DETECTION OF FETAL DRUG ABUSE EXPOSURE IN MECONIUM AND UMBILICAL CORD BLOOD IN OBSTETRIC UNITS IN DAMIETTA GOVERNORATE FROM THE 1ST OF MAY 2014 TO 1ST OF APRIL 2016

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ABSTRCT

Over the past 2 decades, neonatologists have cared for growing numbers of infants who were exposed passively in utero to a variety of licit and illicit drugs consumed by their mothers. Applying specific written guidelines to select newborns for drug testing decreases bias and protects the physicians and hospitals involved. Meconium (MEC) and umbilical cord blood (UCB) are a biological markers of in utero exposure to illicit drugs. So, the purpose of this study was used to detect the exposure of the infant to drug of abuse in MEC and UCB in obstetric units in Al-Azhar University Hospital (New Damietta) from the 1st of may 2014 to 1st of April 2016. for close follow-up of the infant by both medical and social services. It involved 100 infant from a delivery women's in obstetric room in Al-Azhar University Hospital (New Damietta) with history of smoke inhalation by the mother, history of drug of abuse in present or previous pregnancies, maternal report of drug abuse during this pregnancy, demonstration of drug in maternal urine, limited prenatal care (<5 prenatal visits), history of hepatitis C, B, AIDS, syphilis, gonorrhea, unexplained placental abruption and unexplained premature labor or Infants who have any of the following unexplained neurologic complications (e.g., intracranial hemorrhage or infarction, seizures), evidence of possible drug withdrawal (e.g., hypertonia, irritability, seizures, tremulousness, muscle rigidity, decreased or increased stooling) and unexplained intrauterine growth retardation and 50 infant of normal labour without any history of maternal drug abuse or fetal complication as a control group. After free informed consent to participate in this study, all the studied infants were submitted to the following:- full medical history, clinical examination. After delivery, 3 grams of MEC and 10 ml of UCB were collected and extracted for toxic metabolites. Immunoassays as a preliminary test then high performance liquid chromatography (HPLC) were used. Positive drug of abuse metabolites from UCB in the studied groups were, cough suppressant was positive in (50.0%), cannabinoid was positive in (80.0%), morphine was positive in (60.0%), tramadol was positive in (70.0%), methadone was positive in (90.0%), cocaine was positive in (10.0%), diazepam was positive in (56.0%) and amphetamine was positive in (6.0%). Drug of abuse metabolites from MEC in the studied groups were, cough suppressant (codeine) was positive in (40.0%), cannabinoid, morphine and tramadol were positive in (50.0%), methadone and amphetamine were positive in (10.0%) and diazepam was positive in (55.0%).

In conclusion; MEC and UCB were considered as a useful tool to detect the maternal drug abuse, there is a high agreement between results of UCB and MEC testing.

It is recommended that; Identification of drug-of abuse in mothers before or early in pregnancy would be ideal and avoiding intrauterine exposure, the benefits of identifying of drug-of abuse in mothers and her infants could include; programs for improvement of parenting skills with sharing of television, radio and social media, maternal drug treatment, home assistance, focused medical observation during the newborn period, restriction of breast-feeding, close pediatric follow-up emphasizing developmental and social issues and early discovery of maternal with drug-of abuse and successful maternal treatment, leading to decreased postnatal infant exposure, which can have deleterious effects and decreased risk of drug-of abuse in future pregnancies.

INTRODUCTION

During the past two decades, illicit drug use has reached epidemic proportions in North America (1).

In the United States, 10–45% of the women cared for at urban teaching hospitals use cocaine during pregnancy (2).

Estimated rates of infants exposed prenatally to cocaine range between 2.6% and 11% of all live births (3).

As women of reproductive age constitute a large segment of the drug using population, the effects of their drug use on the fetus has been studied extensively (4, 5).

Prenatal cocaine use has been associated with placental abruption and premature labor (6, 7, 8, 10).

Intrauterine cocaine exposure has also been associated with an increased risk of prematurity, small for gestational age status, microcephaly, congenital anomalies including cardiac and genitourinary abnormalities, necrotizing enterocolitis and central nervous system stroke or hemorrhage (11-18).

Some intrauterine cocaine-exposed infants may manifest symptoms of withdrawal including hypertonicity, jitteriness and seizures (19)

Similarly, it is not clear whether cocaine per se, or other risk factors, leads to adverse neurobehavioural effects (20).

