

Pubblicazioni su riviste scientifiche internazionali sull'alcol con almeno un autore affiliato al Reparto di Farmacodipendenza, Tossicodipendenza e Doping (ISS).

1. Assessment of prenatal exposure to ethanol by meconium analysis: results of an Italian multicenter study.

Pichini S, Marchei E, Vagnarelli F, Tarani L, Raimondi F, Maffucci R, Sacher B, Bisceglia M, Rapisardi G, Elicio MR, Biban P, Zuccaro P, Pacifici R, Pierantozzi A, Morini L.

Alcohol Clin Exp Res. 2012 Mar;36(3):417-24.

Abstract

BACKGROUND: This study estimated in 7 Italian cities the prevalence of prenatal exposure to ethanol by determining fatty acid ethyl esters (FAEEs; palmitic, palmitoleic, stearic, oleic, linoleic, linolenic, and arachidonic esters) and ethyl glucuronide (EtG) in neonatal meconium samples.

METHODS: A total of 607 meconium samples were obtained from neonatal wards of 7 public hospitals: Verona and San Daniele del Friuli in the northeast of the country, Reggio Emilia in the middle east, Florence and Rome in the center, and Naples and Crotona in the southwest of the peninsula. Meconium biomarkers were assessed by a validated methodology using liquid chromatography-tandem mass spectrometry and the results categorized using the accepted cutoff of 2 nmol/g total amount of 7 FAEEs and 2 nmol/g EtG, to differentiate between heavy maternal ethanol use during pregnancy and occasional or no use at all.

RESULTS: On the basis of the above-reported cutoffs, the overall prevalence of newborns prenatally exposed to maternal ethanol was 7.9%: 0% in Verona, 4.0% in San Daniele del Friuli, 4.9% in Naples, 5.0% in Florence, 6.2% in Crotona, up to 10.6% in Reggio Emilia, and 29.4% in Rome. Low maternal education level and younger maternal age were associated with biomarker scores over the cutoff. There was also a significant correlation between the highest percentage of prenatal exposure in the capital and certain maternal sociodemographic characteristics.

CONCLUSIONS: These results indicate considerable variability in the prevalence of fetal exposure to ethanol in different Italian cities, as determined by the objective measurement of biomarkers in meconium. These data, together with previous ones obtained in Barcelona, Spain, indicate that gestational ethanol exposure is widespread, at least in parts of Europe.

Fonte: PubMed

2. Determination of maternal-fetal biomarkers of prenatal exposure to ethanol: A review.

Joya X, Friguls B, Ortigosa S, Papaseit E, Martínez SE, Manich A, Garcia-Algar O, Pacifici R, Vall O, Pichini S.

J Pharm Biomed Anal. 2012 Jan 16.

Abstract

The deleterious effects exerted by prenatal ethanol exposure include physical, mental, behavioural and/or learning disabilities that are included in the term fetal alcohol spectrum disorder (FASD). Objective assessment of exposure to ethanol at both prenatal and postnatal stages is essential for early prevention and intervention. Since pregnant women tend to underreport alcohol drinking by questionnaires, a number of biological markers have been proposed and evaluated for their capability to highlight gestational drinking behaviour. These biomarkers include classical biomarkers (albeit indirect) of alcohol-induced pathology (mean corpuscular volume (MCV), gamma glutamyltransferase (GGT), aspartate aminotransferase (AST) and alanine aminotransferase (ALT)) acetaldehyde-derived conjugates, and finally derivatives of non-oxidative ethanol metabolism (fatty acid ethyl esters (FAEEs), ethyl glucuronide (EtG), ethyl sulphate (EtS) and phosphatidylethanol (PEth)). Since ethanol itself and acetaldehyde are only measured few hours after ethanol intake in conventional matrices such as blood, urine and sweat, they are only useful to detect recent ethanol exposure. In the past few years, the non-oxidative ethanol metabolites have received increasing attention because of their specificity and in some case wide time-window of detection in non-conventional matrices from the pregnant mother (oral fluid and hair) and fetus-newborn (neonatal hair, meconium, placenta and umbilical cord). This article reviews bioanalytical procedures for the determination of these markers of ethanol consumption during pregnancy and related prenatal exposure. In addition, clinical toxicological applications of these procedures are presented and discussed. *Fonte: PubMed*

