

Impact of Illicit Drug Use on Pregnancy Outcomes

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Executive Summary

Introduction

Substance misuse is a chronic relapsing condition affecting many populations in the UK. A large proportion of the most chaotic users are women of child bearing age. It is recommended that opiate dependent pregnant women should be treated with opioid replacement therapy (ORT) using Methadone or Buprenorphine. Despite ORT, some patients continue to misuse drugs and lead chaotic lifestyles. Studies have shown that chaotic drug use during the antenatal and perinatal period could compromise pregnancy outcomes. This study aimed to establish if stable drug use is related to better pregnancy outcomes.

Methods

A retrospective longitudinal cohort study was undertaken using a large record-linkage database in Tayside, Scotland. A sample of 44 female patients in contact with the Tayside Substance Misuse Service who fell pregnant between 1 January 2005 and 31 December 2012 and for whom complete datasets were available were selected. Some 51 pregnancies were included in the analysis. Stability of drug use was measured using urine drug screens and attendance records. Pregnancy outcomes were accessed from the relevant Scottish Morbidity Record (SMR02) records.

Results & Discussion

Stability of substance misuse (reflected in drug screens and attendance) was not found to be significantly associated with the pregnancy outcomes measured in this study. Both groups of patients appear to have similar distribution of preterm births (stable 27.8% v non-stable 27.2%), poor birth outcomes (stable 5.6% v non-stable 9.3%), low APGAR score (stable 0% v non-stable 4%) and head circumference (stable 42.9% v 40.2%). Although the non-stable cohort had higher frequency of low birth weight (28.0% v 11.1%), and higher frequency of low crown-heel length (26.7% v 0%), these appear to be statistically non-significant. The limitations in our study were: (1) the wide range of age of patients; (2) data was only collected from people in treatment and were therefore not a full representation of drug using population in Tayside; (3) assumption that the patients drug using habit is the same throughout the study period; (4) missing data on prescription of benzodiazepine meant removing benzodiazepine screens from selection criteria and (5) user dependent measurement of pregnancy outcome.

Conclusion

Stability of drug use in this cohort was poor, with 64.7% of the patients classified as non-stable users. There were no significant associations between stability of drug use (as measured in this study) and better pregnancy outcomes.

Introduction

The Challenge of Substance Misuse

Substance misuse is a chronic relapsing condition that affects a large number of populations in the UK. According to the World Health Organization, approximately 15.3 million people in the world have a drug misuse disorder¹. Throughout the developed world, the funding of care for substance misusers and the provision of methadone has become a highly publicized political issue². In the United Kingdom, the total public expenditure on drug and alcohol service in the year 2010/11 is estimated to be 1.1% of all public sector expenditures on services, an approximate £971.5 million³.

In a report released by NHS Scotland regarding the statistics of drug misuse in 2012⁴, of the population who reported illicit substance misuse, 62% reported heroin use. Amongst the most chaotic users, a large proportion is women of child bearing age. Of the maternity substance misusers recorded in 2009/10, 55% recorded opiates as their main drug of use. Other drugs recorded were cannabinoids (39%) and sedatives (14%)⁴. The general recommendation of the Department of Health is for pregnant women abusing opioids to be kept on maintenance therapy rather than insisting on abstinence as maintenance at a dose that minimises or stops illicit use, is most appropriate for ensuring continuity of contact⁵.

Several obstetric outcomes could be compromised by non-stable drug use during the antenatal and perinatal period. In this study, the relationships between the stability of substance misuse and obstetric outcomes are investigated. It is hypothesized that stable substance misusers would have better obstetric outcomes compared to their more non-stable drug using peers.

Method

Patient Population and Characteristics

This study was carried out in the population of Tayside in Scotland, using the Health Informatics Centre (HIC) record-linkage database. It provided us with datasets on all admissions of maternity patients who had contact with the Tayside Substance Misuse Service, some details of their illicit substance use and their pregnancy outcomes (APGAR score, birth weight, estimated gestation, crown-heel length, head circumference and birth outcome), which are linked by a unique patient identifier called the Community Health Index (CHI) number. The datasets available through HIC are anonymised and the researcher is given no access to patient identifiable data. This research has been approved by the Tayside Academic Health Sciences Centre (TAHSC) and is overseen by HIC standard operating procedures.

Study Population

All maternity patients in contact with the Tayside Substance Misuse Service between 2005 and 2012.