Infants born to mothers using amphetamines have many of the same problems as cocaine-exposed infants, including increased rates of maternal abruption, prematurity and decreased growth parameters such as low birth weight (4).

Intrauterine amphetamine-exposed infants may also have similar postnatal symptoms including hypertonia, tremors, poor feeding and abnormal sleep patterns (11).

In addition to an increased risk of prematurity and being small for gestational age, striking withdrawal symptoms often requiring treatment are frequently observed in infants after in utero opioid exposure. Symptoms include irritability, hypertonia, wakefulness, jitteriness, diarrhea, increased hiccups, yawning and sneezing and excessive sucking and seizures, with onset of withdrawal earlier in heroin-exposed babies compared with methadone-exposed infants (9).

However, because of multiple other reproductive risk factors in women using illicit drugs, it is possible that many of the adverse effects attributed to drugs are caused by other factors (5).

Maternal addiction is a determinant of serious postnatal risk for the infant. Newborns exposed to opioids, barbiturates, benzodiazepines, cocaine, amphetamine or alcohol in utero may experience withdrawal symptoms, often requiring treatment (9, 21).

In the Metropolitan Toronto area, there has been a steady increase in the number of newborns affected by maternal drug use (3).

Fearing legal consequences and embarrassment from admitting illicit substance use, most pregnant mother tend to deny or to under-report drug consumption (12,13).

A major problem in studying the adverse effects of illicit drugs is the lack of standardized techniques to ascertain fetal exposure. The validity of blood and urine tests depends on the elimination half life of the compound in question. Cocaine, has a short elimination half life of less than one hour, so the drug and its metabolites are not likely to be detected for more than a few days in either blood or urine (14)

Other drugs, such as cannabis and opioids, have longer elimination half lives, but even these drugs can be detected for only a maximum of three to four weeks after use (22, 23).

These facts have highlighted an urgent need for a biological marker which will still be positive for weeks after the end of exposure and which may yield a cumulative reflection of long term exposure to illicit drugs (14).

The MEC and UCB testing has proved to be very effective tool for verifying gestational drug exposure **(**13**).**

AIM OF THE WORK

The objective of the present study was used to detect the fetal exposure to drug of abuse in MEC and UCB in obstetric units, in Al-Azhar University Hospital (New Damietta) from the 1st of May 2014 to 1st of April 2016.

PATIENTS AND METHODS

The detection of exposure of the infant to drug of abuse in MEC and UCB in obstetric units, in Al-Azhar university hospital (New Damietta) was from the 1st of May 2014 to 1st of April 2016.

It involved 100 infants from a delivery women's in obstetric room in Al-Azhar university hospital (New Damietta).

-As regarding maternity, the fetus who are recorded with the following;

1. positive history of smoke inhalation,
2. positive history of drug of abuse in the present or previous pregnancies,
3. demonstration of drug of abuse in her urine,
4. limited or no prenatal care (<5 prenatal visits),
5. history of sexually transmitted diseases (hepatitis B, C, AIDS, syphilis or gonorrhea),
6. unexplained placental abruption and unexplained premature labor.

-As regarding infants, the following were recorded;

1. any of unexplained neurologic complications (e.g., intracranial hemorrhage or infarction or seizures),
2. evidence of possible drug withdrawal (e.g., hypertonia, muscle rigidity, irritability, seizures, tremulousness, decreased or increased stooling) and
3. unexplained intrauterine growth retardation.

Beside 50 infants at normal labour without history of any maternal drug of abuse or fetal complication were used as a control group (24).

Free an informed consent from parents to participate in this study was taken.

The infants were submitted to the following:- full medical history, clinical examination: with special attention later on infant Mental Development at 24 months by using a modified Bayley Scales of Infant Development® **(**25**).**

-This test includes:

- The Mental Scale: evaluates sensory/perceptual acuities, discriminations, acquisition of object constancy, memory, learning and problem-solving, vocalization, early verbal communication and abstract thinking, habituation, mental mapping, complex language and mathematical concept formation.

- The Motor Scale: evaluates degree of body control, co-ordination of large muscles, fine manipulation skills, dynamic movement, postural imitation and stereognosis.
- The Behaviour Rating Scale: measures attention, arousal, orientation and engagement, emotional regulation and motor quality.

