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Evaluating a switch from meconium to umbilical cord tissue for newborn drug testing: A retrospective study at an academic medical center

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ABSTRACT

Background: The objective of this study was to compare detection rates of newborn drug exposure at an academic medical center transitioning from meconium to umbilical cord tissue toxicology testing.

Methods: We performed an Institutional Review Board-approved retrospective chart review on all newborns (n = 2072) for whom newborn drug testing was ordered at our academic medical center between June 2012 and August 2015 (in August 2013, umbilical cord tissue became the preferred specimen).

Results: Meconium toxicology testing was positive for at least one compound in 221 cases (21.3% of 1037 total specimens), with non-medical drug use identified in 85 cases (8.2%). Umbilical cord tissue toxicology testing was positive for at least one compound in 302 cases (29.2%), with non-medical drug use identified in 107 cases (10.3%). Of the cases involving non-medical drug use, the most common compounds detected were tetrahydrocannabinol and amphetamines. Non-medical drug use did not differ significantly between meconium and umbilical cord tissue, either as a total or for classes of drugs such as amphetamines, cannabinoids, and opiates. Maternal non-medical use of tramadol (not tested for in meconium) was identified in 5 cases (0.4%). There were significant differences in rate of detection of iatrogenic medications. Specifically, morphine, lorazepam, phenobarbital, and codeine were more commonly detected in meconium, while oxycodone was more commonly detected in umbilical cord tissue.

Conclusions: Umbilical cord tissue toxicology testing yielded a similar detection rate compared to meconium testing. The use of umbilical cord tissue avoids detection of medications given to the neonate prior to meconium collection.

1. Introduction

Non-medical drug use among pregnant women in the United States has an estimated prevalence of 5.4% based on the most recent national survey data from 2012–2013 from the Substance Abuse and Mental Health Services Administration [1]. The extent of maternal non-medical drug use may be underestimated due to underreporting by pregnant women [2]. Studies using biological specimens including maternal urine, maternal hair, and newborn urine or meconium suggest that rates are higher [3,4].

There are currently no standardized indications for newborn drug testing in the United States [3]. Practices vary from state to state, and even hospital to hospital. Decisions regarding testing and reporting are often at the discretion of health providers [5]. Toxicology testing is generally not performed on all pregnant women, because routine drug testing has not been shown to be cost effective and there is the possibility for false positive results which can have significant medicolegal implications [6–8]. The lack of standardized indications for testing has resulted in highly variable testing practices [3,9–11]. While testing indications vary between institutions, many institutions use risk assessment protocols that include various factors such as: maternal history (e.g., history of drug abuse, late or inadequate prenatal care, and history of child abuse or domestic violence), infant history (e.g., unexplained intrauterine growth restriction or evidence of drug intoxication and/or withdrawal), and current maternal alcohol or tobacco use [3]. Formal testing protocols within an institution help to remove potential bias and protect patients from discriminatory testing practices [7]. The goal of newborn drug testing is to assist in identifying neonates at risk for adverse outcomes and to facilitate medical and social work services for the neonate and the family [12–15].

Meconium has traditionally been the gold standard specimen for detection of fetal drug exposure over a long time period in pregnancy (contrasting with newborn urine drug testing which only detects the most recent days prior to birth) [3]. Meconium begins to form around

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the twelfth week of gestation and is passed by the vast majority of full-term newborns within the first 48 h after birth. Analysis of meconium can thus theoretically detect drug exposure over the last two trimesters of pregnancy. Studies suggest that third trimester drug use is more readily identified compared to use in the second trimester, possibly due to drug dilution as the fetus grows and also to drug degradation over time [16,17]. Unfortunately, in addition to maternal prenatal drug use, meconium testing will also detect medications administered to the newborn prior to meconium collection, which can further complicate result interpretation [11,17]. Another disadvantage of using meconium as a drug matrix is that sample collections may not be possible due to in utero meconium passage, late identification of risk factors after meconium has been discarded, delayed meconium passage in premature infants, accidental discarding of specimens, or sample disposal by unsupervised family members [3,11]. Additionally, meconium is a heterogeneous matrix that can present analytical challenges.

Umbilical cord tissue is an alternative matrix used for detection of in utero drug exposure and is gaining popularity [18–22]. A significant advantage of umbilical cord tissue testing is that specimen collection can occur immediately after delivery, in contrast to meconium collection which can be delayed by several days or longer [3]. Universal umbilical cord sample collection is possible, leading to fewer missed collections and protection from parental tampering. Umbilical cord samples obtained at birth can be stored for several weeks or longer, allowing for testing even when risk factors for drug exposure emerge after the opportunity to collect meconium has passed [3,11]. Stored umbilical cord tissue samples can then be discarded if drug testing is not indicated. Analysis of umbilical cord tissue also avoids the detection of medications administered to the newborn after delivery. Previous studies have shown a high rate of concordance between drug detection in meconium and umbilical cord tissue [20,21,23]. Detection of some substances, specifically amphetamines, may even be more sensitive using umbilical cord tissue compared to meconium [21]. Umbilical cord tissue also has disadvantages in that drugs given to the mother at the time of delivery can be detected; this may be explained by blood from cord vessels contaminating the tissue matrix [3]. An additional disadvantage is that umbilical cord tissue may not be available for testing when neonates are transferred from outside hospitals.

