Newborn outcomes exposure to crack cocaine during pregnancy: a critical review

Recém-nascidos expostos ao crack durante a gestação: uma revisão crítica

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Tatiane Britto da Silveira
Doutora em Ciências da Saúde pela Universidade Federal do Rio Grande - FURG
Instituição: Universidade Federal do Rio Grande - FURG
Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.
CEP: 96203-900
E-mail: taty.psic03@gmail.com

Marina dos Santos
Doutora em Ciências da Saúde pela Universidade Federal do Rio Grande - FURG
Instituição: Universidade Federal do Rio Grande - FURG
Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.
CEP: 96203-900
E-mail: marina.wicks@gmail.com

Ronan Adler Tavella
Doutorando em Ciências da Saúde pela Universidade Federal do Rio Grande - FURG
Instituição: Universidade Federal do Rio Grande - FURG
Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.
CEP: 96203-900
E-mail: ronan_tavella@hotmail.com

Rodrigo de Lima Brum
Mestrando em Ciências da Saúde pela Universidade Federal do Rio Grande - FURG
Instituição: Universidade Federal do Rio Grande - FURG
Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.
CEP: 96203-900
E-mail: rodrigo.brum.93@gmail.com

Edariane Menestrino Garcia
Doutora em Ciências da Saúde pela Universidade Federal do Rio Grande - FURG
Instituição: Universidade Federal do Rio Grande - FURG
Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.
CEP: 96203-900
E-mail: nanamenestrino@hotmail.com

Adriane Netto de Oliveira
Doutora em Enfermagem pela Universidade Federal de Santa Catarina
Instituição: Escola de Enfermagem, Universidade Federal do Rio Grande - FURG
Endereço: Rua Visconde de Paranaguá, 102, Centro, Rio Grande - RS, Brasil.
CEP: 96203-900
E-mail: adrianenet@vetorial.net
ABSTRACT
Crack cocaine is a psychotropic and neurotoxic drug with high prevalence of consumption, considerate a public health problem and identified as risk factors to human health. Crack cocaine use among women in reproductive age increased in few year and the literature of the neonatal exposure to this substance during pregnancy are limited. Thus, this critical review discusses the major newborn outcomes reported in original studies, highlighting neurologic abnormalities and malformations outcomes. Sixteen studies were included in this review. The main physiological outcome found in newborn exposure to crack cocaine during gestation were lower birth weight; preterm birth; growth restricted infants; lower 5-minute Apgar scores; small for gestational age; and, small head circumference and congenital malformations. There were several negative neurologic and outcomes were reported on the literature. Moreover, there were still no consensus and the main criticism in this area is the limited studies available.

Keywords: Illicit drugs, gestation, neonate.

INTRODUCTION
Drug abuse is one of the major social and public health problems in the world (UNODC, 2017). Cocaine is a product known since the beginning of history, considered a drug with great...
potential dependence, and it is classified as a stimulant of the Central Nervous System (CNS) (Behnke, Eyler, Garvan, & Wobie, 2001). Cocaine can generate other drugs, such as crack cocaine, a cheap product, which can reach all social classes.

Crack cocaine is a smoked form and almost pure concentrate of cocaine. It is obtained by the conversion of hydrochloride form back into alkalinized form. Crack cocaine may be a more dangerous form of cocaine (dos Santos et al., 2018). There are several psychotropic and neurotoxic effects of crack cocaine use, because of products generated from cocaine pyrolysis (Garcia et al., 2012). Indeed, crack cocaine use lead short-duration euphoria as a consequence of high bioavailability and metabolization.

The economic impact of crack addiction is not only due to the large number of cases, but to the high costs of detoxification, prolonged hospitalization, high morbidity and criminality (Guimarães, Dos Santos, Freitas, & Araujo, 2008). Crack cocaine consumption increased mainly after the 80’s worldwide (Balbinot, Alves, Amaral Junior, & Araujo, 2011). According to the World Drug Report of 2017, presented by the United Nations Office on Drugs and Crime (UNODC, 2017), crack cocaine addiction is one of the public health problems in different countries and is identified as the twenty highest risk factors for human health.

The National Survey of Drug Use and Health, reported an increase of crack cocaine use among women and about 90% are in childbearing age (NSDUH, 2008). However, the exact prevalence of crack cocaine use during pregnancy is still not clear (Aghamohammadi & Zafari, 2016). The prevalence of illicit drug among pregnant women is approximately 5.2% at any time during pregnancy (NSDUH, 2008), which poses great risks to woman and infant health (Schempf, 2007).

