Fisioter Bras. 2023;24:(5):729-40
doi: 10.33233/fb.v24i5.5480

SYSTEMATIC REVIEW PROTOCOL

The use of cocaine and crack during pregnancy and its effects on newborns and children: a systematic review protocol

O uso de cocaína e crack durante a gestação e seus efeitos em recém-nascidos e crianças: um protocolo de revisão sistemática

Raquel Dosares Batista da Silva, Adriana Maria Rêgo Ribeiro, André Silva de Sousa, Reinaldo Oliveira Cunha, Fernanda Gabriella de Siqueira, Juliana Anézia Rodrigues do Amaral, Ana Carolina Pereira Nunes Pinto

[1]*Universidade Federal do Amapá, Macapá, Brasil*

Recebido em: 26 de maio de 2023; Aceito em: 2 de outubro de 2023.
Correspondência: Ana Carolina Pereira Nunes Pinto, anacarolinapnp@hotmail.com

How to cite
Silva RDB, Ribeiro AMR, Sousa AS, Cunha RO, Siqueira FG, Amaral JAR, Pinto ACPN. The use of cocaine and crack during pregnancy and its effects on newborns and children: a systematic review protocol. Fisioter Bras 2023;24(5):729-40. doi: 10.33233/fb.v24i5.5480

Abstract

Introduction: The use of illicit drugs represents an important public health problem in the world, especially when it comes to developing countries like Brazil. *Objective*: To evaluate the effects of cocaine exposure in utero on the motor development and mortality in newborns and children. *Methods*: We will carry out a systematic review including observational studies (cohort or case-control), published in full text or just as an abstract. The study protocol will be registered on the Prospero Platform. We will include newborns and children up to 36 months of age. We will carry out searches in the following databases: Medical Literature Analysis and Retrieval System Online (Medline) via Pubmed, Excerpta Medica dataBASE (Embase) via Elsevier, Cochrane Central Register of Controlled Trials (CENTRAL) via Cochrane Library, Latin American Literature and the Caribbean in Health Sciences (Lilacs) via the Virtual Health Library Portal and Physiotherapy Evidence Database (PEDro), with no restrictions on language or year of publication. We will assess the methodological rigor of the included studies and the

certainty of the evidence of the main results of the systematic review using the Cochrane ROBINS-E- Risk of Bias in Non- randomized Studies- of Exposure (ROBINS-E) tool and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, respectively. Two independent investigators will perform the selection of studies, data extraction, assessment of the risk of bias of included studies and assessment of the certainty of evidence. *Expected Results*: The results of this review are expected to summarize the best scientific evidence currently available regarding the effects of cocaine and crack use during pregnancy on newborns and children, and provide useful information for clinical decision-making. Furthermore, it is believed that the results of this review may expose knowledge gaps and provide a good foundation for future high-quality studies on the subject.
Keywords: pregnancy; drug abuse; crack; cocaine; newborn.

Resumo

Introdução: O consumo de drogas ilícitas representa um importante problema de saúde pública no mundo, especialmente quando se trata de países em desenvolvimento, como o Brasil. *Objetivo*: Avaliar os efeitos da exposição à cocaína durante a gestação no desenvolvimento motor e na mortalidade de recém-nascidos e crianças. *Métodos*: Realizaremos uma revisão sistemática que incluirá estudos observacionais (coorte ou caso-controle), publicados na íntegra ou apenas como resumo. O protocolo do estudo será registrado na plataforma Prospero. Incluiremos recém-nascidos e crianças com até 36 meses de idade. Realizaremos buscas nas seguintes bases de dados: Medical Literature Analysis and Retrieval System Online (MEDLINE) via Pubmed, Excerpta Medica dataBASE (Embase) via Elsevier, Cochrane Central Register of Controlled Trials (CENTRAL) via Cochrane Library, Latin American Literature and the Caribbean in Health Sciences (LILACS) via Portal da Biblioteca Virtual em Saúde e Physiotherapy Evidence Database (PEDro), sem restrições de idioma ou ano de publicação. Avaliaremos o rigor metodológico dos estudos incluídos e a certeza das evidências dos principais desfechos da revisão sistemática usando a ferramenta Cochrane Risk Of Bias In Non-randomized Studies - of Exposure (ROBINS-E) e a abordagem Grading of Recommendations Assessment, Development and Evaluation (GRADE), respectivamente. Dois investigadores independentes realizarão a seleção dos estudos, extração de dados, avaliação do risco de viés dos estudos incluídos e avaliação da certeza das evidências. *Resultados esperados*: Espera-se que os resultados desta revisão resumam as melhores evidências científicas atualmente disponíveis sobre os efeitos do uso de cocaína e crack durante a gravidez em recém-nascidos e crianças, e forneçam informações úteis para a tomada de decisões clínicas. Além disso, acredita-se que os