Study Subjects

Patients were included in the study if the criteria below were all met:

- 1) Tayside patients with the Tayside Substance Misuse Service who were pregnant between 1 January 2005 and 31 December 2012. They were identified from the HIC dataset.
- 2) Tayside patients who had undergone biochemistry urine tests for illicit substances and had recorded results within the HIC dataset from 1 January 2005. Patients whose biochemistry screens results which were missing or incomplete in the database were excluded to avoid distortion of data.

After all these criteria were met, forty four subjects were included in the study of whom 39 patients had 1 pregnancy, 4 patients had 2 pregnancies while 1 patient had 4 pregnancies. A total of 51 pregnancies were therefore included in the analysis. Thirty two patients were excluded due to incomplete information in the database.

Pregnancy Outcomes

From the datasets provided by HIC, we can find out the gestation at birth, birth outcome, APGAR score, birth weight, crown-heel length and head circumference for each pregnancy included in the study cohort. Babies born alive before the 37th week of pregnancy are considered to be preterm birth. There are sub-categories of preterm birth, based on gestational age: moderate to late preterm (32 to <37 weeks); very preterm (28 to <32 weeks); extremely preterm (<28 weeks)⁶. Other pregnancy outcomes were also considered, which includes live birth, still birth and miscarriage. According to the WHO, an APGAR score of more than 8 at birth is a good outcome. The value for birth weight, crown-heel length and head circumference were adjusted for gestational age according to the Fenton growth chart⁷. Values above the 10th centile were accepted as a good outcome while values below the 10th centile were considered poor outcome.

Drug Use

Defining the stability of drug use was slightly more complicated as clinically, there are multiple factors that contribute to stability. These include use of urinalysis, self-reported illicit drug use, attendance at appointments, housing situation, as well as objective observation of patients' behaviour during appointments, illicit drug use of partner and more. However, due to missing data in multiple databases, not all factors can be considered in this study. Instead, stability of drug use was calculated using the following method:

(1) It was assumed that all the patients were being prescribed Methadone. Any patient who has had a biochemistry screen negative for Methadone was defined as 'unstable'.

(2) Any patient with biochemistry screens positive of opioids was defined as 'unstable'.

(3) Attendance at service appointments could also be a useful indicator of stability. Patients with an attendance of more than 80% of appointments were defined as 'stable' while those who attended less than 80% of appointments were defined as 'unstable'. The 80% cut-off point was applied as it has always been used conventionally in clinical trials of safety and efficacy⁸.

Measures

Data analysis was undertaken using SPSS version 21 (SPSS, Chicago, IL, USA). Once the sample has been chosen, frequency distribution study was used to determine the distribution of stable and chaotic users in our cohort. Crosstabulations between stability and pregnancy outcomes were conducted along with Pearson Chi-Square tests. Frequency analysis was carried out for gestation and birth weight to identify the mean and confidence interval. The results of these statistical tests were then analysed to find the relationship between stability of drug use and the pregnancy outcomes measured.

Results

The final cohort consisted of 44 patients who had 51 pregnancies between them.

Stability

As shown in table 1, the distribution between stable and chaotic pregnancies was uneven, with stable samples accounting for only 35.3% while chaotic samples account for 64.7% of the sample.

Table 1: Quantity and percentage of stable and chaotic drug user

	Cases	Percent
Stable	18	35.3
Non-Stable	33	64.7
Total	51 cases	100%

Pregnancy Outcomes

In some cases, some pregnancy outcomes were not recorded, resulting in missing data as shown in table 2.

Table 2: Availability of Data on Pregnancy Outcomes

	Valid		Missing	
	N	Percent	N	Percent
APGAR	40	78.4%	11	21.6%
Birthweight	50	98.0%	1	2.0%
Gestation	51	100.0%	0	0.0%
Crown Heel Length	22	43.1%	29	56.9%
Head Cricumference	22	43.1%	29	56.9%
Birth Outcome	50	98.0%	1	2.0%

Analysis

Statistical analyses were undertaken

Gestation and Stability

Table 3: Association between stability and gestation at birth (n=51)

		Gestation					Total
		Term	Preterm	Very Preterm	Extreme Preterm	< 28 Weeks	
Stable	Cases	13	3	2	0	0	18
	Percentage	72.2%	16.7%	11.1%	0.0%	0.0%	100.0 %
Non-Stable	Cases	24	7	0	1	1	33
	Percentage	72.7%	21.2%	0.0%	3.0%	3.0%	100.0 %
Total	Cases	37	10	2	1	1	51
	Percentage	72.5%	19.6%	3.9%	2.0%	2.0%	100.0 %

The range of gestation of the entire cohort was 12 to 41 weeks. Of the total sample population, 72.5% were born at term. A similar percentage of 72.2% and 72.7% of stable and non-stable drug users carried their pregnancy to term. Some 16.7% of pregnancies were preterm in the stable population while 21.2% of non-stable users had preterm babies. Of the babies born to

stable users, 11.1% were very preterm. In the non-stable population, 3% of the pregnancies resulted in an extremely preterm birth and a similar percentage resulted up with a miscarriage.