Laboratory Analysis:

Soon after delivery, the mothers has been informed that an infant sample has been sent to the laboratory for drug testing, then 10 ml of UCB and 3 grams of MEC were collected from the studied groups and frozen at 4-8°C until analysis for toxic metabolites, the testing of UCB and MEC for analysis of cocaine, its metabolite benzoylecgonine, heroin, morphine, tramadol, codeine, cannabis, methadone, benzodiazepines, barbiturates and amphetamine.

Umbilical cord blood

Ten mL of umbilical cord specimens were collected in EDTA containing test tubes. Immunoassays were used as a preliminary tests for drug of abuse analysis then positive results of drug abuse residues were confirmed by using (HPLC) grade hexane and acetone (2:1) according to method of Verebey et al., (1998). one mL of blood was put in a 50 mL flask for extraction of drug abuse, hexane (6 mL) and acetone (3 mL) were added and the contents were shaken at room temp for 30 min in a mechanical shaker. The extract was centrifuged for 10 min at 2000 rpm and the clear top layer of hexane was collected in a clean test tube. The remaining portion was again extracted twice using the same process and the hexane fractions were added to the previous solvent fractions. Clean up of the samples was done by column chromatography. Elute was collected in a 100 mL beaker and hexane was evaporated to concentrate the samples. The concentrated residues were dissolved in hexane for further analysis.

Meconium testing

MEC is usually passed by full-term newborns within 24 to 48 h, after which transition from blackish-green color to yellow color indicates beginning of passing of neonatal stool (27). For MEC testing, a sample of 3 grams (1 teaspoon) of MEC is needed for maximum sensitivity, approximately 0.2 g wet MEC was extracted with methanol. After centrifugation, the supernatant was diluted 1:5 with phosphate buffered saline and an aliquot was analysed. Immunoassays were also used for drug of abuse analysis then positive results were also confirmed by using (HPLC) as above in umbilical cord blood.

STATISTICAL ANALYSIS

The collected data was organized, tabulated and statistically analyzed using SPSS 13.0 software. For quantitative data, all the values were expressed as mean± standard deviation. For comparison between the two groups, the students (t) test was used. For qualitative data, number and percent distribution were calculated and chi square test was used for comparison between two groups. The value of $P< 0.05$ is considered to denote significance.

RESULTS

Guidelines for medically indicated newborn drug testing: Table (1).

As regarding number of infants whose her mothers have a history of smoke inhalation, history of drug of abuse in the present pregnancy, history of drug of abuse in the previous pregnancies, demonstration of drug of abuse in her urine, limited or no prenatal care (<5 prenatal visits), history of sexually transmitted diseases, unexplained placental abruption and unexplained premature labor were 45,15, 30, 45, 20, 12, 16 and 20 infants respectively.

The number of the affected infants who have unexplained neurologic complications; (intracranial hemorrhage, intracranial infarction and seizures) were 11, 5 and 6 respectively.

Also the number of the affected infant with evidence of possible drug withdrawal as hypertonia, irritability, seizures, tremulousness, muscle rigidity and disturbed bowel habit were 7,8, 8, 8, 7 and 40 infants respectively.

Number of infant with unexplained intrauterine growth retardation was 20 infants.

Clinical manifestation of maternal studied groups. (n=150):Table (2).

As regarding the clinical data, there was no statistically significant difference between cases and controls as regarding systolic blood pressure, diastolic blood pressure, respiratory rate, heart rate and unexplained intrauterine growth retardation ($P>0.05$).

As regarding clinical manifestation of unexplained neurologic complications it was (44.0%) and evidence of possible drug

withdrawal was (78.0%) in the studied groups while in control group the clinical manifestation of unexplained neurologic complications was (4.0%) and evidence of possible drug withdrawal was (6.0%). There were a statistically significant difference between study and control groups (P<0.05).

Bayley Scales of Infant Development: (Table 3). (25).

I- As Regarding Mental Scale:

There was an extremely significant difference by using mental scale between different groups (P<0.05) as regarding, sensory/perceptual acuities, discriminations, acquisition of object constancy, memory, learning and problem- solving, vocalization, early verbal communication abstract thinking, habituation, mental mapping, mathematical concept formation and complex language.

II- As Regarding Motor Scale:

There was an extremely significant difference by using motor scale between different groups (P=0.003) as regarding, degree of body control, co-ordination of large muscles, fine manipulation skills, dynamic movement, postural imitation and stereognosis.