resultados desta revisão possam expor lacunas no conhecimento e fornecer uma boa base para futuros estudos de alta qualidade sobre o assunto.

Palavras-chave: gravidez; abuso de drogas; cocaína; crack; recém-nascido.

Introduction

The use of illicit drugs represents an important public health problem in the world, especially when it comes to developing countries such as Brazil [1]. A recent research conducted by the Brazilian Center for Informtion on Psychotropic Drugs (CEBRID) identified that cocaine consumption has increased considerably in Brazil from the 80s to the present day [2].

Cocaine is an alkaloid obtained from the leaves of Erythroxylon coca, a small tree native to South America [3], which has been used as local anesthetic care in stomatology, ophthalmollogy. Ear nose and throat surgery, as its powerful vasoconstrictive action helps reduce local bleeding [4]. From a pharmacological point of view, cocaine has effects on the cardiovascular system, which depend on an intact sympathetic nervous system and direct stimulation of the myocardium and vessels. On the other hand, crack is a smoked form and an almost pure concentrate of cocaine. It is obtained by converting the hydrochloride form back to the alkalized form. This substance may be a more dangerous form of cocaine [5]. As there are several products generated from the pyrolysis of cocaine, various psychotropic and neurotoxic effects of crack use can occur. Crack use causes short-term euphoria, as a consequence of high bioavailability and metabolism [6]. In addition, it is the free base of cocaine and acts by activating the central nervous system, increasing wakefulness, motor activity and other various changes. Both drugs can increase the irritability of the central nervous system and can lead to fetal vasoconstriction and maternal tachycardia and still cause the appearance of uterine [7].

Among these drugs, cocaine consumption has increased dramatically in the population, including in the obstetric population. Multiple factors are associated with this increase in cocaine use, including sociodemographic characteristics, risk behaviors, exposure to situations of violence and use of legal substances, namely alcohol and tobacco [1,8,4]. Studies indicate that the toxicity of the cardiovascular system with the presence of cocaine in pregnant women, whether acute or chronic use, leads to a significant increase in blood pressure, tachycardia and decrease in cardiac output and heart rate when compared to non-pregnant women. It is known that altered blood flow can trigger placental abruption, preterm delivery, low birth weight, miscarriage and drug withdrawal [8].

In parallel, the National Survey of Drug Use and Health reported an increase in crack use among women. Approximately 1.4 million people 12 to 65 years old reported having used crack cocaine and similar at some point in their lives, which corresponds to 0.9% of the population with a pronounced differential between men (1.4%) and women (0.4%) [9].

In the National Survey of Drug Use and Health, it was also possible to identify that about 90% of women whose crack consumption has increased are at the reproductive age [10]. Thus, this same problem becomes more severe in pregnant women [11], since the drugs used by the mother during pregnancy can reach the baby through the maternal-fetal circulation, and constitute a high risk factor for the intrauterine life of the baby and for its postnatal development [12,13]. In addition, the use of cocaine and/or crack during pregnancy has been associated with several risks for the development of the baby [11,14], namely: prematurity and low birth weight, neurological problems, risks of sexually trasmitted infections, higher incidence of fetuses with intrauterine growth restriction, premature births, placental abruption, preeclampsia, cognitive deficits, difficulty verbalizing, aggressiveness and depression [15,16]. In addition, they may be associated with deleterious effects, especially generating deficits in the growth and neuropsychomotor development of the child [18-20].

Given this, it is of paramount importance to conduct a systematic review on the subject, since it can fill the gaps in the literature, in addition to encourage the initiation of public policies to reduce drug use during pregnancy. Therefore, the aim of this study is to systematically review the literature to evaluate the currently available evidence on the effects of exposure to cocaine and/or crack in utero (intrautero) on the mortality rate and motor development of children after their birth.

