



SPECIAL ARTICLE

Toxicology screening in paediatrics[☆]



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Abstract The prevalence of acute or chronic exposure to substances of abuse in paediatric patients, from the neonatal period to adolescence, is not well established as most cases go unnoticed. Regardless of clinical cases of acute poisoning leading to visits to emergency room, the exposure is usually detected by a questionnaire to the parents or children.

In the last few years, new validated analytical methodologies have been developed in order to detect parent drugs and their metabolites in different biological matrices. These biological matrices have different time windows for detection of the exposure: acute (i.e., urine, blood, oral fluid), and chronic (i.e., hair, meconium or teeth).

The aim of this paper was to review the scenarios where the use of biological matrices is indicated for the detection of acute or chronic exposure to substances of abuse.

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PALABRAS CLAVE

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alternativas

Utilidad del cribado toxicológico en pediatría

Resumen La prevalencia de la exposición aguda o crónica a sustancias de abuso en pediatría, desde la época neonatal hasta la adolescencia, no está bien establecida porque la mayoría de los casos pasan inadvertidos. Independientemente de los casos clínicos de intoxicaciones agudas que generan visitas a servicios de urgencias, las herramientas para la detección de la exposición que se han empleado clásicamente se reducen al cuestionario a los padres o los niños.

En los últimos años se han desarrollado metodologías analíticas validadas que permiten detectar la presencia de las sustancias madre y sus metabolitos en distintas matrices biológicas.

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Estas matrices biológicas ofrecen distintas ventanas de detección de la exposición: agudas (orina, sangre o saliva, entre otras) y crónicas (pelo, meconio o dientes, por ejemplo).

El objetivo de este manuscrito es revisar las situaciones en las que está indicada la utilización de las diferentes matrices biológicas para la detección de la exposición aguda o crónica a sustancias de abuso.

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The consumption of drugs of abuse in the general population has remained stable for most substances in the last decade. In Spain, cocaine is now the most frequently consumed drug after cannabis in the population aged 15–64 years, and is the most frequently consumed illegal stimulant.¹ Although the prevalence of cocaine use in Europe has been decreasing after peaking at 3% in 2007, in the past decade there has been an increase in the use of cannabis and cocaine in Spain of up to 7.1% and 8.8%, respectively.^{2–4}

A previous study conducted on newborns by our research group found an overall prevalence of prenatal exposure to drugs of abuse of 10%.⁵ Another study conducted on the patients that visited the paediatric emergency department in our hospital and that used hair as an alternative matrix found that 23.3% of children aged 1–5 years and 13.5% of children aged 10–14 years are chronically exposed to drugs of abuse in their immediate environment.^{2,6,7}

The documented cases demonstrate that acute intoxication with drugs of abuse in children is often the first clinical evidence of chronic repeated exposure.^{6,8} Newborns, infants and young children can be passively exposed to such substances, for instance by inhaling the smoke produced by their consumption or by hand-to-mouth behaviours leading to ingestion of traces of drugs present in the residence of an active user. They may also be passively exposed through the placenta, breastfeeding, or the saliva or sweat of the user, and there is always the possibility of intentional administration by the adult. However, there is a dearth of published evidence on the subject of chronic exposure to drugs of abuse after the neonatal period. This possibility has already been documented in several published clinical cases.^{5,6,8,9}

Diagnosis

Acute intoxications give rise to highly diverse clinical manifestations, often of a neurologic nature. Doses that are usually harmless to adults may lead to severe conditions in children, especially when different substances are consumed simultaneously. On the other hand, chronic intoxications due to continued exposure to drugs of abuse rarely produce specific symptoms, and are usually discovered by toxicological analysis of biological matrices.⁶

Aside from clinical cases of acute intoxications that result in emergency department visits, the means that have been traditionally used for detecting exposure have been limited to taking a history from the parents or the child. Questionnaires continue to be the most commonly used tool for identifying prenatal and postnatal exposure to drugs of

abuse, but there is evidence that diagnosis of drug intake by means of questionnaires is not reliable and has a low diagnostic yield, as drug use tends to be underreported or not reported at all.^{8,10}

There is no consensus-based standardised toxicology screen for implementation in paediatric emergency departments. Each laboratory has some of the various commercial rapid detection tests available, with the inherent differences in the substances they may detect and the cut-off points that define positive results. The most frequently used methods have urine as the biological matrix and involve semiquantitative detection by enzyme immunoassay. The tests available in hospitals can usually detect the presence of cannabis, cocaine, amphetamines, opioids, methadone, benzodiazepines, barbiturates and tricyclic antidepressants.⁹ Except for very specific cases, such as the habitual use of cannabis or long half-life benzodiazepines, urine tests will only be able to detect substances that have been actively or passively consumed in the hours or days immediately preceding sample collection.

In recent years, analytical methods have been developed and validated that allow the objective detection of parent drugs and their metabolites (biomarkers) in different biological matrices, and thus a definitive diagnosis, which provides the foundation for the appropriate treatment and followup of newborns and children passively exposed to drugs of abuse. These biological matrices have different time windows for detection of drug exposure: acute (for example, urine, blood or saliva) and chronic (hair or meconium).