III- As Regarding Behaviour Rating Scale:

Also, there was an extremely significant difference by using behaviour rating scale between different groups (P=0.012) as regarding, attention, arousal, orientation and engagement, emotional regulation and motor quality.

Positive drug abuse metabolites from UCB in the studied groups: (Table 4).

As regarding positive drug of abuse metabolites from UCB in the studied groups, cough suppressant (codeine) was positive in 50 cases (50.0%), cannabinoid was positive in 80 cases (80.0%), morphine was positive in 60 cases (60.0%), tramadol was positive in 70 cases (70.0%), methadone was positive in 90 cases (90.0%), cocaine was positive in 10 cases (10.0%), diazepam was positive in 56 cases (56.0%) and amphetamine was positive in 6 cases (6.0%). While in control group, cough suppressant (codeine), morphine, cocaine and amphetamine were positive in one case (2.0%), cannabinoids and diazepam were positive in 5 cases (10.0%), tramadol was positive in 20 cases (20.0%) and methadone was positive in 9 cases (9.0%). There is a significantly difference between a studied groups (P≤0.05).

Positive drug abuse metabolite from MEC in the studied groups: (Table 5).

As regarding positive drug of abuse metabolites from MEC in the studied groups, cough suppressants (codeine) was positive in 40 cases (40.0%), cannabinoids, morphine and tramadol were positive in 50 cases (50.0%), methadone and amphetamine were positive in 10 cases (10.0%) and diazepam was positive in 55 cases (55.0%). While in control group, cough suppressants (codeine), morphine, cocaine and amphetamine were positive in one case (2.0%), cannabinoid and diazepam were positive in 5 cases (10.0%), tramadol was positive in 20 cases (20.0%) and methadone was positive in 9 cases (9.0%). There is a significantly difference between the studied groups (P≤0.05).

Results of fetal exposure to illicit drugs using UCB Versus (Vs) MEC:(Table 6).

There were no statistically significant difference as a comparison results of fetal exposure to illicit drugs using UCB vs MEC in cough suppressant, cannabinoid, morphine, tramadol, diazepam and amphetamine (P>0.05), while there was a statistically significant difference as comparison a results of fetal exposure to illicit drugs using UCB vs. MEC in methadone and cocaine (P<0.05).

Table (1): guidelines for medically indicated newborn drug testing. (n=100)

Parameters			no, %
Number of infants whose mothers have any of the following	History of smoke inhalation		45 (45.0%)
	History of drug of abuse in the present pregnancy		15 (15.0%)
	History of drug of abuse in the previous pregnancies		30 (30%)
	Demonstration of drug of abuse in her urine		45 (45.0%)
	Limited or no prenatal care (<5 prenatal visits)		20 (20.0%)
	History of sexually transmitted diseases		12 (12.0%)
	Unexplained placental abruption		16 (16.0%)
	Unexplained premature labor		20 (20%)
Victim Infants who have any of the following	Unexplained neurologic complications	Intracranial hemorrhage	11 (11.0%)
		Intracranial infarction	5 (5.0%)
		Seizures	6 (6%)
	Evidence of possible drug withdrawal	Hypertonia	7 (7.0%)
		Irritability	8 (8.0%)
		Seizures	8 (8%)
		Tremulousness,	8 (8.0%)
		Muscle rigidity,	7 (7%)
		Disturbed bowel habit	40 (40.0%)
	Unexplained intrauterine growth retardation		20 (20%)

Table (2): Clinical manifestation of maternal studied groups. (n=150).

Parameters	Study group 100	Control group 50	p Value
Systolic blood pressure (mean±SD).	125.70±10.76	110.00±6.53	0.82 (NS)
Diastolic blood pressure (mean±SD).	70.88±7.36	85.25±6.15	0.28 (NS)
Respiratory rate. cycle/min.	20.32±1.09	18.53±1.61	0.33 (NS)
Heart rate. beats/min.	100.10±1.70	85.23±6.04	0.12 (NS)
Unexplained neurologic complications.	44 (44.0%)	2 (4.0%)	0.01 (S)
Evidence of possible drug withdrawal	78 (78.0%)	3 (6.0%)	0.01 (S)
Unexplained intrauterine growth retardation	20 (20.0%)	1 (2.0%)	0.51 (NS)

Significant difference (S) if $P \leq 0.05$.
Non-significant difference (NS) if $P > 0.05$.