Objective

To evaluate the effects of exposure to cocaine and/or crack in utero on mortality and motor development of children.

Methods

Type of study

This is a systematic review protocol that was reported as per the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) to Protocol (PRISMA-P) [21]. The review will be conducted in

accordance with the methodological recommendations of the Cochrane Handbook [22] and will be reported following the recommendations of PRISMA [23]. This protocol will be registered in PROSPERO platform.

Ethical aspects and location of research

The review protocol will be recorded on the PROSPERO Platform. This study will be conducted at the Federal University of Amapá (UNIFAP).

Types of studies included

We will include observational studies, such as cohort and case-control studies, published in full text.

Types of participants

We will include newborns and children up to 36 months of age.

Types of exposure

Exposure to cocaine or crack during pregnancy.

Types of comparisons

No exposure to cocaine or crack during pregnancy.

Outcomes measures

Delay in the neuropsychomotor development of the NB and mortality, evaluated by any validated and recognized instrument and newborn and children mortality.

Literature search strategy

We will perform sensitive searches (Appendix A), without limitation of year of publication or language, in the following databases : Medical Literature Analysis and Retrieval System Online (Medline) via Pubmed, Excerpta Medica dataBASE (Embase) via Elsevier, Cochrane Central Register of Controlled Trials (CENTRAL) via Cochrane

Library, Latin American and Caribbean Literature in Health Sciences (Lilacs) via Virtual Health Library Portal and Physiotherapy Evidence Database (PEDro). We will use pre-specified relevant terms and descriptors (Chart I)

Chart I - *Search strategy*

MEDLINE via PubMed

#1 pregnancy[Mesh] OR mother* OR maternal* OR pregnan* OR gestation* OR in utero OR prenatal OR pre-natal

#2 abus* OR addict* OR overdos* OR use* OR intoxication OR Intoxication[Mesh] OR exposure OR utilization

#3 Cocaine[Mesh] OR cocain* OR "Crack Cocaine"[Mesh] OR Crack OR "Cocaine Smoking"[Mesh]

#4 #2 AND #3

#5 infant, newborn[MeSH] OR infan* or neonat* OR "Infant"[Mesh] OR newborn OR pre school OR pre-school OR child* OR baby OR babies

#6 #1 AND #4 AND #5

#7 (animals [mh] NOT humans [mh])

#8 #6 NOT #7

Excerpta Medica dataBASE (Embase) via Elsevier

#1 'pregnancy'/exp OR pregnan* OR 'child bearing' OR 'childbearing' OR gestation* OR gravidity OR 'maternal'/exp OR maternal OR 'mother'/exp OR mother* OR 'prenatal'/exp OR prenatal OR pre-natal OR 'in utero'

#2 abus* OR addict* OR overuser OR use* OR intoxication OR 'exposure'/exp OR exposure OR utilization

#3 'cocaine'/exp OR cocain* OR '2beta carbomethoxy 3beta benzoxytropane' OR 'benzoylmethyl ecgonine' OR codrenine OR 'crack'/exp

#4 #2 AND #3

#5 'newborn'/exp OR newborn OR 'full term' OR infant* OR neonat* OR 'newly born' OR 'infant'/exp OR infant* OR 'baby'/exp OR baby OR babies OR 'child'/exp OR child*

#6 #1 AND #4 AND #5

#7 ([animals]/lim NOT [humans]/lim)

#8 #6 NOT #7

#9 #8 AND [embase]/lim NOT ([embase]/lim AND [medline]/lim)

Cochrane Central Register of Controlled Trials (CENTRAL) via Cochrane Library

#1	MeSH descriptor: [Pregnancy] explode all trees	24097
#2	mother* OR maternal* OR pregnan* OR gestation* OR in utero OR prenatal OR pre-natal	100821
#3	#1 OR #2	101006
#4	bus* OR addict* OR overdos* OR use* OR intoxication OR exposure OR utilization	1879591
#5	MeSH descriptor: [Cocaine] explode all trees	973
#6	cocain* OR crack	3796
#7	MeSH descriptor: [Crack Cocaine] explode all trees	85
#8	MeSH descriptor: [Cocaine Smoking] explode all trees	0
#9	{OR #5-#8}	3796
#10	#4 AND #9	3795
#11	#3 AND #10	242

