Ecstasy abuse during pregnancy associated with cerebral leucomalacia in a preterm infant

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Introduction

The use of psychostimulant agents such as cocaine and amphetamine during pregnancy has increased during the last ten years and is associated with high risk of maternal complications and poor perinatal outcome. Psychostimulant-using women have a higher rate of spontaneous abortion, abruptio placentae and preterm labour.[1,2] Perinatal morbidity as well as the occurrence of growth retardation and neurological disorders are significantly increased after prenatal exposure to stimulant drugs.[2,3] A marked increase of echoencephalographic abnormalities, mainly hemorrhages, has been observed in cocaine- and amphetamine-exposed neonates.[4] Cerebral infarction and hemorrhage due to ecstasy (methylenedioxymethamphetamine, MDMA) are common in adults.[5] To our knowledge, this is the first report of cerebral complication in a newborn infant following intrauterine ecstasy exposure.

Case report

A preterm infant with gestational age of 32 weeks, birth weight of 1575 g, length of 43 cm and head cir-cumference of 29 cm was born by caesarean section because of precocious amniorhexis and severe variable deceleration. Routine echoencephalography scans on days 1 and 5 showed nothing abnormal. A third routine echoencephalography scan at 28 days showed distinct bilateral periventricular leucomalacia that was subsequently confirmed by magnetic resonance imaging (Fig.).

There were no such risk factors as peripartal hypoxia, circulatory failure, infections or seizures being able to explain marked leucomalacia. The pregnancy-history revealed two previous abortions and no prophylactic prenatal examination until week 30 of gestation. Moreover, the abuse of ecstasy was conceded until one week before delivery.

During the first month of life, the child developed a remarkable increase in muscle tone. The neurologic follow-up examinations until the age of 18 months showed severe psychomotor retardation with disturbance of coordination and muscle tone.

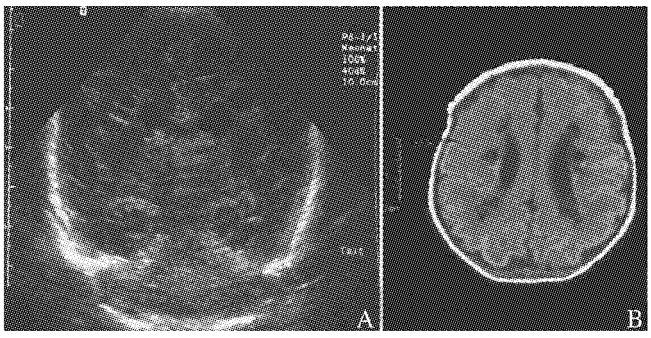

Fig. Periventricular leucomalacia following maternal MDMA abuse. **A**: echoencephalography; **B**: magnetic resonance imaging.

Discussion

The consumption of MDMA (ecstasy) has dramatically increased in recent years, particularly in adolescents and young adults including women of child bearing age.[6] Since ecstasy is known as a "recreational drug" and few or conflicting data are related to its toxicity in pregnancy,[7,8] this substance may be underestimated regarding its potential danger to mother and fetus.

In prenatally MDMA-exposed neonates, increased incidence of congenital malformations has been described.[7] Most data on abuse of stimulants during pregnancy refer to cocaine and amphetamine, which lead to an elevated rate of spontaneous abortion, abruptio placentae, preterm labour, perinatal morbidity, neurological defects, growth retardation, and various late sequelae in newborns.[1-3,9] The rise of vascular reactivity is suggested being responsible for the observed

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complications. In neonates exposed to cocaine and amphetamine in utero, cerebral abnormalities, mainly hemorrhages, have been observed increasingly.[4] Following MDMA-consumption, several severe short-term and long-term effects have been described in human adults and animals. In adults, MDMA consumption is associated with severe neurotoxic and vascular side-effects as cerebral infarction and hemorrhage.[5] A recent study in healthy, non drug addict adults showed a marked increase of arterial blood pressure, heart rate and blood cortisol level.[10] Animal studies have shown loss of cerebrovascular autoregulation in rats [11,12] and several neurotoxic side-effects of MDMA in primates. [13,14] In neonatal rats, a lack of neurotoxicity of MDMA is suggested because of insufficient maturity of the serotoninergic and dopaminergic system in newborns. [15] Nevertheless, in utero MDMA exposure produced significant long-term effects on ce-rebral function by an unknown mechanism in neonatal rats.[15] In human newborns neither neurotoxic nor cerebrovascular complications following prenatal MDMA-exposure have been reported. Solely an increased risk of congenital anomalies, mainly congenital heart disease and talipes, has been reported so far.[7] Moreover, the incidence of 7%-10% of poor MDMA metabolizers in the caucasian population, deficient in debrisoquine hydroxylase (CYP2D6),[16] fatal intoxications following relatively low doses of MDMA and non linear MDMA pharmacokinetics in good metabolizers leading to an inappropriate increase in MDMA plasma levels after small increase of ingested dose[17] underlie the possibility of uncalculatable risk of MDMA abuse in women of child bearing age. Furthermore, it is not clear whether toxic effects after ingestion of ecstasy are caused by MDMA or by other psychoactive compounds of ecstasy tablets. However, confounding risk factors in women using MDMA as heavy smoking, polydrug use and further pre-morbid factors are often observed.[18]

In conclusion, further investigations are necessary to elucidate possible toxic effects of ecstasy to the human fetus, mother and newborn. In psychomotor retardation of unknown origin, the possibility of a drug history including ecstasy should be considered.

Funding: None.
Ethical approval: Not needed.
Competing interest: None.
Contributors: UK wrote the main body under supervision of MN. ZZ provided advise on medical aspects. OL is the guarantor.

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Received April 1, 2005
Accepted after revision May 4, 2005