3. Validity of a maternal alcohol consumption questionnaire in detecting prenatal exposure.

Manich A, Velasco M, Joya X, García-Lara NR, Pichini S, Vall O, García-Algar O.
An Pediatr (Barc). 2012 Jun;76(6):324-8. Epub 2011 Nov 21

Abstract

Ethanol consumption by pregnant women can produce severe effects in the foetus and the newborn, mainly in neurological and weight-height development, and are included in the term FASD (Fetal Alcohol Spectrum Disorder). Questionnaires are the most used screening method to detect prenatal exposure, but a previous population study questioned its reliability. The objective of this study was to compare alcohol prenatal exposure detection by questionnaire compared with biomarkers in meconium.

Fonte: PubMed

4. Fetal alcohol syndrome: new perspectives for an ancient and underestimated problem.

de Sanctis L, Memo L, Pichini S, Tarani L, Vagnarelli F
J Matern Fetal Neonatal Med. 2011 Oct;24 Suppl 1:34-7.

Abstract

The knowledge of the dangers of alcohol consumption during pregnancy isn't indeed a new issue, but the recent evidences of ethyl-glucuronide and ethyl-sulfate in meconium as novel biomarkers of prenatal ethanol exposure open new perspectives for the early diagnosis of the alcohol-related birth defects. This is crucial for a better developmental outcome of the affected patients and for preventing additional cases in at risk families. The fetal alcohol syndrome is not a single entity but represents the most severe form of a spectrum of disorders, including distinctive craniofacial alterations, stunted growth and behavioral abnormalities, caused by complex gene-environment interactions. FAS must always be a diagnosis of exclusion and have to be differentiated from many conditions caused by other embryotoxin agents and genetic syndromes that share some phenotypic features. Even if the first trimester is considered the most vulnerable period, nowadays is known that a fetal damage might occur throughout all gestation. Since ethanol consumption is constantly increasing among young women, a substantial amount of work has to be made to implement the knowledge on alcohol fetal effects among women of childbearing age; moreover, awareness and training among professionals in the health care system might play a critical role in the early diagnosis of these serious conditions.

Fonte: PubMed

5. Fetal alcohol syndrome: new perspectives for an ancient and underestimated problem.

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Fonte: PubMed

6. A survey of Italian and Spanish neonatologists and paediatricians regarding awareness of the diagnosis of FAS and FASD and maternal ethanol use during pregnancy.

Vagnarelli F, Palmi I, García-Algar O, Falcon M, Memo L, Tarani L, Spoletini R, Pacifici R, Mortali C, Pierantozzi A, Pichini S.

BMC Pediatr. 2011 Jun 6;11:51

Abstract

Ethanol is the most widely used drug in the world and a human teratogen whose consumption among women of childbearing age has been steadily increasing. There are no Italian or Spanish statistics on ethanol consumption during pregnancy nor any information regarding prevalence of fetal alcohol syndrome (FAS) and fetal alcohol spectrum disorders (FASD). There is also a reasonable suspicion that these two diseases are underdiagnosed by professionals from the above-reported countries. The objectives of this study were: 1) to evaluate the experience, knowledge and confidence of Italian and Spanish neonatologists and paediatricians with respect to the diagnosis of FAS and FASD, and 2) to evaluate professionals awareness of maternal drinking patterns during pregnancy.

Fonte: PubMed

7. Population Baseline of Meconium Ethyl Glucuronide and Ethyl Sulfate Concentrations in Newborns of Nondrinking Women in 2 Mediterranean Cohorts.