Filter: Trials = 167

Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) via Portalda Biblioteca Virtual em Saúde (BVS)

#1 mh:Gravidez OR Gestação* OR mh:G08.686.784.769$ OR mãe* OR matern* OR "in utero" OR prenatal OR pre-natal

#2 abuso* OR vício* OR overdose* OR uso* OR intoxicação OR exposição OR utilização

#3 Mh:Cocaína OR cocaína OR mh:D02.145.074.722.388$ OR mh:D03.132.889.354$ OR mh:D03.605.084.500.722.388$ OR mh:D03.605.869.388$ OR mh:"Cocaína Crack" OR Crack OR mh:D02.145.074.722.388.250$ OR mh:D03.132.889.354.250$ OR mh:D03.605.084.500.722.388.250$ OR mh:D03.605.869.388.250$ OR mh:D26.878.250$ OR mh:"Fumar Cocaína" OR mh:F01.145.805.250.250$

#4 mh:"Recém-Nascido" OR Recém-Nascid* OR neonat* OR RN OR mh:M01.060.703.520$ OR infan* OR mh:Lactente OR mh:M01.060.703 OR lactent* OR pré-escolar OR pré escolar OR criança* OR bebê*

#5 #1 AND #2 AND #3 AND #4

Filter: LILACS e IBECS

(mh:gravidez OR gestação* OR mh:g08.686.784.769* OR mãe* OR matern* OR "in utero" OR prenatal OR pre-natal) AND (abuso* OR vício* OR overdose* OR uso* OR intoxicação OR exposição OR utilização) AND (mh:cocaína OR cocaína OR mh:d02.145.074.722.388* OR mh:d03.132.889.354* OR mh:d03.605.084.500.722.388* OR mh:d03.605.869.388* OR mh:"Cocaína Crack" OR crack OR mh:d02.145.074.722.388.250* OR mh:d03.132.889.354.250* OR mh:d03.605.084.500.722.388.250* OR mh:d03.605.869.388.250* OR mh:d26.878.250* OR mh:"Fumar Cocaína" OR mh:f01.145.805.250.250*) AND (mh:"Recém-Nascido" OR recém-nascid* OR neonat* OR rn OR mh:m01.060.703.520* OR infan* OR mh:lactente OR mh:m01.060.703 OR lactent* OR pré-escolar OR pré escolar OR criança* OR bebê*) AND (db:("LILACS" OR "IBECS"))

We will also check the reference lists of relevant publications. In addition, to identify recently published, ongoing and unpublished studies , we will perform searches on clinical trial platforms such as the World Health Organization (WHO) database, the International Clinical Trials Registry Platform (ICTRP) (https://www.who.int/clinical-trials-registry-platform/the-ictrp-search-portal) which includes the registration of different websites such as ClinicalTrials.gov, base widely used in Brazil and also includes the Brazilian registry (REBEC). Finally, we will contact the authors of the primary studies to identify additional studies potentially important to this review and request additional information when needed.

Selection of studies

Two fully independent authors (R.D.B.S) and (A.M.R.R.) will select the studies based on the pre-specified eligibility criteria. Initially, studies that have been indexed in more than one (duplicate) database will be excluded. In the event that there are reports with the same participants, but with different outcome measures or using different follow-up times, both reports will be included, but both reports will be considered as parts of only one study. After the analysis of potential duplicates, the evaluation will be carried out based on the titles and abstracts and, finally, the reading of the full texts for further analysis. Disagreements between authors regarding the inclusion of studies will be resolved by a third reviewer (A.C.P.N.P). We will use the Rayyan application (https://www.rayyan.ai/) to optimize the selection process [24]. The results related to the process of selection of studies will be presented in a flowchart, as recommended by PRISMA (Figure 1).

