
Unbound serum drug levels
Pregnancy

ABSTRACT

We present a child in utero exposed to valproic acid with congenital malformations due to fetal valproate syndrome and with toxic effects. Directly postnatal, a high-unbound serum level of valproic acid was measured. The total serum level of valproic acid was in the therapeutic range. Measuring unbound serum levels during pregnancy and postnatal period in the child provides more information about real-time exposure than measuring total serum levels.

© 2016 Published by Elsevier, a division of RELX India, Pvt. Ltd on behalf of Indian Epilepsy Society.

1. Introduction

Valproic acid (VPA) is a commonly used antiepileptic drug for juvenile myoclonic epilepsy. Superior efficacy of VPA compared to lamotrigine or topiramate was suggested in the Standard and New Antiepileptic Drugs (SANAD) trial.[1,2] Young women first diagnosed with juvenile myoclonic epilepsy and reaching the age of child-bearing potential are a challenging group to treat. Together with the patient a risk-benefit analysis should be performed by the neurologist to determine the right antiepileptic drug treatment.

The usage of VPA in women of child-bearing age is controversial due to the risk of major congenital malformations, withdrawal symptoms and poorer cognitive development later in life of the unborn child.[2,3] Spina bifida aperta, cardiovascular and urogenital malformations combined with skeletal defects and specific facial malformations, also called fetal valproate syndrome, are seen with VPA use during pregnancy.[3] Symptoms of withdrawal seen are irritability, jitteriness, abnormalities of tone, seizures, and feeding problems.[4] Alternative treatment options for VPA in juvenile myoclonic epilepsy are not always available or effective.[5] For women without the desire to become pregnant in the near future VPA treatment is a very effective treatment option when combined with effective contraception.[5]

If women become pregnant during VPA treatment stopping VPA is not always an option. Untreated epilepsy during pregnancy is associated with higher health risks for women and fetus.[3,6] Furthermore switching to another antiepileptic drug may cause additional risks of major congenital malformations and increase of maternal epileptic attacks.[5] The additional risk for maternal epileptic attacks due to stopping VPA before reaching the new steady state concentrations of the new antiepileptic drug is present.

VPA dosages and serum levels both as low as possible combined with the clinical assessment of the neurologist is a tool to optimize treatment during pregnancy. Hereby reducing the exposure of the unborn child.

We present a neonate, in utero exposed to VPA, with congenital malformations due to fetal valproate syndrome, withdrawal symptoms and toxic unbound VPA levels with a follow-up time of four years.

2. Case report

At the age of 11 years the mother was diagnosed with juvenile myoclonic epilepsy for which she received VPA. Seven years later,

* Corresponding author. Present address: Sint Jansdal ziekenhuis, Wethouder Jansenlaan 90, 3844 DG Harderwijk, The Netherlands.
E-mail address: sca.sparla@stjansdal.nl (S. Sparla).

http://dx.doi.org/10.1016/j.ijep.2016.11.001
2213-6320/© 2016 Published by Elsevier, a division of RELX India, Pvt. Ltd on behalf of Indian Epilepsy Society.

Please cite this article in press as: Sparla S, et al. Valproic acid during pregnancy: Case report of a child with congenital malformations due to fetal valproate syndrome, and a high unbound serum level of valproic acid at birth, *Int J Epilepsy.* (2016), http://dx.doi.org/10.1016/j.ijep.2016.11.001

at 18 years, she had an unplanned pregnancy. At that time she used VPA 1000 mg twice daily. In the second trimester, after four months, the neurologist was informed. Considering that the embryonic phase of development had passed and organogenesis was finished VPA dosage was not adjusted. Therefore the risk for epileptic attacks with lower dosage was considered to be a higher risk than congenital malformation at that stage of the pregnancy.

After six weeks of gestation the mother started with folic acid (5 mg daily) prescribed by her general practitioner. At 36 weeks of gestation her gynecologist prescribed phytomenadione (10 mg daily).

No abnormalities were seen at the 18 and 26 weeks echo. No serum levels of VPA were obtained during pregnancy. The most recent VPA total serum level was 117 mg/L (reference 50–100 mg/L) nine months before conception.[9] The second last was 37 months before conception with total serum level of 83 mg/L (reference 50–100 mg/L) and unbound serum level of 14 mg/L (reference 5–10 mg/L) using the same dosage of 2000 mg/day. No albumin concentrations were available. Due to therapy resistance higher unbound and total serum levels were accepted. Dosage was determined based on clinical presentation and higher serum levels were deliberately accepted.

At 40 weeks a male child was born after uncomplicated vaginal delivery with a birth weight of 3095 gram. APGAR scores were 7 after one minute, 7 after five minutes and 8 after ten minutes. Because of postnatal groaning the child received PEEP (oxygen and positive end expiratory pressure ventilation) for a short period of time.

