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REVIEW ARTICLE

Factors medicated that influence the production of breast milk.

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Breast Feeding,
Lactation,
Lactation Disorders,
Drug Therapy,
Weaning.

Abstract

Introduction: Several factors may affect the production of breast milk - among them, the difficulty in breastfeeding per se, the reduction of oxytocin due to stress, and the use of medication. In this study, a systematic review of the subject has been made through the use of the following databases: PubMed, Scielo, and LILACS. **Objective:** To evaluate the factors medicated that influence breas tmilk production. **Discussion:** Medications such as galactagogues and lactation inhibitors interfere in the process - either increasing or decreasing the volume of milk produced by the mothers. **Conclusão:** On the other hand, medications like metoclopramide, sulpiride, and domperidone are galactagogues, that is, they increase milk production. Among the medications that may inhibit lactation, pseudoephedrine stands out. However, further studies are necessary to evaluate the actual safety of mothers use of medication while breastfeeding.

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INTRODUCTION

Human milk plays a fundamental role in the growth, development and maintenance of a child's health. Currently, the recommendation of breast milk for newborn children, including preterm and low birth weight newborns, is unanimous and the World Health Organization (WHO) recommends exclusive breastfeeding in the first six months of life.[1,2]

According to ENANI - 2019 (National Study of Child Food and Nutrition), which evaluated the prevalence and practices of breastfeeding in Brazilian children under 2 years of age with a sample composed of 14,558 children living in 12,424 households. In Brazil, 96.2% of children under two years of age were ever breastfed, and 62.4% were breastfed within the first hour of life. The prevalence of exclusive breastfeeding in children under 6 months was 45.8% in Brazil, with a higher prevalence in the southern region (54.3%), followed by the Southeast (49.1%), Central-West (46. 5%), North (40.3%) and Northeast (39%), with no statistically significant differences among the regions.[3]

Ensuring exclusive breastfeeding until the ideal age still constitutes an important challenge in Brazil. In this sense, there are several factors that influence the early interruption of exclusive breastfeeding, from false information to difficulties in offering breast milk. However, it is up to healthcare professionals to fully understand the aspects related to the benefits of breast milk for the health and well-being of infants and women to provide better assistance in their follow-up. Exclusive Breastfeeding has benefits beyond the nutritional field and offers a lower risk of developing chronic diseases such as diabetes, hypertension, obesity and provides protection against different types of neoplasms to the mother. On the other hand, there are still obstacles in promoting quality breastfeeding, especially for mothers and infants in situations of greater social vulnerability, an aspect that must be considered in healthcare.[4]

The use of medications is one of the factors that can affect mothers' milk production, as some types can increase or decrease milk production by the nursing mother. The use of medications by breastfeeding mothers is a very common practice and even though they have all the benefits of breast milk, there are situations in which the risk/benefit of drug therapy must be considered, as some medications can pass into breast milk, which could be harmful to the newborn. Therefore, mothers report that, out of fear, they often end up interrupting breastfeeding when there is a need to use medication.[5]

During breastfeeding, the use of medications by mothers is often necessary to protect, improve or restore maternal health. However, it may result in unintentional exposure of the infant to the medicine.[6] It is important to advise the use of only effective and safe medications during lactation. Even though there is a limited number of medications identified as potentially or probably harmful to infants; still, breastfeeding mothers are often told to stop breastfeeding while taking medications.[7]

The importance of identifying the factors that affect and interfere with milk production is due to breastfeeding being associated with nutritional, immunological, affective, economic and social benefits. Therefore, it is of fundamental importance to identify mainly the medicinal factors associated with low or high milk production.[8] Given these settings; the present study aimed to analyze the medicinal factors that influence mothers' milk production.

METHODOLOGY

Study type

Narrative review paper.

The study carried out followed the principles of exploratory study, through bibliographical search.

Step - Sources

We ran a search on the subject, using PubMed, Scielo and LILACS databases.

Inclusion criteria:

For source selection we used references that addressed the topic of factors that influence milk production, use of medications by mothers during breastfeeding, galactagogues, metoclopramide, domperidone, sulpiride and lactation inhibitors.

All original papers indexed in the period between January 1, 1995 and December 31, 2022, with an experimental design (clinical trials, randomized or not), observational (case-control studies, cohort studies and before and after studies) and systematic review papers were included.

Exclusion criteria:

All original papers indexed in the period prior to 1995 were excluded.

References that did not address the subject of the present study and meta-analyses were excluded.

Time limit

We selected papers published between 1995 and 2022, including those available online in 1994 that were published in 1995.

Languages

We selected papers written in English, Portuguese or Spanish.

Data collection

a) Exploratory reading of all selected material (quick reading that aims to check whether the study consulted is of interest to our paper);

b) Selective reading (more in-depth reading of papers directly related to the topic);

c) Record of information extracted from sources (authors, year, method, results and conclusions).

Analysis and Interpretation of results

At this stage, an analytical reading was carried out with the purpose of ordering and summarizing the information contained in the sources.

Discussion of Results

Analysis and discussion of data obtained in the previous stage.