The objective of this study was to compare rates of detection of drugs and drug metabolites in meconium and umbilical cord specimens at an academic medical center transitioning from meconium testing to umbilical cord tissue testing. We hypothesized that the two specimens would yield similar rates of detection for maternal non-medical drug use but that fewer iatrogenic medications would be detected in umbilical cord tissue given that newborn medications would only be detectable by meconium analysis.

2. Materials and methods

2.1. Retrospective analysis at academic medical center

This study had approval from the University of Iowa Institutional Review Board (protocol # 201508705) as a retrospective study. Retrospective analysis was conducted of the medical records of all newborns who had drug analysis studies performed over a three year period (June 1, 2012 to August 2, 2015; n = 2072) at the University of Iowa Hospitals and Clinics (UIHC). A transition from meconium to umbilical cord tissue testing was made on August 27, 2013. Neonates prior to that date had analysis performed only on meconium. After August 27, 2013, meconium testing was performed only when umbilical cord tissue was not available – primarily in the case of patients transferred from other institutions to UIHC. UIHC is a state academic medical center that provides high-risk obstetric services and has a level IV neonatal intensive care unit (NICU).

Detailed chart review was performed on all cases (n = 221) from June 1, 2012 to August 27, 2013 for which one or more drugs or drug metabolites were identified and confirmed in meconium. Chart review was performed on all cases after August 27, 2013. As detailed in Fig. 1 and within the Results section, four groups were defined based on drug(s) and/or drug metabolite(s) detected by meconium and/or umbilical cord tissue drug analysis: Group A - cases where testing for drugs/metabolites was completely negative; Group B - cases in which all compounds detected were potentially explained by iatrogenic medications given to mother and/or newborn; Group C - cases where maternal non-medical drug use was detected; Group D - cases where compounds detected were not explained by iatrogenic medications known to be given to the mother or newborn, but where there was insufficient evidence to conclusively identify maternal non-medical drug use. Categorization of drugs detected in Group C is summarized in Table 1. Categorization of Group B drugs detected is summarized in Table 2.

2.2. Drug testing analysis

Meconium samples were analyzed by a national reference laboratory (ARUP Laboratories, Salt Lake City, UT) using enzyme-linked immunosorbent assay (ELISA) followed by confirmation by gas chromatography/mass spectrometry (GC/MS) or liquid chromatography tandem mass spectrometry (LC/MS/MS) testing. In an effort to reduce likelihood of false positives, results were only reported if the screening and confirmation methods agreed. Details on the methodology for meconium analysis have been previously published [24].

Umbilical cord tissue testing was also referred to ARUP Laboratories which performed analysis using liquid chromatography coupled with time-of-flight mass spectrometry (LC-ToF-MS), with the exception of tetrahydrocannabinol (THC) which was detected with ultra-sensitive ELISA [18,20]. Validation of the umbilical cord tissue testing included 27 neonates from UIHC that had both meconium and umbilical cord tissue toxicology analysis performed [20]. A comparison of the drugs and drug metabolites detected in the meconium and umbilical cord tissue panels is in Supplemental Table 1. It should be noted that the umbilical cord tissue drug panel included more drugs and drug metabolites than the meconium panel; some of the compounds available for umbilical cord tissue but not meconium included buprenorphine, fentanyl, tramadol, and zolpidem. Both panels included similar coverage of amphetamines, barbiturates, benzodiazepines, cocaine, traditional and semi-synthetic opiates (e.g., codeine, hydrocodone, hydromorphone, morphine, oxycodone, and oxymorphone), and THC.

2.3. Statistical analysis

Statistical analyses were carried out in SPSS (PASW Statistics 18, Chicago, IL). Differences between drugs detected by meconium and umbilical cord tissue were tested by Fisher's exact method.

3. Results

3.1. Overall rates of drug testing

During the period of study at UIHC, 6578 live births occurred. Newborn drug testing (meconium or umbilical cord tissue) was ordered in 31.5% of live births (n = 2072). Fig. 1 summarizes the results of testing in the study population.

3.2. Meconium testing results

There were 1037 cases with meconium toxicology results, with 122 cases following the switch to umbilical cord tissue as the primary specimen (these 122 cases were almost entirely on neonates transferred from outside hospitals where umbilical cord was not available to UIHC for toxicology testing). Fig. 2A summarizes the results in meconium. Of the total number of meconium specimens analyzed, 816 (78.7%)