

No intrauterine growth retardation in babies of mothers stabilized on methadone before conception and throughout their pregnancies

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Summary

The aim of the present study is to explore the maturity of neonates of women who had conceived while being stabilized on methadone and who remained stabilized throughout their pregnancies. The sample comprised ten women and their neonates. All the neonates were eutrophic and nine of them were full-term. Mean birth weight of the neonates was 3,193 g. None of the measures of maturity differed from the data for the general population. The results obtained do not indicate any negative effect of methadone alone on neonatal maturity.

Key Words: Methadone Maintenance - Methadone Stabilization
- Pregnancy - Intrauterine Growth Retardation
- Neonatal Maturity

Introduction

Despite the better prognosis, in terms of morbidity and mortality, accorded to the fetuses and neonates of mothers on methadone maintenance treatment (MMT), compared with (1) mothers detoxified during pregnancy, or (2) those who continued to use illicit opiates [2, 7], the results of most observational studies have shown a higher incidence of intrauterine growth retardation and more frequent prematurity than those observed in the general population [1, 4, 5, 8-10, 12]. In the meta-analysis carried out by Hulse et al. [6], the mean reduction in birth weight which could be accounted for by methadone was 279 g (with a range of 229-328 g) in neonates of mothers who did not use heroin

during pregnancy.

It is very hard to determine to what extent these problems are caused by the dosing regimen applied, by recourse to other drugs (a very common problem), by other factors related to the lifestyle of an addict, or by methadone alone.

Plenty of studies have documented the benefits brought by the stabilization of a pregnant opioid-dependent woman on methadone, but there are no data, or very few, on the maturity of the neonates of mothers who had conceived them while being stabilized on methadone and who remained stabilized throughout their pregnancy. The present study aims to cover this subpopulation.

Our working hypothesis was that the maturity of neonates born to women who had conceived while being stabilized on methadone and then remained stabilized throughout their pregnancy might not differ from the maturity of neonates in the general population.

Patients and Methods

The treatment approach to pregnant women in MMT programmes in Bratislava is characterized by the following parameters (the first two apply to all MMT patients): (1) no ceiling for methadone doses; (2) methadone doses individually tailored to meet patients' needs according to their cravings, clinical signs of withdrawal and urinalyses; (3) where it is needed, a gradual increase in methadone dose is applied in the last three months of pregnancy.

We have conducted a retrospective audit among women — some current, some ex-MMT programme patients — at the Centre for Treatment of Drug Dependencies in Bratislava.

An optimal cohort approach was applied. The criteria for inclusion were:

- 1) if conception occurred after the woman had been on methadone maintenance treatment for at least 8 weeks;
- 2) if the results of the randomly conducted urinalyses were consistently negative for all the drugs screened (opiates, cocaine, amphetamines, methamphetamines, barbiturates and benzodiazepines) throughout her pregnancy.

One woman was excluded from the study because she was suffering from HIV/AIDS and obstetric complications related to that medical condition.

Ten women with their neonates (N=10) were included in the study. Their mean age at delivery was 23.4 years (SD±1.7, range 21-26). They had been using heroin for an average of 5.9 years, with a range of 2-11 years, before entering into MMT. 70% of the mothers had a history of polydrug use on entry into MMT. Six (60%) of them proved to be positive for HCV antibodies. None were HIV- or HBV- positive. Eight women smoked tobacco during their pregnancy, one did not, and in one case the smoking status was unknown. The mothers' mean methadone dose on the day before delivery was 106.5 mg (SD±51.9 mg, range 40-190 mg).

All these women were asked to provide a medical report on their babies. Data on

the age of gestation, neonate's maturity, birth weight, and so on, were analysed.

In assessing the influence of methadone maintenance treatment on the neonates' condition, we decided on comparison of our sample with national data as being methodologically the most correct procedure in checking the status of all possible local differences and time trends. Descriptive statistics was used to describe the biological maturity of the neonates. Normality of data distribution was tested using both the Kolmogorov-Smirnov and the Shapiro-Wilk Test, while the One-Sample T-Test was applied to compare the data for babies born to mothers stabilized in MMT with the general population data. Pearson product-moment correlation and partial correlation was used to further analyse the data. SPSS software was used.

The study was approved by the Ethical Committee at the Centre for Treatment of Drug Dependencies in Bratislava.