In the non-stable group, mean gestation was 37.09 weeks (95% CI 34.9 – 38.7) while in the stable group, the mean gestation was 37.33 weeks (95% CI 35.5-39.0). There was no statistically significant association between stability of drug use and duration of pregnancy ($\chi^2 (4) = 4.881, p=0.300$).

Birth Outcomes and Stability

There were relatively similar numbers of life births and still births amongst both stable and non-stable users (Table 5). However, there was one incidence of miscarriage in the non-stable sample. No statistically significant associations were identified ($\chi^2 (2) = 0.590, p=0.745$).

Table 4: Association between stability and outcome of birth (n=50)

		Outcome			Total
		Live birth	Stillbirth	Miscarriage	
Stable	Cases	17	1	0	18
	Percentage	94.4%	5.6%	0.0%	100%
Non-Stable	Cases	29	2	1	32
	Percentage	90.6%	6.2%	3.1%	100%
Total	Cases	46	3	1	50
	Percentage	92.0%	6.0%	2.0%	100%

APGAR Score and Stability

The APGAR score for the entire cohort ranged from 5 to 10. There were 11 cases in which data on APGAR scores were missing. This occasionally reflected recording in cases of stillbirths and miscarriage (4cases).

Table 5: Association between stability and APGAR score (n=40)

		APGAR		Total
		< 8	> 8	
Stable	Cases	15	0	15
	Percentage	100.0%	0.0%	100.0%
Non-Stable	Cases	24	1	25
	Percentage	96.0%	4.0%	100%
Total	Cases	39	1	40
	Percentage	97.5%	2.5%	100%

As shown in table 5, of the stable population, 100% had pregnancies which ended with a good APGAR score of more than 8 while the non-stable population had 96% of good APGAR and 4% with poor APGAR. No statistically significant differences were identified ($\chi^2 (1) = 0.615, p=0.433$).

Birth Weight and Stability

The birth weight of the entire cohort ranged from 940 grams to 3750 grams.

Table 6 shows that 88.9% of children born to stable drug users had a normal birth weight while 11.1% had a low birth weight. This is comparable to 71.9% of babies born to non-stable drug users having normal birth weight while 28.1% had a low birth weight.

The mean birth weight was 2859 grams (95% CI, 2444.2, 3197.5) in the stable population and was 2724 grams (95% CI 2516.6, 2931.63) in the non-stable population. There is no apparent linear association between stability of drug use and normal birth weight ($\chi^2 (1) = 1.943, p=0.163$) from the cohort.

Table 6: Association between stability of drug use and birth weight (n=50)

		Birth weight		Total
		Normal	Low	
Stable	Cases	16	2	18
	Percentage	88.9%	11.1%	100.0%
Non-Stable	Cases	23	9	32
	Percentage	71.9%	28.1%	100.0%
Total	Cases	39	11	50
	Percentage	78.0%	22.0%	100.0%

Crown-Heel Length and Stability

The Crown-Heel length is the longest measurement of the newborn from end to end in full extension. Table 7 shows a 100% normal crown heel length for babies born to stable drug users. Of the non-stable population, 73.3% had babies with normal crown heel length while 26.7% had a significantly shorter crown heel length which is below the 10th centile on the Fenton growth chart. However, this result was statistically non-significant ($\chi^2 (1) = 2.281$; $p=0.131$).

Table 7: Association between stability and crown-heel length (n=22)

		Crown Heel Length		Total
		Normal	Low	
Stable	Cases	7	0	7
	Percentage	100.0%	0.0%	100.0%
Non-Stable	Cases	11	4	15
	Percentage	73.3%	26.7%	100.0%
Total	Cases	18	4	22
	Percentage	81.8%	18.2%	100.0%

Head Circumference and Stability

Table 8 shows a relatively similar distribution of head circumference distribution between the stable and non-stable users. There appears to be no significant relationship between stability and measurement of head circumference ($\chi^2 (1) = 0.016$; $p=0.899$).

Table 8: Association between stability of drug use and head circumference (n=22)

		Head Circumference		Total
		Normal	Low	
Stable	Cases	4	3	7
	Percentage	57.1%	42.9%	100.0%
Non-Stable	Cases	9	6	15
	Percentage	60.0%	40.0%	100.0%
Total	Cases	13	9	22
	Percentage	59.1%	40.9%	100.0%

Discussion

The main findings of this study were there were no apparent linear association between stability of drug use as defined in this study and any of the pregnancy outcomes investigated.