The negative effects of crack cocaine use are well recognized. However, physiological changes during pregnancy increase crack cocaine effects, especially its cardiovascular toxicity (Botelho, Rocha, & Melo, 2013). In addition, chemical substances present in crack cocaine can cross the placental blood barrier and may affect intrauterine fetal development (Matos, Melo, Colombo, & Melo, 2011). The influences of this substance to newborn health are a concern (Aghamohammadi & Zafari, 2016). The literature identified newborn crack cocaine intoxicated as “crack babies” (Duailibi, L.B.; Ribeiro, M.; Laranjeira, 2008).

The literature about crack cocaine use during pregnancy and its effects in newborn are still controversial and restrict. Thus, the purpose of the study was evaluated, through a literature review, studies that reported neonatal outcomes exposure to crack cocaine during pregnancy.

2 MATERIAL AND METHODS

Search strategy
This study is a critical review of the literature on the topic of unfavorable outcomes in newborns from crack cocaine use during pregnancy. The research was carried out in August 2018, through the databases: Pubmed/Medline (Medical Literature Analysis and Retrieval System Online), Lilacs (Literatura Latino-Americana e do Caribe em Ciências da Saúde), Scielo (Scientific Electronic Library Online), Web of Science and Google Scholar.

The data search occurred from the descriptors: "crack", "pregnant women", "child OR children OR newborn", without date, country and language restrictions. The titles and abstracts were independently screened by two reviewers (RAT and MS). After consulting the databases and the application of the search strategies, duplicates between studies in different databases were identified. All pre-selected abstracts were read. In cases where the abstract reading was not sufficient, the full article was read to ensure its inclusion. After that, the integral reading of each study was performed, and the thematic analysis of content of the articles was carried out.

Inclusion and exclusion criteria
To be included in this review, studies must followed criteria adopted: studies addressing newborn outcomes from pregnant users of crack cocaine. Articles were excluded when they presented some of the following criteria: a) literature reviews, b) articles with socioeconomic outcomes, c) articles that did not provide the text in full or without a summary; d) articles that did not involve human beings; e) articles selected by the search system, but did not cover the outcome; and f) articles that addresses the outcomes of cocaine instead of crack in their results.

Data extraction and statistical analysis
Information was extracted from all eligible studies, including publication date, country, study design, sample size and newborn outcomes. In clinical trials studies were used only baseline data from the crack cocaine users.

3 RESULTS
A total of 188 titles were identified by searching the electronic databases, of which 172 were excluded during screening based on the inclusion and exclusion criteria (Figure 1).
Thus, a total of 16 studies were included. The extracted data for each study are presented in table 1. The main birth outcomes found were: lower birth weight; preterm birth; growth restricted infants; lower 5-minute Apgar scores; small for gestational age; and, small head circumference. Regarded to neurologic outcomes, several behavior abnormalities were cited. While, just one study observe association with malformations (Xavier, Gomes, Ribeiro, Mota, & Alvarez, 2017).
| Sample size | Neomatal repercussions | Neurologic and malformations outcomes |
|-------------|------------------------|---------------------------------------|
| Leblanc, 1987 | EUA | Case-control | 38 | Low birth weight | Premature delivery | Abnormal neuromuscular symptoms | Tremulousness | Irritability | Muscular rigidity |
| Cheruku, 1987 | EUA | Cohort | 25 | Low birth weight | Premature delivery | Abnormal neuromuscular symptoms | Tremulousness | Irritability | Muscular rigidity |
| Cheruku, 1988 | EUA | Cohort | 55 | Low birth weight | Premature delivery | Abnormal neuromuscular symptoms | Tremulousness | Irritability | Muscular rigidity |
| Bateman et al., 1993 | EUA | Cohort | 748 | Low birth weight | Premature delivery | Not verified |
| Eyler et al., 1994 | EUA | Cohort | 340 | Congenital anomalies | Placental abruption | Not verified |
| Sprauve et al., 1997 | EUA | Cohort | 483 | Growth-restricted infants | Not verified |
| Eyler et al., 1998 | EUA | Cohort | 308 | Premature delivery | Not verified |
| Behnke et al., 2001 | EUA | Cohort | 272 | Lower birth weight | Not verified |
| Fiocchi & Kingress, 2001 | EUA | Cross-section | 76 | Low birth weight | Premature delivery | Not verified |
| Zeviachi et al., 2014 | Brazil | Cross-section | 12 | Low birth weight | Premature delivery | Not verified |
| Reis & Lourenco, 2015 | Brazil | Cross-section | 14 | Premature delivery | Small for gestational age | Not verified |
| Madini et al., 2016 | Brazil | Cross-section | 57 | Lower birth weight | High inflammatory state | Not verified |
| Agahamohammadi & Zafar, 2016 | Iran | Control case | 88 | Lower birth weight, Premature delivery | Not verified |
| Madini et al., 2017 | Brazil | Cross-section | 57 | Lower birth weight | High lipid peroxidation | Not verified |
| Xavier et al., 2017 | Brazil | Qualitative research | 15 | Premature delivery | Cleft palate and cleft lip | Not verified |
| Parcianello et al., 2017 | Brazil | Cross-section | 57 | Low birth weight | Lower 5-minute Apgar score | Not verified |