Themes:

The following topics will be covered: Difficulties During Breastfeeding, Change in Oxytocin Production, Regulation of the Volume of Milk Produced, Lactation Feedback Inhibitor (LFI), Galactagogues, Metoclopramide, Domperidone, Sulpiride, Other Galactagogue Drugs and Lactation Inhibitors .

DISCUSSION

Breastfeeding comprises a remarkable and complex process, and it is essential to consider the physiological aspects, economic, social and cultural conditions of the mother and her child. The resolution of difficulties related to breastfeeding depends, to a large extent, on maternal attitudes, the link between the family/social support received by the woman and the influence of healthcare professionals in this process.[9]

Difficulties During Breastfeeding

Most problems related to breastfeeding arise in the first days of the baby's life and may persist in the following weeks. Among the difficulties, the following stand out: babies who do not suck or have weak suction; delays in milk letdown, that is, delay in the gestation process; inadequate grip and positioning; reduced milk production; flat or inverted nipples; breast engorgement, which refers to the excessive accumulation of milk in the breasts; pain and/or cracks in the nipples; mastitis; among others. Considering the practice of breastfeeding as a dynamic and persuadable process, family members are considered the main responsible and influencers on the woman's decision to breastfeed, the perpetuation of this act and the success of breastfeeding. In this way, the family represents the fundamental pillar for health actions and encouraging breastfeeding.[10]

Change in Oxytocin Production

Oxytocin is released in response to breastfeeding, causing milk ejection and inducing physiological and psychological changes that promote milk production. Increased milk production occurs through the release of prolactin. Furthermore, oxytocin also induces anti-stress effects, including lowering blood pressure and cortisol levels.[11]

Since birth, there are several factors that interfere with milk production, including maternal stress and anxiety. Sucking induces the release of oxytocin from the central nervous system, facilitating physiological and psychological adaptations to breastfeeding and motherhood.[11,12] Factors related to childbirth and the type of anesthesia used also interfere with the production of oxytocin, as stress and medical interventions during childbirth can negatively influence and affect the initiation of breastfeeding. Maternal obesity can also interfere with milk production, since adipose tissue has the ability to concentrate progesterone, causing a reduced response of prolactin, a hormone that stimulates milk production.[11.13]

Regulation of the Volume of Milk Produced

Shortly after birth, a small volume of milk is produced, around 37 to 169 ml of colostrum during the first 48 hours.[13] From the 5th day after giving birth, a woman can produce 500 to 750 ml of milk daily, and after the 14th day, 700 to 1000 ml daily. 14 Mothers of twins or triplets can produce 2 liters or more of milk per day, demonstrating that physiological mechanisms can adapt milk production to the nutritional needs of infants. They can regulate the volume of milk produced by mothers through the mechanism of feeding frequency, as an increase in feeding frequency is associated with an increase in the volume of milk produced.[15]Adequate attachment of the areola-nipple complex by the infant promotes complete emptying of the breasts and increased milk production through lactation feedback inhibition (LFI). This procedure also prevents nipple trauma and pain, which is a symptom associated with ejection reflex inhibition.[16]

Lactation Inhibitor Feedback (LIF)

It is a low molecular weight glycoprotein synthesized by the mammary gland and secreted into milk. This substance reversibly blocks protein synthesis by breast cells. LIF accumulates in the mammary alveoli between feedings, blocking protein secretion. When the breast is emptied, the blockage quickly ends and the breast cells restart the production of protein and lactose, responsible for milk volume. In this way, LIF action can explain the effect of breast emptying on milk production.[16]

When it is necessary to prescribe medications during breastfeeding, it is essential to know the conditions that can determine their safety for use during this period. They may be related to the metabolic and physiological aspects of human milk, the woman, the infant or the medication. The composition of breast milk varies depending on the stage of lactation (colostrum versus mature milk) or even during feeding (foremilk versus hindmilk). Such changes influence the extent of drug transfer from plasma to milk, causing variations in breast milk concentrations.[17]

Galactagogues

The use of galactagogues should be reserved for situations in which treatable causes of hypogalactia have been ruled out (e.g., maternal hypothyroidism or use of medications) and, mainly, after evaluating the breastfeeding technique and measures that are known to increase milk production; such as greater frequency of feedings and adequate emptying of the breasts. Mechanical stimulation of the nipple-areolar region by sucking and secreting milk are the most important stimuli for maintaining lactation. Such stimuli promote the secretion of prolactin by the anterior pituitary and oxytocin by the posterior pituitary.[18]

Galactagogue medications increase the production and volume of breast milk, helping to initiate and maintain milk production.[19] Galactagogue drugs act as dopaminergic antagonists, reducing the inhibitory action of dopamine on prolactin secretion.