Morini L, Groppi A, Marchei E, Vagnarelli F, Garcia Algar O, Zuccaro P, Pichini S

Ther Drug Monit. 2010 Mar 23.

Abstract

The detection of ethyl glucuronide (EtG) and ethyl sulfate (EtS) in meconium has been investigated recently as an alternative to meconium fatty acid ethyl esters (FAEEs) measurement as an objective estimate of prenatal alcohol exposure, independent of maternal self-reporting. We report the results of the first study conducted to investigate the concentrations of EtG and EtS in meconium from newborns with and without intrauterine exposure to ethanol, defined by questionnaire and meconium FAEEs concentration. FAEEs, EtG, and EtS were quantified by liquid chromatography tandem mass spectrometry in meconium samples obtained from the Arcispedale Santa Maria Nuova, Reggio Emilia, Italy (n = 80) and from the Hospital del Mar in Barcelona, Spain (n = 105). Median EtG and EtS values in meconium from newborns without intrauterine exposure to ethanol varied between 0.100 and 0.140 nmol/g and 0.010 and 0.020 nmol/g in Reggio Emilia and Barcelona samples, respectively. In meconium from newborns with uncertain prenatal ethanol exposure, the EtG median value was 0.160 nmol/g in the Italian cohort and 0.250 nmol/g in the Spanish one. The median EtS concentration was 0.020 in both cohorts. EtG and EtS median values in 5 meconium samples from newborns of heavily drinking mothers were 7.240 nmol/g and 0.033 nmol/g, respectively. A positive cutoff of 2.0 nmol/g for EtG yielded the best sensitivity and specificity (100%) to discriminate for true prenatal exposure to ethanol. It was not possible to establish a proper cutoff for EtS because of the low number of positive samples. Based on our results, meconium EtG can be proposed as an alternate biomarker for intrauterine alcohol exposure. In contrast to the 7 FAEEs, EtG is just one molecule that could be screened in meconium samples from all newborns by a simple, low-cost, easy-to-perform immunoassay, which can be routinely applied in neonatology wards for the early diagnosis of prenatal exposure to ethanol.

Fonte: PubMed

8. Population Baseline of Meconium Ethyl Glucuronide and Ethyl Sulfate Concentrations in Newborns of Nondrinking Women in 2 Mediterranean Cohorts.

Morini L, Groppi A, Marchei E, Vagnarelli F, Garcia Algar O, Zuccaro P, Pichini S.
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Fonte: PubMed

9. Ethyl glucuronide and ethyl sulfate in meconium and hair-potential biomarkers of intrauterine exposure to ethanol.

Morini L, Marchei E, Vagnarelli F, Garcia Algar O, Groppi A, Mastrobattista L, Pichini S.
Forensic Sci Int. 2010 Mar 20;196(1-3):74-7.

Abstract

This study investigated ethyl glucuronide (EtG) and ethyl sulfate (EtS) concentration in meconium and in maternal and neonatal hair (HEtG and HFAEEs, respectively) as potential markers of intrauterine exposure to ethanol together with meconium fatty acid ethyl esters (FAEEs) in a cohort of 99 mother-infant dyads, 49 coming from the Arcispedale of Reggio Emilia (Italy) and 50 from the Hospital del Mar of Barcelona (Spain). FAEEs, EtG and EtS were measured in meconium samples using liquid chromatography-tandem mass spectrometry. A head space-solid phase microextraction-gas chromatography-mass spectrometry was used to test HEtG and HFAEEs in hair samples from mothers and their newborns. Eighty-two meconium samples (82.8%) tested positive for EtG, 19 (19.2%) for EtS while 22 (22.2%) showed FAEEs levels higher than 2 nmol/g, the cut-off used to differentiate daily maternal ethanol consumption during pregnancy from occasional or no use. Although EtG and EtS in meconium did not correlate with total FAEEs concentration, a good correlation between EtG, EtS and ethyl stearate was observed. Moreover, EtG correlated well with ethyl palmitoleate, while EtS with ethyl laurate, myristate and linolenate. Neither maternal nor neonatal hair appears as good predictors of gestational ethanol consumption and subsequent fetal exposure in these mother-infant dyads. In conclusion, these data show that meconium is so far the best matrix in evaluating intrauterine exposure to ethanol, with EtG and EtS being potentially good alternative biomarkers to FAEEs.

