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THE USE OF INJECTABLE CONTRACEPTIVES IN NURSING MOTHERS

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Abstract: Faced with changes in women's reproductive rights, the use of contraceptives has become increasingly routine. One of the options being explored is monthly and quarterly injectable contraceptives. A point discussed is about this method and its relationship with lactation. This systematic review evaluates injectable contraceptives and assesses the risks of exposing the newborn to steroidal hormones from breast milk, when the mother decides to use this method in the postpartum period. For a better extraction of results, the research was carried out by searching for clinical studies, systematic reviews and meta-analyses published in English and Portuguese, in the PubMed, LILACS, Scielo databases, and in the Portal Periódicos CAPES from August 2021 to February 2022. Thus, the objective was to identify the mechanism of action of injectable contraceptives, evaluating their advantages and disadvantages. In this context, it became evident that the quarterly injectable has few adverse effects on lactation and on the growth and development of newborns. The use of combined contraceptives, such as monthly injectables and oral hormonal contraceptives, must be discouraged among nursing mothers, as they negatively interfere with the composition, quality and quantity of breast milk, as well as adversely affect the baby's health, as there are mechanisms that present a higher risk of transferring hormones to the newborn and the possibility of alterations in child development, due to their non-metabolization by the immature liver and the difficulty of excretion by the still-developing kidneys.
Keywords: Female Contraception. Estrogens. Progesterone. Breastfeeding. Child development. Kidney. Liver.

INTRODUCTION

More than half a century ago, in 1961, the first oral hormonal contraceptive appeared. This fact took place through a real struggle in favor of women's sexual and reproductive rights, giving them the ability to control their fertility. This event allowed women to have more autonomy, information, professionalization and competition with men in the labor market, thus changing the vector of power in society and bringing a new profile (BRANDT et al., 2018).

In recent years, there has been a noticeable reduction in the fertility rate in Brazil, from 6.16 children in 1940 to 1.90 children in 2010, largely due to the increasing number of women entering the labor market, which increased the search for other contraceptive methods. However, to determine the choice of method, deep dilemmas arise about its benefits and harms (CUNHA; VASCONCELOS, 2016).

The main mechanism of action of hormonal contraceptives is blocking ovulation, inhibiting the secretion of FSH and LH, thickening the cervical mucus, making sperm transport difficult, making the endometrium inopportune for implantation and altering the secretion and movement of the tubes. This drug is useful both for pregnancy precautions and for regulating the menstrual cycle, available in versions for oral or injectable use (FERRARI, 2015).

An effective option for women who do not intend to use oral contraceptives are monthly or quarterly injectable contraceptives. These drugs represent the most used long-term methods due to the lower risk of failure, since they do not depend on daily reminders. Furthermore, the mechanism of action is the same, as both perform ovulatory blockade (SILVEIRA et al., 2014).

There are two basic types of formulations: combination injectables (monthly) and progestogen-only injectables (quarterly). In those monthly, the first injection must be made until the fifth day of the cycle and the others every 30 days. In monthly there is a

combination of progestogen and estrogen. This method is highly effective, as long as it is used correctly. In addition, the return of fertility occurs around 8 weeks after the last injection, being smaller when compared to the quarterly (14 weeks) (POLI et al., 2009).

The three-monthly contraceptive has only progestogen in its composition, being a formulation of depot medroxyprogesterone acetate (DMPA), at a dose of 150 mg, applied to the buttocks or deltoids (intramuscularly) every three months. When injected into the muscle, it is deposited and absorbed slowly. This contraceptive method is an excellent option for women who cannot use estrogen. (PANISSET *et al.*, 2015).

One point to be addressed is the relationship between this type of contraceptive method and lactation, since this period is of great nutritional, immunological, cognitive and psycho-affective importance for the newborn (NB). Furthermore, the World Health Organization (WHO) recommends exclusive breastfeeding until the sixth month of life. Normally, the return of fertility after childbirth occurs around the twenty-seventh day in women who are not breastfeeding. In nursing mothers, this period is variable and can be prolonged for several months, especially during exclusive breastfeeding. However, the return of fertility is unpredictable. Therefore, many lactating women seek contraceptive methods to prevent a new pregnancy (BORGES et al., 2021).

Thus, nursing mothers who intend to use monthly injectable contraceptives must be aware of the risks of exposure to steroid hormones by the infant, especially when the NB is premature, due to the immaturity of the renal and hepatic systems. In addition, they must be avoided in the puerperium because estrogen impairs the quality and quantity of breast milk by inhibiting the production of prolactin, the hormone responsible for milk production (VIEIRA et al., 2008).

Therefore, it is hypothesized that the use of monthly injectable contraceptives can cause alterations in the renal and hepatic metabolism of infants due to the presence of estrogen, in addition to implying possible alterations in the production of breast milk, thus affecting the development of the puerperal.

METHODOLOGY

A systematic review was carried out on the use of monthly and quarterly injectable contraceptives and how they cause changes in the production and composition of breast milk, and evaluated their effects on the renal and hepatic metabolism of infants.

The research was carried out by searching for clinical studies, systematic reviews and meta-analyses published in English and Portuguese, in the PubMed, LILACS, Scielo databases, and in the Portal Periódicos CAPES from August 2021 to February 2022. found in a general search in the same databases with the same keywords, but addressing their use in titles and abstracts.