Data extraction and management

To extract the data from the included studies, we will use a spreadsheet in the Microsoft Excel 365 software. Two authors (R.D.B.S) and (A.M.R.R) will independently extract the following data: 1) Details regarding the identification (title, authors, place and date of the study) of the study; Methods (study design, total duration of the study, assessment instrument (Ex: Bayley Scales of Infant Development PDI, Infant Monitoring Questionnaire (IMQ); 2) Participants: Age at evaluation, gestational age, mother's age, mother's educational level, use of cigarettes, alcohol and other drugs (Ex: marijuana), type of delivery, complications during childbirth, inclusion and exclusion criteria; 3) Exposure: type of exposure (cocaine or crack or both); exposure details: (dose, duration, frequency and gestational age of use); 4) Results: NPMD: time points collected and relayed, number of participants lost/not evaluated, method to deal with missing

prticipants data; 5) Notes: occurrence of funding for the study and potential conflicts of interest of the study authors. Disagreement or disagreements will be resolved by a third part author (A.C.P.N.P). In the absence of information or incomplete information, the authors of the studies will be contacted.

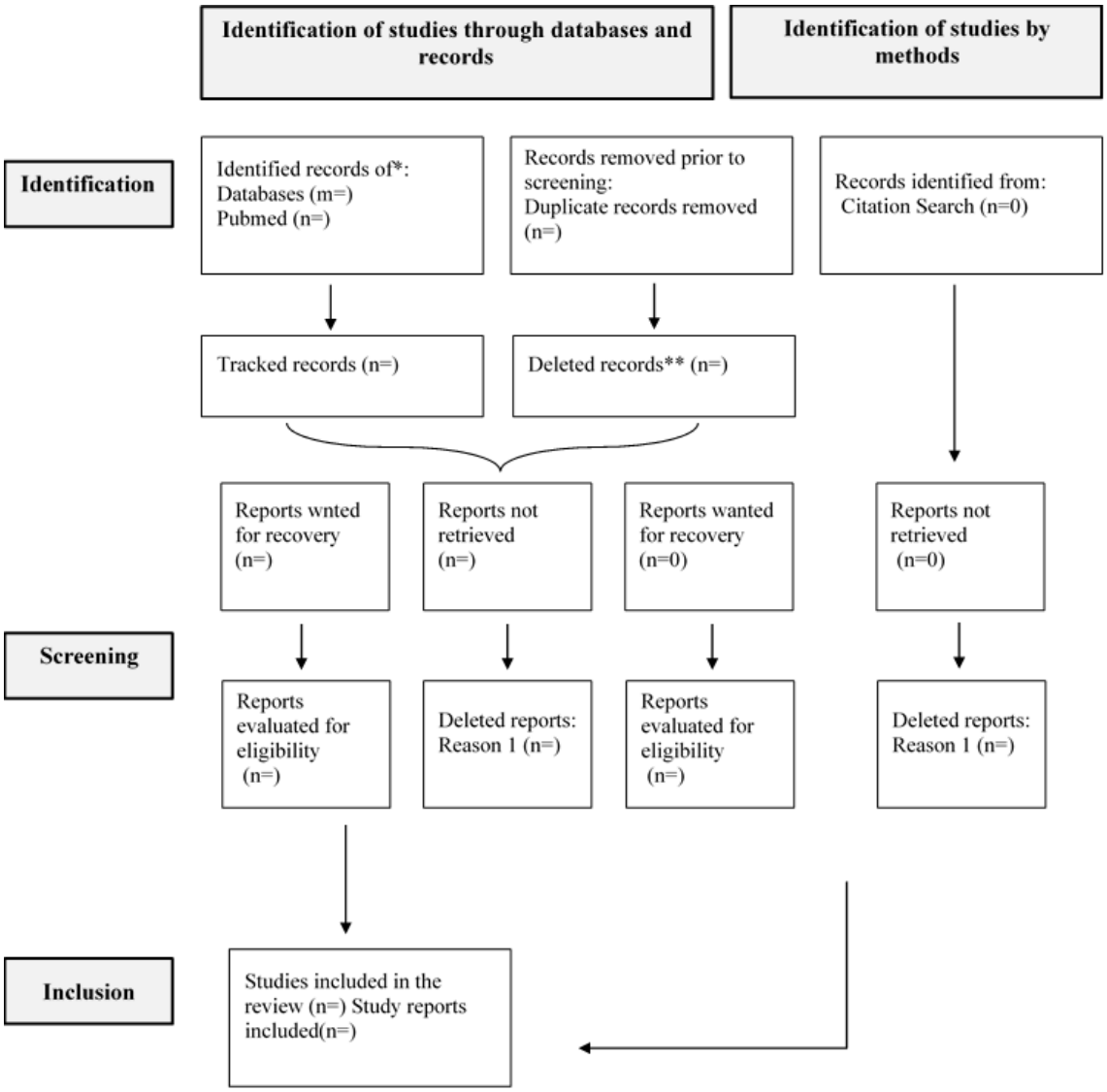

Figure 1 - *Demonstration on how studies will be presented in a flowchart in the systematic review*