Table (3): Clinical evaluation of Bayley Scales Affections of Infant Development. (n=150).

Variable	Results of Scales.		P Value
	Cases (100)	Control (50)	
	Positive no, %	**Positive** no, %	
I- Mental Scale Affection:			
1. Sensory/perceptual acuities.	51 (51%)	4 (8%)	0.002(S)
2. Discriminations.	55 (55%)	3 (6%)	
3. Acquisition of object constancy.	55 (55%)	3 (6%)	
4. Memory.	22 (22%)	1 (2%)	
5. Learning and problem solving.	20 (20%)	1 (2%)	
6. Vocalization.	77 (77%)	1 (2%)	
7. Early verbal communication abstract thinking.	70 (70%)	3 (6%)	
8. Habituation.	11 (11%)	2(4%)	
9. Mental mapping.	11 (11%)	2 (4%)	
10.Mathematical concept formation	23 (23%)	1 (2%)	
11.Complex language	33 (33%)	4 (8%)	
II- Motor Scale Affection:			
1. Degree of body control.	33 (33%)	3 (6%)	0.003(S)
2. Co-ordination of large muscles.	23 (23%)	4 (8%)	
3. Fine manipulation skills.	33 (33%)	3 (6 %)	
4. Dynamic movement.	15 (15%)	1 (2%)	
5. Postural imitation.	24 (24%)	2 (4%)	
6. Stereognosis.	44 (44%)	2 (4%)	
III- Behaviors Rating Scale Affection:			
1. Attention.	40 (40%)	4 (8%)	0.012(S)
2. Arousal.	50 (50%)	5 (10%)	
3. Orientation and engagement	44 (44%)	11 (22%)	
4. Emotional regulation.	80 (80%)	21 (42%)	
5. Motor quality.	45 (45%)	8 (16%)	

Significant difference (S) if P≤ 0.05

Table (4): Positive drug abuse metabolites from UCB in the studied groups. (n=150).

Drug metabolite	Study group no, %	Control group no, %	P value
Cough suppressants (Codeine)	50 (50.0%)	1 (2.0%)	0.001 (S)
Cannabinoids*	80 (80.0%)	5(10.0%)	0.001 (S)
Morphine	60 (60.0%)	1 (2.0%)	0.001 (S)
Tramadol	70 (70.0%)	20 (40.0%)	0.001 (S)
Methadone	90 (90.0%)	9 (18.0%)	0.001 (S)
Cocaine*	10 (10.0%)	1 (2.0%)	0.001 (S)
Diazepam	56 (56.8%)	5 (10.0%)	0.002 (S
Amphetamine	6 (6.0 %)	1 (2.0%)	0.001 (S)

Significant difference (S) if P≤ 0.05

*Tetrahydrocannabinol and/or tetrahydrocannabinol-9-carboxylic acid.

*Cocaine and/or benzoylecgonine.

Table (5): Positive drug abuse metabolite from MEC in the studied groups. (n=150).

Drug metabolite	Study group no, %	Control group no, %	P value
Cough suppressants (Codeine)	40 (40.0%)	1 (2.0%)	0.001 (S)
Cannabinoids*	50 (50.0%)	5(10.0%)	0.001 (S)
Morphine	50 (50.0%)	1 (2.0%)	0.001 (S)
Tramadol	50 (50.0%)	20 (40.0%)	0.001 (S)
Methadone	10 (10.0%)	9 (18.0%)	0.001 (S)
Cocaine*	0 (0.0%)	1 (2.0%)	0.001 (S)
Diazepam	55 (55.8%)	5 (10.0%)	0.002 (S
Amphetamine	10 (10.0 %)	1 (2.0%)	0.001 (S)

Significant difference (S) if P≤ 0.05

*Tetrahydrocannabinol and/or tetrahydrocannabinol-9-carboxylic acid.

*Cocaine and/or benzoylecgonine.

Table (6): Results of fetal exposure to illicit drugs using UCB Vs MEC.