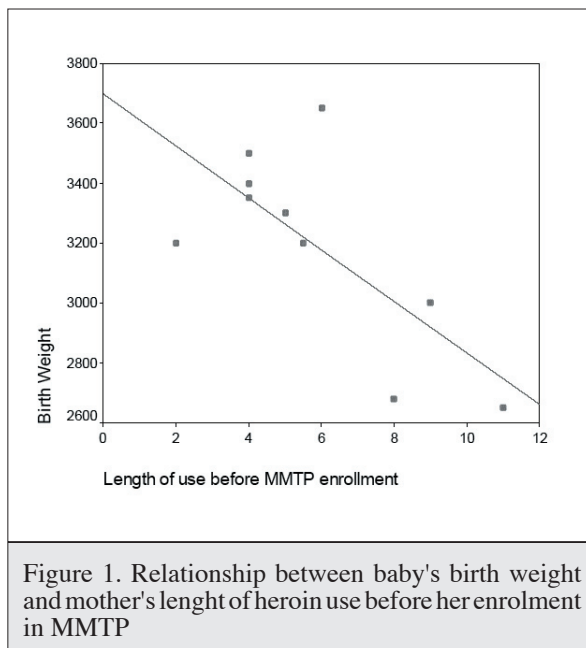
Results

40% of the births were spontaneous. All the neonates were eutrophic (birth weight between 5th and 95th percentile of fetal growth) and nine of them were full-term, with gestational age ranging between 38th and 42nd week. One baby was born in the 37th week (partus inductus). In his mother, lues latens and lymphadenopathia were diagnosed shortly before conception. Mean birth weight of the neonates was 3,193 g, median 3,250 g (SD±329.6 g; ranging between 2,650 and 3,650 g). Their mean gestational age was 39.2 weeks, median 39 (SD±1.3; range 37-41 weeks). The average birth length was 48.8 cm, median 49.5 cm (SD±1.9; from 46 to 51 cm). Median Apgar score was: 9.5/10/9 (the third measurement was only performed in 5 neonates).

Since the data from the studied sample showed a normal distribution, it enabled us to use the One-Sample T-Test to compare the sample data with those for the general population. In 2002 and 2003, the mean birth weight of all live births in Slovakia was 3,255 g and 3,259 g, respectively; mean gestational age was 39 weeks and mean birth length was 50 cm (Ustav zdravotnických informácií a štatistiky, response to request IC-548-2004. Selected Data on Neonates in the Slovak Republic. E-mail dated December 16, 2004.). Results of the comparison are shown in Table 1.

Table 1. Comparison of data on babies of the optimal cohorts, who conceived on methadone with the general population data (one-sample T-test)					
	General population 2002 data	General population 2003 data	Methadone babies	T	p
Mean birth weight	3.255 gr	3.259 gr	3.193 gr	-0.595 -0.633	0.567 0.542
Mean birth length	50 cm	50 cm	48.8 cm	-1.964	0.081
Average gestational age	39 weeks	39 weeks	39.2 weeks	0.480	0.642

Birth weight of the neonates was, to a significant degree, negatively correlated with the length of heroin use history of their mothers before the beginning of methadone maintenance treatment (Pearson $r=-0.717$, $p=0.02$, see Figure 1). This correlation remained significant even after checking for mother's age (partial $r=-0.708$, $p=0.033$). However, birth weight was not correlated with the length of stay in MMT before delivery. Also, the dose of methadone on the day before delivery failed to show statistically significant correlation with birth weight.



Discussion

Birth weight as well as gestational age of methadone babies born to mothers who were stabilized throughout their pregnancies did not reveal statistically significant differences from the general population data in the present study.

Several studies had analysed this problem and showed similar results, except for the findings on the maturity of newborns whose mothers were in MMT. One study reported the beneficial effects of a longer period of methadone maintenance and a higher methadone dose^[4]. Even so, very little research has been done while taking precautions to eliminate all possible interference factors, such as: late beginning of MMT in an already pregnant woman, being in the induction phase into methadone maintenance during pregnancy, incomplete stabilization on MMT, continued drug use, smoking habits and so on. Each of these factors might play an important role in retarding fetus development. A recent study by Sharpe and Kuschel^[11], who studied the outcomes of infants born to mothers receiving methadone for pain management during pregnancy

reported results similar to those of the present study, except for a higher incidence of preterm birth, which could be related to other factors in their sample (the mothers studied by them had multiple health problems).

Another important factor seems to be the length of heroin use before MMT programme enrolment. In our sample, this was negatively correlated with weight of the baby at birth. This could be due to long-term damage to the mother's body deriving from drug use. As a result, studies carried out on methadone patients with a long history of drug use could yield worse outcomes for their neonates.

It is hard to reach conclusions about the net effect of methadone on the maturity of neonates, because of the possible impact of other factors. It is, however, clear that in the presence of other possible teratogens, the maturity and health condition of the observed neonates were good, which implies that methadone itself had had no clinically significant negative impact.

Despite our encouraging findings, there is still the problem that there is a relatively large proportion of women in methadone maintenance treatment programmes who either use drugs other than methadone or enter methadone treatment very late, at an advanced stage of pregnancy. Either condition could have a negative impact on the maturity and health of their neonates. Further research should be carried out to discover how to successfully eliminate substance use during pregnancy, as well as how to encourage pregnant women to participate in an appropriate substitution programme, comprising prenatal care, as early as possible, preferably before their pregnancy. The results of a contingency management approach to eliminating drug use are promising^[3], but further research is needed. Encouraging planned parenthood, with the use of contraception until the mother achieves stabilization, is another option.

Study Limitations

The most important limitations on the present study include its small sample size and the lack of checks on other factors which might have an impact on the maturity of the neonates. For instance, eight out of ten women continued to smoke tobacco during their pregnancies, most of the mothers were polydrug users before entering into MMT, and a high proportion had blood samples that tested positive for HCV antibodies. All these noxious factors are much less frequent among pregnant women from the general population in the Slovak Republic.

Conclusions

We can conclude that the findings of the present study confirm the good level of maturity of neonates born to women stabilized in methadone maintenance treatment throughout their pregnancy. A clinical priority for the future should be to maximize the proportion of pregnant women with opioid dependence who are treated and stabilized in this way.

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