Fonte: PubMed

10. Ethylglucuronide and ethylsulfate in meconium to assess gestational ethanol exposure: preliminary results in two Mediterranean cohorts.

Pichini S, Morini L, Marchei E, Palmi I, Rotolo MC, Vagnarelli F, Garcia-Algar O, Vall O, Zuccaro P. *Can J Clin Pharmacol*. 2009 Summer;16(2):e370-5.

Abstract

In recent years, fatty acid ethyl esters (FAEEs) in meconium emerged as reliable, direct biological markers for establishing gestational ethanol exposure. Among the minor nonoxidative products of ethanol metabolism, there are ethyl glucuronide (EtG) and ethyl sulfate (EtS).

The aim of the study was to analyse meconium specimens from two different Mediterranean cohorts to check for the presence of EtG and EtS, and to investigate the eventual correlation between meconium FAEEs and these two metabolites and their possible application as direct biomarkers of gestational ethanol exposure.

FAEEs, EtG and EtS were quantified by liquid chromatography tandem mass spectrometry in meconium samples obtained from the Neonatal Intensive Care Unit of Arcispedale Santa Maria Nuova, Reggio Emilia, Italy (N= 96) and from the Pediatric Service of the Hospital del Mar in Barcelona, Spain (N=81).

EtG was present in more than 80% meconium samples while EtS only in 50% specimens. Although the samples from Spain and Italy originated from similar socio-demographic cohort, EtG values in the Barcelona samples (median value: 101.5 ng/g) were statistically higher than those from Reggio Emilia ones (median value: 15.6 ng/g). In the Barcelona cohort, EtG values could differentiate between samples with FAEEs below and those equal or above 2 nmol/g - the cut-off used to differentiate heavy maternal ethanol consumption during pregnancy from occasional or no use.

For the first time the presence of EtG and EtS in meconium has been proven, with EtG concentration likely to discriminate heavy maternal ethanol consumption during pregnancy disclosed by FAEEs concentration in this matrix. Further investigations are needed to verify the use of these two ethanol metabolites as alternative biomarkers of chronic in utero exposure to ethanol.

Fonte: PubMed

11. Liquid chromatography with tandem mass spectrometric detection for the measurement of ethyl glucuronide and ethyl sulfate in meconium: new biomarkers of gestational ethanol exposure?

Morini L, Marchei E, Pellegrini M, Groppi A, Stramesi C, Vagnarelli F, Garcia-Algar O, Pacifici R, Pichini S.

Ther Drug Monit. 2008 Dec;30(6):725-32

Abstract

A liquid chromatography tandem mass spectrometric (LC-MS/MS) method with postcolumn addition of acetonitrile for the determination of ethyl glucuronide (EtG) and ethyl sulfate (EtS) in meconium was developed and validated using pentadeuterated EtG and pentadeuterated EtS as internal standards. The analytes were extracted from the matrix by acetonitrile, concentrated by solid phase extraction, separated using a reversed-phase chromatographic column, and quantified within 9 minutes. Lower limits of quantification were 5 and 1 ng/g meconium for EtG and EtS, respectively. Calibration curves were linear from lower limits of quantifications to 500 ng/g, with a minimum $r > 0.999$. At 3 concentrations spanning the linear dynamic range of the assay, mean recoveries ranged between 78.7% and 96.8% for EtG and between 72.1% and 95.6% for EtS. Inaccuracy was better than 8.1%, with intra-assay and interassay imprecision better than 7.2% and 10.5%, respectively. Matrix effects (ion suppression/enhancement) were found to be negligible. The analytes of interest were stable at room temperature, at 4 degrees C, when exposed to 3 freeze-thaw cycles, and when stored at -20 degrees C for up to 6 months. This sensitive and specific method was used to assess the presence of these alcohol biomarkers in meconium samples from 2 different city cohorts

Fonte: PubMed

12. Liquid chromatography-tandem mass spectrometry for fatty acid ethyl esters in meconium: assessment of prenatal exposure to alcohol in two European cohorts.