Drug metabolite	UCB no, %	MEC no, %	P value
Cough suppressants (Codeine)	50 (50.0%)	40 (40.0%)	0.811 (NS)
Cannabinoids*	80 (80.0%)	50 (50.0%)	
Morphine	60 (60.0%)	50 (50.0%)	
Tramadol	70 (70.0%)	50 (50.0%)	
Methadone	90 (90.0%)	10 (10.0%)	0.021 (S)
Cocaine*	10 (10.0%)	0 (0.0%)	0.001 (S)
Diazepam	56 (56.8%)	55 (55.8%)	0.761 (NS)
Amphetamine	6 (6.0 %)	10 (10.0 %)	

Significant difference (S) if P≤ 0.05

*Tetrahydrocannabinol and/or tetrahydrocannabinol-9-carboxylic acid.

*Cocaine and/or benzoylecgonine.

DISCUSSION

Drug abuse is considered as one of the most serious problem in Egypt that worries the government and the society (28).

This phenomenon causes a hard currency leaking from the Egyptian economy as much as 2 billions of U.S dollars every year (29).

As illicit drug use reaches epidemic proportions, protecting the wellbeing of the fetus and offspring of drug users is a serious challenge for health professionals and social services. Because UCB is always available and often allows more rapid reporting of results compared to testing other specimen types and because MEC contains the amniotic fluid swallowed by the fetus in the last half of pregnancy (from the second trimester of pregnancy onwards) and is released as the first stools after birth and it is easier to collect than neonatal urine, so positive MEC test can reflect maternal use of illicit drugs from the second trimester of pregnancy onwards (38).

So the aim of this work was to detect the exposure of the infant to drug of abuse in MEC and UCB in obstetric units, in Al-Azhar university hospital (New Damietta) from the 1st of May 2014 to 1st of April 2016.

It involved 100 infants from a delivery women's in obstetric room in Al-Azhar university hospital (New Damietta) and 50 infants as a control group.

As regarding guidelines or choice for medically indicated newborn drug testing as in Table (1). Infants whose their mothers have a history of smoke inhalation, history of drug of abuse in the present pregnancy, history of drug of abuse in the previous pregnancies, demonstration of drug of abuse in her urine, limited or no prenatal care (<5 prenatal visits), history of sexually transmitted diseases, unexplained placental abruption and unexplained premature labor which are corresponding with the guidelines of (Tai, et al., 2014).

The choice of the affected infant who have unexplained neurologic complications, infant with evidence of possible drug withdrawal and

infant with unexplained intrauterine growth retardation which were corresponding with guidelines of (Ryan et al., 2014), who was documented the chart for indication for the infant drug test (Sydney, 2003).

As regarding clinical data as in Table (2). There was no statistically significant difference between cases and controls as regarding systolic and diastolic blood pressure, respiratory rate, heart rate and unexplained intrauterine growth retardation. These results are in agreement with United States National Library of Medicine 2009), who reported that the majority of cases in their study were mild according to Glasgow Coma Scale. In addition to (Gerra et al., 2003), who reported significant but no differences were observed between studied patients as regard clinical data (United States National Library of Medicine (2009). While there a statistically significant difference as regarding unexplained neurologic complications and evidence of possible drug withdrawal.

There was an extremely significant difference by using Bayley Scales of Infant Development in mental, Motor and behavior rating scales between different groups (Table 3). making this scales as a useful tools for mental development index, it was found a significant adverse impact of offspring drug of abuse level and mental development index score (Gerra, 2003).

As regarding positive drug of abuse metabolites from UCB in the studied groups, cough suppressant (codeine) was positive in (50.0%), cannabinoid was positive in (80.0%), morphine was positive in (60.0%), tramadol was positive in (70.0%), methadone was positive in (90.0%), cocaine was positive in (10.0%), diazepam was positive in (56.0%) and amphetamine was positive in (6.0%). Which is a significantly significant. These results are in accordance with (Tai et al., 2014; Bayley 2016).

As regarding positive drug of abuse metabolites from MEC in the studied groups, cough suppressant (codeine) was positive in (40.0%), cannabinoid, morphine and tramadol were positive in (50.0%), methadone and amphetamine were positive in (10.0%) and diazepam was positive in (55.0%). Which is a significantly significant. These results are in accordance with (Casanova et al., 2014).

Cocaine was not detected in the MEC as a cocaine has a short elimination half life of less than one hour. These result is in accordance with (Ostrea 2003), who reported that cocaine and its metabolites are not likely to be detected for more than a few days in either blood or urine.