Physical examination revealed remarkable major congenital malformations of the head such as trigonocephaly due to stenosis of sutura metopica and plagiocephaly, combined with facial dysmorphic features such as deformed and small ears, epicanthic fold, long philtrum, small lips, and high-arched palate (Fig. 1). Furthermore inverted nipples, hypospadias and cryptorchidism, long fingers and toes with syndactyly at the right hand and both feet were observed.

Laboratory results showed an albumin level of 22 g/L (reference 24–39 g/L). Valproic acid levels were measured immediately after birth. Total VPA serum level was 76 mg/L (reference 50–100 mg/L). The unbound serum level was increased, i.e. 17 mg/L (reference 5–10 mg/L).

The neonate was observed at the neonatal department and received 1 mg phytomenadione. During the first day of his life the child showed hypoglycemia, tremors and apneas with decrease in saturation and bradycardia, due to withdrawal. After administration of oxygen and positive end expiratory pressure ventilation these parameters recovered to normal. After 24 hours he was transferred to the neonatal intensive care unit of the children's hospital for further examination. Due to decrease in saturation, cerebral function monitoring was performed, showing no abnormalities. Echocardiography showed no cardiac abnormalities except atypical structure of the aorta without clinical signs of

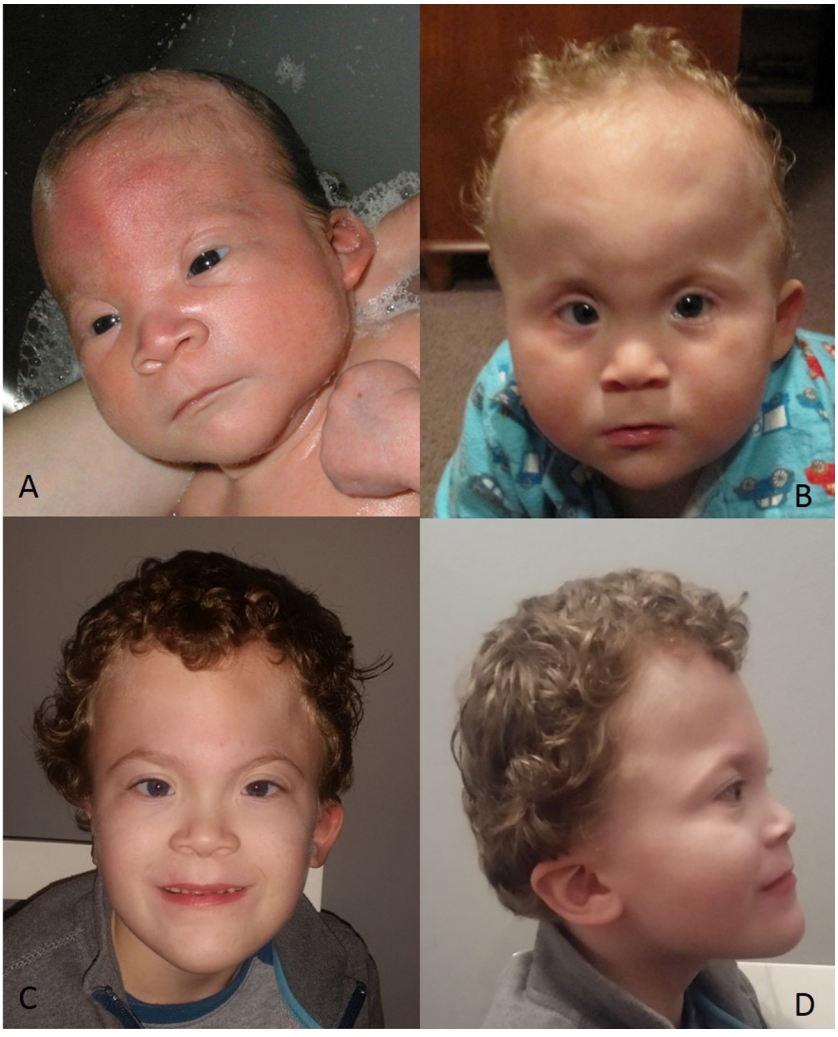

Fig. 1. Patient at the age of 3 days (A), 1 year and 11 months (B) and 8 years and 10 months (C, D). Informed consent for these photographs has been obtained.

Please cite this article in press as: Sparla S, et al. Valproic acid during pregnancy: Case report of a child with congenital malformations due to fetal valproate syndrome, and a high unbound serum level of valproic acid at birth, *Int J Epilepsy.* (2016), http://dx.doi.org/10.1016/j.ijep.2016.11.001

Download English Version:

https://daneshyari.com/en/article/8838652

Download Persian Version:

https://daneshyari.com/article/8838652

Daneshyari.com