Low milk production may be associated with inadequate breastfeeding technique, incomplete emptying of the breasts and low frequency of feedings; therefore, before using galactagogues it is necessary to evaluate the frequency and technique of breastfeeding because most of the problems in breastfeeding can be prevented and resolved with known practices that maintain physiological lactation, such as breastfeeding on demand, adequate attachment of the areolar-nipple complex and emptying of the breasts.[20] Many medications are used to increase milk production. Although numerous drugs have the potential to increase milk volume or induce lactation, metoclopramide and domperidone are the most used in clinical practice.[21]

Metoclopramide

It has a dose-dependent prolactinogenic effect. It is a safe and effective medicine for initiating and maintaining lactation.[22] The most commonly used dose for inducing lactation has been 10 mg, 3 times a day. However, dosages of 10 mg 2 to 4 times a day have been prescribed.[5]

Among the drugs with galactagogue properties, metoclopramide is the most studied. A small amount is transferred to the milk, with reported concentrations ranging from 28 to 157 µg/l in the immediate postpartum period. This medication can cause extrapyramidal side effects, such as tremor, bradykinesia and other dystonic reactions, especially in the mother.[21]

Domperidone

Domperidone is an antidopaminergic medication, used as a gastrokinetic in the treatment of nausea and vomiting. Also presented It has the property of stimulating prolactin secretion.

It has lower lipid solubility and higher molecular weight than metoclopramide, which makes it less permeable to the blood-brain barrier and, therefore, safer than metoclopramide due to the lower risk of extrapyramidal effects. The dose used to induce and maintain lactation varies from 10 to 30 mg, three times a day.[21] According to a randomized, double-blind, placebo-controlled study, domperidone increases milk volume by 44.5% after 7 days of use, with milk levels of 1.2 ng/ml.[23]

Sulpiride

Sulpiride is a dopaminergic antagonist used as an antidepressant and antipsychotic. It acts to increase serum prolactin levels similar to other galactagogues.[19] It is used as a psychotherapeutic agent and galactagogue;[24,25] however, its clinical value for increasing milk production is questionable. Further studies, which include potential endocrine effects on the infant, are needed before sulpiride can be recommended to increase milk production. Sulpiride appears in breast milk[24,25] and may be associated with adverse effects on the infant.[25,26,27] It has been recommended that it should not be used to increase milk production,[25,26] although some studies have not shown the occurrence of adverse reactions in infants.[25] Other authors describe that sulpiride is compatible with breastfeeding, but like other antipsychotics, it must be used judiciously[25,26] when in high doses or prolonged use, as it can cause drowsiness and lethargy in the infant. Postpartum mothers have a relatively high risk for postpartum depression and sulpiride can cause depression as a side effect. Fatigue and headache were reported as adverse reactions by mothers who used sulpiride as a galactagogue.[27]

Other Galactagogue Drugs

Other drugs reported to have galactagogue action are chlorpromazine, growth hormone and thyrotropin-secreting hormone (TSH), but there is a need for greater clinical experience before they can be recommended for this purpose.[20] The antipsychotic chlorpromazine has very limited use as a galactagogue due to the potential risk of side effects.[27]

Lactation inhibitors

Some medications are well known for reducing milk production. As the infant's growth is directly related to the synthesis and ingestion of breast milk, the use of any of these medications may represent a risk, especially during the immediate postpartum period, the most sensitive time for lactation suppression. If the use of any of these medications is unavoidable, the healthcare professional should delay their introduction as much as possible and prescribe them for the shortest possible time.[28]

Drugs with a risk of reducing milk production are alcohol, bromocriptine, bupropion, cabergoline, ergometrine, ergotamine, estrogens, such as ethinyl estradiol, levodopa, lisuride, modafinil, nicotine, pseudoephedrine and testosterone.[17]

In the study by Aljazaf et al., pseudoephedrine has been shown to cause a significant reduction in breast milk volume after use. The study is a warning about the use of this medication, which is widely used as a nasal decongestant

associated with antihistamines, which is considered compatible with breastfeeding according to the American Academy of Pediatrics.[29,30] Metronidazole is a medication that also requires concern, as it can cause breastfeeding to be suspended for 12 to 24 hours during treatment and is classified by the American Academy of Pediatrics as medications with unknown effects and with recommendations for caution when breastfeeding, the concern is due to the risk of carcinogenesis and the high bioavailability of the drug.[31]

The number of women who wean their children from using medicines is significant. Studies in many countries estimate that 90 to 99% of breastfeeding women will receive at least some medication during the first week postpartum. Other studies suggest that medication use is one of the main reasons women stop breastfeeding prematurely.[7]

CONCLUSION

Certain medications are well known for increasing or decreasing milk production; however, the use of these medications requires specific care and caution to avoid compromising the health of babies; as the growth of infants is directly related to the synthesis and intake of breast milk.

Therefore, during breastfeeding, it is of fundamental importance to assess whether or not it is necessary to use medications to increase milk production, as breastfeeding women often just need to adapt the correct breastfeeding techniques to their daily routines.

Regarding the use of medications by mothers during breastfeeding, more clinical studies are needed to ensure the safety of newborns and assessments regarding whether or not drugs pass into breast milk. It is important to study and continuously update the subject, in order to detect the possible passage or not of medications into breast milk, and possible adverse reactions for both mothers and newborns.

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