**Exacerbated Micro reflex, Exacerbated heightened hypoactivity irritability hypoactivity weak sucking reflex lethargy Tremulousness**
DISCUSSION

The majority of studies reports assessment of alcohol, marijuana or cocaine use during pregnancy (Addis, Moretti, Ahmed Syed, Einarson, & Koren, 2001; Castro, Guilam, Sousa, & Marcondes, 2013; Frank, Augustyn, Knight, Pell, & Zuckerman, 2001; Gouin, Murphy, & Shah, 2011). In this critical review, it was availed studies that reported newborn outcomes exposure to crack cocaine during the pregnancy. Worldwide, crack cocaine use is a severe public health (UNODC, 2017), being one of the most prevalent form of the drug abused, mainly between EUA and Brazil (Rotta & Cunha, 2000). According to the literature, pregnant women among the lower economic classes used this drug, especially, due to the lower prices (Behnke, Eyler, Garvan, Wobie, & Context, 2017; Eyler, Behnke, Conlon, Woods, & Wobie, 1998).

The prevalence of intoxicated children by crack cocaine increased (dos Santos et al., 2018), because its metabolites cross the placenta and reach fetal tissues in high concentrations, which might affect child development (Zavaschi et al., 2014). The negative effect of crack cocaine do not depend on the dose, suggesting that any exposure levels increase the risk to newborn (White & Lambe, 2003). Indeed, crack cocaine effects in utero are very different for each newborn (Mardini et al., 2017; Parcianello et al., 2018) and the exposure impact may continue after birth, resulting in long-term effects on the child’s organism (dos Santos et al., 2018; Jones, 2015).

The results show innumerous negative outcomes for newborn health. Concerning the common physiological outcomes, low birth weight (Aghamohammadi & Zafari, 2016; Bateman, Ng, Hansen, & Heagarty, 1993; Behnke et al., 2001; Bender et al., 1995; R Cherukuri, Minkoff, Feldman, A, & Glass, 1988; Radha Cherukuri, Howard, Parekh, Feldman, & Glass, 1987; Fiocchi & Kingree, 2001; Leblanc, 1987; Mardini et al., 2016, 2017; Parcianello et al., 2018; Sprauve, Lindsay Michael K., Herbert, & Graves, 1997; Zavaschi et al., 2014) preterm delivery (Aghamohammadi & Zafari, 2016; Bateman et al., 1993; Behnke et al., 2001; R Cherukuri et al., 1988; Radha Cherukuri et al., 1987; Eyler et al., 1998; Fiocchi & Kingree, 2001; Leblanc, 1987; Reis & Loureiro, 2015; Sprauve et al., 1997; Xavier et al., 2017) and small for gestational age (Behnke et al., 2001; Leblanc, 1987; Reis & Loureiro, 2015) were well establish risk between newborn exposure to crack cocaine during pregnancy (dos Santos et al., 2018). The low 5-minute Apgar score (Parcianello et al., 2018; Sprauve et al., 1997) and small head circumference (Behnke et al., 2001; R Cherukuri et al., 1988; Radha Cherukuri et al., 1987; Leblanc, 1987) were also reported as a risk to crack cocaine exposure.