Traditionally, the biological matrices most frequently used for toxicology screening have been blood and urine, in which recent consumption can be detected¹¹:

1. The detection window for drug testing of blood is very short, between zero and 1 h after consumption or exposure, although it can extend to up to 24 h for some substances. The chief limitation is that the procedure for sample collection is invasive.
2. The detection window for drugs of abuse in urine is somewhat longer, ranging from half to five hours from intake or exposure, although it can extend to 24–48 h for cannabis, or even one week.

The alternative or nonconventional biological matrices (hair, meconium, sweat, saliva) used for detection of drugs of abuse offer advantages compared to traditional matrices: the collection method is usually noninvasive, and some have very broad retrospective detection windows, for example, the past two trimesters in the case of meconium, while each

centimetre of hair, starting at the scalp, is equivalent to one month in the past^{8,9}:

1. Hair is considered the matrix of choice to rule out chronic exposure to drugs of abuse in children presenting with acute intoxication or living in a high-risk environment.^{8,10,11} The Society of Hair Testing has established guidelines for the washing and processing of samples to avoid external contamination as well as reference values for the detection and quantification of various substances in hair, and the clinical interpretation of the findings.^{11,12} Maternal hair testing is also used for detection of prenatal passive exposure due to substance use during pregnancy.¹⁰
2. Meconium allows assessment of prenatal exposure to substances of abuse in the second and third trimesters of gestation, including foetal production of metabolites starting on weeks 12–16.^{5,8}

The detection of drugs of abuse in hair is a unique analytical method in pharmacotoxicology, as it allows the retrospective confirmation of a history of consumption or passive exposure over a period of several months.¹² In addition to its well-known application in forensic toxicology, the detection of drugs of abuse in hair can be used to perform epidemiological studies to objectively assess passive exposure in at-risk populations such as pregnant women, newborns or children that live in environments where drugs are used.^{2,4,13,14} Previous cohort studies in Spain have demonstrated the exposure of paediatric populations to drugs of abuse,^{2,7,15} with a high rate of detection of the same drugs in the parents. As described in the scientific literature, such passive or active exposure carries a high risk of severe harmful effects.¹⁴

The purpose of urine screens for drugs of abuse is to confirm acute exposure to these substances in cases of suspected intoxication. Thus, a positive result should be followed by confirmation by testing of traditional biological matrices (urine) and ruling out chronic exposure by testing of alternative matrices (hair) with highly specific and sensitive methods (liquid or gas chromatography and mass spectrometry). Therefore, whenever a clinical presentation is suggestive of intoxication with drugs of abuse, and especially if the suspicion is confirmed by rapid urine testing, a urine sample must be preserved for a confirmatory test and a hair sample collected (a lock from the nuchal region, 2–3 cm in diameter and cut as close as possible to the scalp, fixed at the proximal end to a sheet of paper with a paperclip, and stored in an envelope at room temperature).

When exposure to drugs of abuse is confirmed in a child, the corresponding department of social services should be contacted, and samples collected from adults and other children residing in the household of the intoxicated child.

The confirmatory urine test can be performed in the reference laboratories of hospitals, but hair analysis requires an exceptional route through centres specialising in legal medicine or clinical research.

Indications for toxicology screening

Newborns, children and adolescents may be exposed to drugs of abuse through different mechanisms, and exposure

can be acute (acute intoxication) or chronic. The possible scenarios include: (1) accidental active intake; (2) passive exposure to smoke produced by consumption of substances; (3) intentional recreational use (adolescents); (4) intentional self-administration in a suicide attempt; (5) intentional forced exposure (child abuse, Munchausen syndrome by proxy, attempted murder, drug-facilitated crime, etc.); (6) prenatal exposure due to maternal use during pregnancy; (7) exposure through breast milk or sweat.

Therefore, the indications for toxicology screening (rapid urine test with confirmation in reference laboratory in cases of acute intoxication, and hair testing in reference laboratory in cases of chronic exposure) in the paediatric practice would be: (1) suspected acute intoxication or chronic exposure (both based on history taking or clinical manifestations); (2) all cases of acute intoxication; (3) known accidental exposure; (4) reported intake, and (5) suspected prenatal exposure (based on history of maternal use or clinical manifestations) or postnatal exposure.^{8,9}

Since the detection of drugs of abuse by hair testing is still a costly technique with limited availability, we cannot propose that it be used for widespread screening. Consequently, we suggest that it be indicated for paediatric patients that seek care in the primary care or hospital systems in any of the following scenarios⁴:

1. Geographical area with a high prevalence of substance use and of low socioeconomic status.
2. Clinical suspicion of acute intoxication with any drug of abuse.
3. Clinical suspicion of chronic intoxication with any drug of abuse.
4. Suspicion, evidence or report of substance use by the adult accompanying the child.
5. Evidence of a high-risk environment for the child.
6. Newborn at risk of or with suspected prenatal exposure.

The assessment of acute and chronic exposure to drugs of abuse in children must be considered part of routine medical care in emergency settings.⁹ In order to prevent drug exposure and intake in newborns, children and adolescents, the public health system and social services must carry out interventions to make the population aware of the risks to child health and the need to avoid substance use during pregnancy and in settings where children spend time with adults. Furthermore, clinical practice guidelines must be developed and implemented for the health care and social work professionals that confront exposure to drugs of abuse in newborns, children and adolescents.

Conflict of interests

The authors have no conflict of interests to declare.

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