There appeared to be a similar percentage of preterm births in both groups of patients. This is not in keeping with the findings of other studies which indicated that less stable users tend to have a higher frequency of preterm birth^{9, 10}. This could be due to the significantly smaller sample of stable users compared to non-stable users in this study. A study with a larger population is needed to validate the effects of stability on the duration of pregnancy.

Similarly, there were only slight differences in the numbers of live and still births in both cohorts, although there was one miscarriage in the non-stable group. Some 6% of the total cohort had experienced stillbirths. This is approximately 20 times higher than the normal rate of stillbirths in the UK, which was quoted as 3.8 per thousand live births in 2010¹¹. Despite the use of methadone, the rate of stillbirths is still significantly higher in the drug using population compared to the general population.

There is a higher frequency of low APGAR score in the non-stable group, but this was shown to be statistically non-significant. Other literature on similar samples has found similar results¹². Although there was no breakdown of the APGAR score available in this study, it is possible that the lower APGAR score is because of poorer respiratory effort and decreased pulse rate reflecting the cardiorespiratory depressive effects of opioids¹³.

Although not significant, there is a higher incidence of low birth weight amongst the non-stable drug using population (28.1% v 11.1%). The better results in birth weight amongst the stable users could be attributed to their adherence to Methadone treatment as the use of Methadone is associated with a significantly smaller drop in birth weight of infants born to substance misusing patients^{14, 15}. The incidence of low birth weight in the stable population is comparable to the incidence of low birth weight in the UK population in 2009 (7.5%)¹⁶.

There was a 100% normal crown-heel length in babies born to mothers with stable drug use habit compare to 73.3% in babies born to non-stable mothers. There was no significant literature on this issue, making it difficult to determine if this was in keeping with the norm.

Previous studies have shown a reduced head circumference in children of mothers exposed to heroin¹⁷. Despite this, our study found head circumference to be relatively similar for both

stable and non-stable pregnancies. Significant missing data on head circumference could have contributed to this.

Limitations and Strengths

The patients involved in this study were of a wide range of age. The youngest patient was 17 years old at time of delivery while the oldest patient was 38 years old. Teenage pregnancies often result in a higher rate of premature births and lower birth weight and this could affect the results of the study.

The study involved only patients who were receiving treatment from or were in contact with the Tayside Substance Misuse Service. This is not a full representation of the drug using population as a large number of populations who abuse illicit substances are not in contact with specialist services. However, as substance misusers who are not in contact with specialist services are unlikely to have a stable drug use pattern; this does not affect the study population.

The biochemistry data used in monitoring the drug use habits of the patients were conducted as a 2 year follow-up study. However, some of the pregnancies occurred outwith the 2 year follow-up period. In these patients, the assumption that they maintained the same substance misuse habit had to be made as there were no further data regarding this. Although this is a fair assumption to make, some patients may have stabilised their drug use during pregnancy as pregnancy is a strong motivator to stabilise their drug use¹⁸.

Due to missing data on benzodiazepine prescriptions, we were unable to determine the stability of some patients who tested positive for benzodiazepines on biochemistry screens. As a result, a positive screen of benzodiazepine was omitted as the selection criteria for chaotic patients. This could have had a significant effect on the results as benzodiazepine abuse has been shown to significantly affect the same pregnancy outcomes this study looks at^{19, 20}.

Certain parameters of the outcome were very user dependant. For example, the measurement of crown-heel length in newborns requires the full extension of lower limbs. This is a difficult method and is dependent on the user's technique. As this is carried out by different users, the accuracy of the data could be affected.

One of the most notable strengths in our study was the use of an electronic database provided by HIC. As it records the biochemistry screens of all patients, it provides a more objective view of stability of drug use. Besides that, the patients recruited into the study all had a diagnosis of substance misuse.

Conclusion

In conclusion, the non-stable group had a higher frequency of low APGAR score (4.0% v 0%), higher frequency of lower birth weight (28.0% v 11.1%), higher frequency of low crown-heel length (26.7% v 0%) and higher frequency of poor birth outcome (9.3% v 5.6%). However, the percentages of preterm birth in both groups are similar (27.8% v 27.2%) for both stable and non-stable group. Similarly, the frequency of low head circumference length was similar in both groups (stable 42.9% v non-stable 40.2%). There were no statistically significant differences in the birth outcomes of stable users compared to non-stable users. Hence, further work needs to be done to ascertain the effects of stability illicit substance misuse on pregnancy outcomes.

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