The most common outcomes in children exposure to crack cocaine were preterm delivery, low birth weight, small for gestational age and small head circumference, when compared with the drug-free groups. These outcomes were possibly associated with nutrition problems during pregnancy, due to the gradual reduction in placental blood flow produced by vasoconstriction,
decreasing oxygen and nutrient transfer to the fetus (Aghamohammadi & Zafari, 2016) and complications in brain development (McCarthy, Kabir, Bhide, & Kosofsky, 2014; Nordstrom-Klee, Delaney-Black, Covington, Ager, & Sokol, 2002). Also, it is important that pregnant crack cocaine users usually present inadequate nutrition intake (Eide, Stevens, Schuetze, & Dombkowsko, 2006; Fajemirokun-Odudeyi & Lindow, 2004).

It is important to highlight the fact that newborn of crack cocaine user mothers are private of breastfed, do not receiving benefits of breast milk, which get worse birth outcomes and may affect the health adult life (Xavier et al., 2017). Breast milk is an extremely complex and highly variable fluid to nourish infants and protect them from disease whilst their own immune system matures. The composition of human breast milk changes matching the infant’s requirements (Fujita et al., 2012; Michaelsen, Skafte, Badsberg, & Merete, 1990). Therefore, the breast milk is vital for health development of newborn (Andreas, Kampmann, & Mehring Le-Doare, 2015).

Another important physiological newborn outcome reported were several congenital malformations such as, cleft palate and cleft lip, anomalies of mandible and ear, microcephaly, born without a lung and congenital malformation (Xavier et al., 2017). Regarding malformations outcomes, there were still no consensuses (Sprauve et al., 1997). In relation to neurologic outcomes, studies observed tremulousness; irritability, muscular rigidity (R Cherukuri et al., 1988; Leblanc, 1987) neuromuscular symptoms (Radha Cherukuri et al., 1987); abnormal receptive language and visual motor (Bender et al., 1995); exacerbated motor reflex, exacerbated/heightened hypoactivity, irritability hypotonia, weak sucking reflex, lethargy and tremors (Reis & Loureiro, 2015). It was observed high lipid peroxidation, representing the inflammatory response system exacerbated.

Neurologic abnormalities are frequently reported in newborn of crack cocaine user mothers, although, biological mechanisms of these alterations are still unclear. It was suggest that crack cocaine acts on maternal and fetus central nervous system, inhibiting dopamine, noradrenaline and serotonin reuptake at the presynaptic terminals, and exacerbating their effects (Span, 2011). Additionally, the use of crack affects the monoamine neurotransmitter functions of the developing fetal brain (McCarthy et al., 2014). All these factors can generate inadequate neuronal functions development and potentiating neurological effects of newborn.

Also, newborn from crack cocaine user mothers frequently receive inadequate prenatal care (Sprauve et al., 1997) or abnegate the addiction on this moment, which make more difficult the identification of newborn at risk (Camargo & Martins, 2014). Indeed of physiological outcomes observed, series of psychological consequence on postnatal may affect the newborns, since their mothers, in general, do not form affective bonds, experience mothering and frequently abandoned their babies (Xavier et al., 2017; Yabuuti & Bernardy, 2014).
Crack cocaine use during pregnancy cause serious health outcomes and social consequences for newborn. Since, only a few pregnant women report drug use, the prevalence of treatment is low during pregnancy. Indeed, symptoms of crack cocaine addiction can be confused with the effects by other substances or with diseases (Rayburn, 2007). Thus, the number of newborns exposure to crack cocaine may be higher than the reported in the found literature. Although recent research has shown more robustly the impact of crack cocaine on neonatal health, this is a field of research that must be explored, since it has a multifactorial effect. Countries with a crack cocaine epidemic, such as Brazil, should prioritize actions to minimize the harm to these children, aiming at social equity.

5 CONCLUSION

This review show the most common birth outcomes in newborn exposure to crack cocaine during pregnancy were preterm delivery, low birth weight, small for gestational age and small head circumference, highlighting neurologic abnormalities and malformations outcomes. There were several negative neurologic and malformations outcomes observed, however, there were still no consensus when compared newborn from drug-free mothers.

This research corroborates the need of further studies on the subject. Thus, future studies are needed to known how crack cocaine exposure during pregnancy may affect in long-term the development of these newborns, since, this population grows gradually. Besides that, it is need education as well as health professionals prepared to deal with this emerging demand.

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