Data extraction and management

To extract the data from the included studies, we will use a spreadsheet in the Microsoft Excel 365 software. Two authors (R.D.B.S) and (A.M.R.R) will independently extract the following data: 1) Details regarding the identification (title, authors, place and date of the study) of the study; Methods (study design, total duration of the study, assessment instrument (Ex: Bayley Scales of Infant Development PDI, Infant Monitoring

Questionnaire (IMQ); 2) Participants: Age at evaluation, gestational age, mother's age, mother's educational level, use of cigarettes, alcohol and other drugs (Ex: marijuana), type of delivery, complications during childbirth, inclusion and exclusion criteria; 3) Exposure: type of exposure (cocaine or crack or both); exposure details: (dose, duration, frequency and gestational age of use); 4) Results: NPMD: time points collected and relayed, number of participants lost/not evaluated, method to deal with missing prticipants data; 5) Notes: occurrence of funding for the study and potential conflicts of interest of the study authors. Disagreement or disagreements will be resolved by a third part author (A.C.P.N.P). In the absence of information or incomplete information, the authors of the studies will be contacted.

Evaluation of methodological rigor and certainty of evidence

The assessment of the risk of bias of the included studies will be carried out by two independent authors (R.D.B.S.) and (A.M.R.R.) through the tool developed by Cochrane, called Risk of Bias in No- randomized Studies- of Exposure – ROBINS-E) [22]. Disagreements will be resolved by consensus or, if necessary, by a third party reviewer (A.C.P.N.P). The following domains will be evaluated: bias due to confounding factors, bias due to exposure assessment, bias in the selection of participants for the study (or for analysis), bias due to post-exposure interventions, bias due to missing data, bias in the evaluation of the outcome, and bias in the selection of the reported outcome. Each domain will be judged as: low risk of bias, some concerns about the risk of bias, high risk of bias, or very high risk of bias. We will contact the authors of the studies to clarify any unclear or missing information about the domains evaluated.

We will use the Grading System of Recommendations Assessment, Development and Evaluation (GRADE, 2004) to classify the certainty of evidence. To achieve this goal, we will consider factors that may decrease certainty in the evidence: (i) the overall risk of bias of the included studies; (ii) the indirection of evidence; (iii) the inconsistency of the results; (iv) the accuracy of the estimates; and (v) the risk of publication bias. We will also evaluate three factors that can increase the certainty of the evidence, which are: (i) high magnitude of effect; (ii) residual confounding factors; and (iii) dose-response gradient. The assessment of the risk of bias and the certainty of the evidence will be carried out by two evaluators independently (R.D.B.S. and A.M.R.R.) and any disagreements will be resolved through analysis by a third examiner (A.C.P.N.P). We will use the GRADE profiler software, available online (https://gdt.gradepro.org/app/) to summarize our judgments about the certainty of the evidence for each major outcome. As recommended by the Cochrane Library, the

judgment and reasons for the trial will be presented in a table containing the main findings for the outcome evaluated, at all points of time found.

Statistical analysis

Provided that at least two studies present sufficient homogeneity regarding the participants, interventions and outcomes evaluated, we will group the results into meta-analyses. If the data are insufficient to be included in a meta-analysis, we will contact the authors of the studies to request access to the missing data. If the data are insufficient even after contact with the author, the results of the study will be summarized only in narrative synthesis.

When it is possible to perform meta-analyses, we will group data using the inverse variance method and the random effects model in Software Review Manager 5.4 [25]. When possible, continuous variables will be summarized through the difference of means (post and pre-intervention) with a 95% CI. In the absence of results reported as differences in means, we will use the data reported after the intervention. If studies use different measurement instruments to assess continuous outcomes, we will group the data reporting them as differences in standardized means. The dichotomous variables will be summarized using odds ratio (OR) with a 95% CI.