As regarding the results of fetal exposure to illicit drugs using UCB vs MEC. There were no statistically significant difference as a comparison results of fetal exposure to illicit drugs using UCB vs MEC (Table 6). in cough suppressant, cannabinoid, morphine, tramadol, diazepam and amphetamine, while there were a statistically significant difference as a comparison of results of fetal exposure to illicit drugs using UCB vs MEC in methadone and cocaine. These result are in accordance with (Ostrea et al., 2009; Casanova et al., 2014). As they were reported that the MEC specimens from 20 neonates of drug-dependent mothers and five control neonates, was analyzed by radio immunoassay for metabolites of heroin, cocaine, and cannabinoids. (40) They also were reported that MEC of the controls had no drugs detected while that from neonates of drug-dependent mothers invariably showed the presence of at least one drug metabolite**.**

In these study there is a high agreement between results of UCB and MEC testing except cocaine which was detected in 10% in UCB not in MEC table (6). These results are in agreement with (Cirimele et al., 2007; Graham et al., 2008), which were postulated that the agreement between results of UCB and MEC testing ranged from 90.7 to 100% concordance with sensitivity ranging from 75 to 95.24% where calculations were possible and specificity from 91.18 to 100% where MEC samples were considered the Gold, 21 MEC samples screened positive for amphetamines while 20 of the matched UCB also screened positive. Of the 97 MEC samples that screened negative for amphetamines, 94 of the matched cords also screened negative, but three screened positive. The three samples screening as positive for amphetamines in UCB, but negative in MEC, were confirmed as methamphetamine-positive specimens using GC–MS. It was observed that 94.9% concordance for opiates, 99.2% concordance for cocaine, 90.7% for cannabinoids.

In the present study the percentage or numbers of drug of abuse were detected more in UCB than MEC table (6). These are in accordance with (Cirimele et al., 2007; Graham et al., 2008), who were hypothesized that drug testing could be carried out on UCB. If correct, this might have certain advantages over MEC or hair testing. For instance, UCB could be sent for testing immediately after delivery, while for preterm infants sometimes MEC is not passed for several days. Also, fetuses that are stressed often pass MEC in utero, making that source

unavailable for testing. However, MEC testing might have an advantage over UCB testing, if the maternal drug abuse was not suspected at delivery and the cord discarded, yet MEC could still be collected.

CONCLUSION

1. The MEC and UCB were considered as a useful way to detect maternal drug use.
2. There is high agreement between results of cord and MEC testing. But if correct the number of drug of abuse was detected more in UCB than MEC, because it could generally be sent for analysis sooner than could MEC. Moreover, UCB might be a more suitable screening method of unknown epidemiologic testing, with fewer inherent problems than with MEC collection,.

Its recommended that;

1. Identification of drug-of abuse in mothers before or early in pregnancy would be ideal and avoiding intrauterine exposure.
2. Close pediatric follow-up emphasizing developmental and social issues. In addition, currently unidentified problems caused by drug-of abuse may be discovered in the future.
3. Early discovery of maternal with drug-of abuse and successful maternal treatment, leading to decreased postnatal infant exposure, which can have deleterious effects and decreased risk of drug-of abuse in future pregnancies.

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الكشف عن التعرض الجنيني للأدوية الغير مشروعة من التبرز الأول للجنين ودم الحبل السري في وحدة الولادة في محافظة دمياط في الفترة من مايو 2014 إلى مايو 2016