Pichini S, Pellegrini M, Gareri J, Koren G, Garcia-Algar O, Vall O, Vagnarelli F, Zuccaro P, Marchei E.
J Pharm Biomed Anal. 2008 Nov 4;48(3):927-33.

Abstract

Fatty acid ethyl esters (FAEEs) in meconium emerged as a reliable, direct biological marker for establishing fetal exposure to ethanol. We developed an LC-MS/MS method for ethyl laurate, ethyl myristate, ethyl palmitate, ethyl palmitoleate, ethyl stearate, ethyl oleate, ethyl linoleate, ethyl linolenate, and ethyl arachidonate using ethyl heptadecanoate as the internal standard. The analytes were extracted from meconium with hexane, followed by solid-phase extraction with aminopropyl-silica columns. Chromatography was performed on a C(8) reversed-phase column using water/isopropanol/acetonitrile (20:40:40, v/v/v) as a mobile phase. A triple quadrupole mass spectrometer that monitored the transitions in multiple reaction-monitoring mode was used for the detection of the analytes. Limits of quantification (LOQs) varied between 0.12 and 0.20 nmol/g. Calibration curves were linear from LOQs to 50 nmol/g for all analytes, with a minimum $r(2) > 0.99$. At three concentrations spanning the linear dynamic range, mean recoveries ranged between 53.6 and 86.7% for the different analytes. The validated method was applied to analysis of meconium in newborns of two European cities. The two cohorts presented with different prevalence of gestational ethanol consumption during pregnancy.

Fonte: PubMed

13. Alarming prevalence of fetal alcohol exposure in a Mediterranean city.

Garcia-Algar O, Kulaga V, Gareri J, Koren G, Vall O, Zuccaro P, Pacifici R, Pichini S.
Ther Drug Monit. 2008 Apr;30(2):249-54.

Abstract

The prevalence of gestational ethanol exposure and subsequent fetal exposure has been assessed in a cohort of mother-infant dyads in a Mediterranean city (Barcelona, Spain) by meconium analysis of fatty acid ethyl esters (FAEEs) after showing in this population a high prevalence of meconium opiates (8.7%), cocaine (4.4%), and cannabis (5.3%). Of the 353 meconium samples analyzed for FAEEs, 159 (45%) contained a total amount of seven FAEEs equal or above 2 nmol/g meconium, the cutoff internationally accepted to differentiate heavy maternal alcohol consumption during pregnancy from occasional use or no use at all. No parental sociodemographic differences or maternal features differentiated exposed from unexposed newborns. The prevalence of gestational consumption of ethanol was similar between women using and not using drugs of abuse during pregnancy (45.7% and 44.7% of samples with total FAEEs equal or higher than 2 nmol/g meconium, respectively). Meconium samples from newborns exposed in utero to ethanol, and positive for at least one illicit drug (cocaine, opiates, or cannabis), had total FAEEs and five of nine individual FAEEs statistically higher than the meconium samples that were negative for the most frequently used illicit drugs of abuse. Among the most prevalent FAEEs, oleic acid ethyl ester showed the best correlation to total FAEE concentration followed by palmitoleic acid ethyl ester. This study, which highlights a 45% ethanol consumption during pregnancy in a low socioeconomic status cohort, may serve as an eye opener for Europeans that gestational alcohol exposure is not endemic only in areas outside of Europe.

Fonte: PubMed