To estimate the heterogeneity between the studies in each meta-analysis, we will use the I2 statistic. If heterogeneity is significant (I2 > 50%), we will explore the sources of hethoregeneity in subgroup or sensitivity analyses as recommended by the Cochrane Manual for Systematic Reviews of Interventions [22]. If there is slight clinical or methodological heterogeneity, we will also investigate the sources of heterogeneity through subgroup analyses, considering maternal age, drug use, dose of exposure. We will also perform sensitivity analyses, considering only studies with a low risk of bias. In the event that at least 10 studies are included in a meta-analysis, the risk of publication bias will be assessed through the analysis of the funnel plot and the Egger test in Software R ((https://www.r-project.org/) [22].

Impacts and expected results

The present study proposes to perform a systematic review update investigating the use of cocaine and crack during pregnancy and its effects on newborns and children and, if possible, to gather the data in meta-analyses to reduce the probability of type 2 error in comparisons. The results of this review will help clarify if there are new studies

to be published on the subject, as well as to alert to the health care of the child. In addition, notify public policies to pay attention to this point.

Possible limitations can be found, such as the presence of biased studies or studies that do not make it possible to accurately estimate the effects of esxposition to cocaine or crack during pregnancy. However, transparency, methodological rigor, evaluation of the certainty of evidence for each outcome and extensive and careful searches will enable a safer and more reliable clinical response, providing useful information for clinical decision-making in physical therapy practice, based on the best evidence currently available. In addition, it is believed that the results of this review may expose knowledge gaps and support future high-quality studies on the subject.

Conflitos de interesse
Não há

Fontes de financiamento
Um dos autores é bolsista do Programa Institucional de Bolsas de Iniciação em Desenvolvimento Tecnológico e Inovação – CNPq

Contribuição dos autores
Concepção e desenho da pesquisa: Silva RDB, Ribeiro AMR, Pinto ACPN; *Coleta de dados*: Silva RDB, Ribeiro AMR; *Análise e interpretação de dados*: Silva RDB, Ribeiro AMR, Sousa AS, Cunha RO, Pinto ACPN; *Análise estatística*: Silva RDB, Ribeiro AMR, Pinto ACPN; *Redação do manuscrito*: Silva RDB, Ribeiro AMR, Pinto ACPN*; Revisão crítica do manuscrito quanto ao conteúdo intelectual importante*: Silva RDB, Ribeiro AMR, Sousa AS, Cunha RO, Nogueira FGSB, Amaral JAR, Pinto ACPN

Referências

1. Guimarães RA, Souza MM, Caetano KAA, Teles SA, Matos MA. Use of illicit drugs by adolescents and young adults of an urban settlement in Brazil. Rev Assoc Med Bras. 2018;64(2):114-118. doi: 10.1590/1806-9282.64.02.114
2. Escritório das Nações Unidas sobre Drogas e Crime. Relatório Mundial sobre Drogas 2015. 2015 [citado 2017 Jan 6]. Disponível em: https://www.unodc.org/documents/wdr2015/World_Drug_Report_2015.pdf
3. Aghamohammadi A, Zafar, M. 2016. Crack abuse during pregnancy: Maternal, fetal and neonatal complication. Journal of Maternal-Fetal and Neonatal Medicine 2016;29(5):795–97. doi: 10.3109/14767058.2015.1018821
4. Dia Nacional de Combate às Drogas e ao Alcoolismo. Biblioteca Virtual em Saúde. [citado 2023 fev 20]. Disponível em: https://bvsms.saude.gov.br/20-02-dia-nacional-de-combate-as-drogas-e-ao-alcoolismo/
5. Santos JF, Cavalcante CMB, Barbosa FT, Gitaí GLD, Duzzioni M, Tilleli CQ, et al. Maternal, fetal and neonatal consequences associated with the use of crack cocaine during the gestational period: a systematic review and meta-analysis. Arch Gynecol Obstet. 2018;298(3):487-503. doi: 10.1007/s00404-018-4833-2
6. Garcia RCT, Dati LMM, Fukuda S, Torres LHL, Moura S, Carvalho, et al. 2012. Neurotoxicity of anhydroecgonine methyl ester, a crack cocaine pyrolysis product. Toxicological Sciences 2012;128(1):223–34. doi: 10.1093/toxsci/kfs140
7. Hoffman RS, Henry GC, Howland MA, Weisman RS, Weil L, Goldfrank LR. Associação entre a toxicidade da cocaína com risco de vida e a atividade da colinesterase plasmática. Ann Emerge Med 1992; 21:247-253.
8. Eduardo Tsuyoshi Yamaguchi, Mônica Maria Siaulys Capel Cardoso, Marcelo Luis Abramides,Torres Arthur Guerra de Andrade. Abuso de drogas durante a gravidez. Arch. Clin. Psychiatry. 2008;35(suppl 1). doi: 10.1590/S0101-60832008000700010