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إنه على مدار العقدين الماضيين, لاحظ أطباء حديثي الولادة (المبتسرين) بوجود أعداد من المواليد حديثي الولادة الذين تم تعرضهم إلى الإصابة الغير مباشرة لأنواع من الأدوية المحرمة أو الغير محرمة عن طريق الأم. ومن ثم فإن تطبيق دليل استرشادي خاص دقيق و مكتوب (برتوكول) للمواليد لاختبار تعرضهم لبعض الأدوية, يقلل الجدل والنزاع, ومن ثم يحمى الأطباء والمستشفى من الاتهام بالتقصير. لذا يعتبر التبرز الأول (الميكونيوم) ودم الحبل السري من الدلائل الحيوية الهامة والتي تظهر تعرض الأم للأدوية المحرمة أو الغير محرمة والتي تؤثر بدورها على صحة الطفل. لذلك كان الهدف من البحث هو الكشف عن التعرض للأدوية الغير مشروعة من التبرز الأول للجنين ودم الحبل السري في وحدة الولادة في محافظة دمياط في الفترة من مايو 2014 إلى ابريل 2016, وذلك لمتابعتهم بواسطة الأطباء و الأخصائيين الاجتماعيين. وقد شملت هذه الدراسة مائة من الأطفال حديثي الولادة الذين تم ولادتهم في وحدة الولادة بمستشفى الأزهر الجامعي بدمياط الجديدة, وقد تم اختيار الأطفال إما على أساس تعرض الأمهات (للتدخين أو تناول أدوية غير مشروعة أثناء الحمل أو وجود نواتج أدوية غير مشروعة في البول أو وجود تاريخ طبي لتناول أدوية غير مشروعة في هذا الحمل أو في حامل سابق أو كان عدد الزيارات لمتابعة الحمل اقل من 5 زيارات, أو وجود تاريخ مرضى لفيروس الكبد الوبائي (س) , (ب) أو إصابة الأم بالايدز, الزهري, السيلان أو انفصال غير متوقع للمشيمة أو دخول الأم في ولادة مبكرة بدون سبب واضح) أو اختيار أطفال حديثي الولادة إما على أساس (مضاعفات عصبية غير معروفة السبب, أو وجود أعراض الانسحاب للأدوية الغير مشروعة أو وجود إعاقة للنمو داخل الرحم غير معروفة السبب). كما تم اختيار خمسون من الأطفال حديثي الولادة تم ولادتهم ولادة طبيعية بدون مشاكل أو بدون تاريخ مرضى يفيد تعرض الأمهات للأدوية غير مشروعة كمجموعة ضابطة. بعد اخذ الموافقة للمشاركة في الدراسة, تم أخذ التاريخ الطبي للأطفال , الفحص الإكلنيكى لهم مع التركيز على المضاعفات العصبية أو وجود أعراض الانسحاب. ثم تم جمع 3 جرام من أول تبرز و 10 مل من دم الحبل السري للكشف عن نواتج الأدوية المشروعة. تم حفظ العينات في درجة 4-8 درجة مئوية تحت الصفر لحين عمل التحاليل المعملية مستخدمين في ذلك جهاز المناعة الإنزيمية بواسطة كواشف جهاز" سيفا سولارز للمناعة الأنزيمية" كاختبار مبدئي وجهاز الفصل الكروماتوجرافى السائلي عالي الجودة كتأكيد للنتائج . وقد أظهرت نتائج التحاليل لدم الحبل السري و التي كانت إيجابية في (الكودايين بنسبة 50%, مشتقات الحشيش بنسبة 80%, المواد الأفيونية بنسبة 60%, الترامادول بنسبة 70%, الميثادون بنسبة 90% , والكوكيين بنسبة 10%, البنزوديازبين بنسبة 56% و الامفيتاميين بنسبة 6%). بينما أظهرت نتائج التحاليل للبراز الأول والتي كانت إيجابية في (الكودايين بنسبة 40% بينما مشتقات الحشيش, المواد الأفيونية و الترامادول بنسبة 50%, أما الميثادون و الامفيتاميين كانت نسبتهم 10%, و البنزوديازبين بنسبة 55%).
وتخلص الدراسة إلى أن فحص دم الحبل السري والبراز الأول يعتبران طريقة مفيدة وفعالة للكشف عن نواتج الأدوية الغير مشروعة لدى الأطفال حديثي الولادة. كما أظهرت وجود توافق إلى حد كبير في نتائج كلا من دم الحبل السري والبراز الأول.
لذا بناءا على ما سبق نوصى بوضع نظام دقيق للكشف عن الأدوية الغير مشروعة لدى الأم والطفل لاكتشاف الأعراض مبكرا, علاجهم, مساعدتهم اجتماعيا, متابعتهم طبيا وخصوصا أثناء فترة حديثي الولادة, كما ينصح بمنع الرضاعة الطبيعية لهذه الأمهات أثناء الإصابة والكشف الدوري عن الأمهات الراغبين في الإنجاب لاحقا وذلك لتفادى التأثيرات الضارة لهن ولأطفالهن مع الأخذ في الاعتبار, التوعية الإعلامية والتركيز على خطورة تعاطي الأمهات وتأثيره الضار جدا على أطفالهن.