9. National Survey on Drug Use and Health (NSDUH-2015). [citado 20 fev 2023]. Disponível em: https://catalog.data.gov/dataset/national-survey-on-drug-use-and-health-nsduh-2015
10. National Survey on Drug Use and Health (NSDUH-2008). Data.Gov. [citado 20 fev 2023]. Disponível em: https://catalog.data.gov/dataset/national-survey-on-drug-use-and-health-nsduh-2008
11. Reis FT, Loureiro RJ. Repercussões neonatais decorrentes da exposição ao crack durante a gestação. Rev Eletrônica Saúde Mental Álcool Drog. 2015;11(4):217-24. doi: 10.11606/issn.1806-6976.v11i4p217-224
12. Matos JC, Mello JM, Colombo JVP, Melo SR. Efeitos neurológicos da exposição pré-natal à cocaína/crack. Arquivos do Mudi 2011;15:8-16. Disponível em: https://periodicos.uem.br/ojs/index.php/ArqMudi/article/view/21067
13. LENAD – II Levantamento Naciona de Álcool e outras Drogas - 2012. Organizado por: Ronaldo Laranjeira; et. al. São Paulo: Instituto Nacional de Ciência e Tecnologia para Políticas Públicas de Álcool e Outras Drogas (INPAD). UNIFESP; 1014.
14. National Survey on Drug Use and Health (NSDUH-2008). Data.Gov. Disponível em: https://catalog.data.gov/dataset/national-survey-on-drug-use-and-health-nsduh-2008.
15. Moreira DJS, Santos IM, Dunningham WA. Crack exposure during pregnancy and its maternal, fetal and neonatal repercussions: a systematic review. Revista Brasileira de Neurologia e Psiquiatria 2022 set/dez;26(3):84-90. Disponível em: http://www.revneuropsiq.com.br/rbnp/article/view/946
16. Burkett G, Bandstra ES, Cohen J. Cocaine-related maternal death. Am J Obstet Gynecol. 1990;163:40–41. doi: 10.1016/s0002-9378(11)90662-0
17. Serino, MA, Dana, Bradley S. Peterson, MD, and Tove S. Rosen, MD. Psychological functioning of women taking illicit drugs during pregnancy and the growth and development of their offspring in early childhood. Journal of Dual Diagnosis 2018;14.3:158-170. doi: 10.1080/15504263.2018.1468946
18. Hurt H. Crianças expostas à cocaína: acompanhamento até 30 meses. Journal of Developmental & Behavioral Pediatrics 1995;16(1):29-35.
19. Messinger D. The maternal lifestyle study: cognitive, motor, and behavioral outcomes of cocaine-exposed and opiate-exposed infants through three years of age. Pediatrics 2004;113(6):6:1677-1685. doi: 10.1542/peds.113.6.1677
20. Midon MZ, Gerzon LR, Almeida CS. Crack and motor development of babies living in an assistance shelter. ABCS Health Sciences. 2019. doi: 10.7322/abcshs.2019159.1428
21. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1. doi: 10.1186/2046-4053-4-1
22. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane, 2022. Available from www.training.cochrane.org/handbook
23. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:71. doi: 10.1136/bmj.n71
24. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev 2016;5(1):210. doi: 10.1186/s13643-016-0384-4
25. Review Manager (RevMan). Versão 5.3. Copenhagen: Nordic Cochrane Centre, Cochrane. 2020. (computer program)

This is an open access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.