The keywords used were: injectable contraception; steroid hormones; breast-feeding; infant; neonatal development; renal metabolism; hepatic metabolism.

The following filters were used: clinical trials, systematic review and meta-analysis in humans, full text and publication in the last 10 years.

TYPES OF HORMONAL CONTRACEPTIONS

Contraceptive methods are diverse, being chosen according to the patient's need and guidance from the health professional. They are divided into two large groups, reversible and permanent. Among the reversible ones, there is the most used type, the hormonal method, in which oral and injectable hormonal contraceptives, transdermal patch,

vaginal ring, intrauterine device (IUD) and implants stand out, in addition to behavioral methods, barrier methods and of emergency contraception (morning after pill). The definitive ones are surgical methods or sterilization (tubal ligation and vasectomy) (BRANDT et al., 2018).

ORAL HORMONAL CONTRACEPTIVES (CHO)

According to the UN, the contraceptive method most accepted by women is the contraceptive pill, because it is low cost and easy to access, since some of them are made available by the SUS (OLIVEIRA, 2021).

CHOs have their main composition of steroids used alone in mini-pills, with only progesterone, or in association when there is a combination of estrogen and progesterone forming various derivatives of this composition. Thus, these steroids are a classification of hormones derived from cholesterol that move to their target cells through the bloodstream, bound to carrier proteins, a process that limits their diffusion through tissues, but protects them from enzymatic degradation (FERREIRA, 2019).

CHO can be divided into monophasic, biphasic and triphasic. In this first, all pills have the same hormone dosage and composition, being the most used; the biphasics have two phases of dosage and the triphasics have, finally, three distinct phases of hormone doses. Thus, from these dosages it is possible to understand the changes generated in the body by this method (BORGES *et al*., 2021).

There are positive actions by use such as reduced risk of ovarian cysts, ovarian and endometrial cancer and benign breast disease, a lower incidence of pelvic inflammatory disease (PID) and ectopic (tubal) pregnancy, in addition to improvement in premenstrual symptoms, dysmenorrhea, endometriosis and decreased flow in the menstrual cycle. However, there are also negative actions. The method can trigger several adverse effects such as headache, weight gain, acne, mood swings, libido and some complications such as cardiovascular disease and venous thromboembolism (CORRÊA et al., 2017).

Combination pills work by blocking ovulation. Progestogens, in association with estrogens, prevent the peak of luteinizing hormone (LH), which is responsible for ovulation. This effect is called gonadotrophic blockade and is the main mechanism of action of the pills. Furthermore, oral contraceptives have a strong influence on metabolic pathways (FIGUEIREDO et al., 2021).

In protein pathways, this action promotes LH suppression, resulting in inhibition of androgen biosynthesis and stimulation of SHBG (sex hormone binding protein), which binds to free androgens and leads to the downfall of biologically active androgens. This fall leads to bone degeneration, reduced muscle strength, rarefaction of hair and alteration of memory and cognitive function (FERREIRA, 2019).

In the lipid pathways, CHO are capable of modifying the metabolism of lipoproteins, promoting an increase in total cholesterol and triglyceride levels. Leading to increased lipid stock and causing weight gain. Therefore, in hemostasis pathways, there is a vasoconstriction process stimulating platelet aggregation process, which causes platelets to bind to collagen fibers and form a hemostatic plug. This whole process takes place in the "coagulation cascade", stimulating the formation of thrombin, which transforms soluble fibrinogen into insoluble fibrin, in addition there is an increase in coagulation factors and a reduction in natural coagulation inhibitors, thus there is a direct relationship with the amount of SHBG and the onset of thrombosis. Therefore, the higher the SHBG concentration, the greater

the risk of thrombosis. The risk of venous thromboembolism in women using oral contraceptives is low, but it is higher than that found in the general population (FARIAS et al., 2016).

INJECTABLE HORMONAL CONTRACEPTIVE

There are two types of injectable hormonal contraceptives: combined (monthly use) and isolated (quarterly use). They have a good adherence of users who generally do not adapt to the pill, either due to forgetfulness, gastrointestinal discomfort or other adverse effects that oral use can cause. In addition, their main quality is the non-occurrence of the first-pass effect in the liver (BRANDT et al., 2018).

MONTHLY COMBINED

Monthly combined injectable contraceptives are composed of estrogen and progestogen. Those available in Brazil are Perlutan® and Preg-Less® (estradiol enanthate 10 mg + algestone acetophenide (dihydroxyprogesterone) 150 mg), Mesigyna® and Noregyna® (estradiol valerate 5 mg + norethisterone enanthate 50 mg) and Ciclofemine ® (estradiol cypionate - 5mg + medroxyprogesterone acetate - 25mg). The first application must be carried out intramuscularly until the fifth day of the cycle and the following, every 30 days (FARIAS et al., 2017).

The mechanism of action is the same as combined pills. In this context, progesterone has an effect at a central level (hypothalamus and pituitary) inhibiting the production and release of LH, thus preventing ovulation. It also acts by altering tubal movement, reducing it, acts by thickening the cervical mucus, which makes sperm transport difficult, and by inducing endometrial atrophy, making it inhospitable to implantation. Estrogen, on the other hand, has a negative central action in relation to the production and release of FSH, inhibiting follicular growth. In addition, it helps to stabilize the endometrium, regulating the menstrual cycle (HAIDER; DARNEY, 2007).

The effectiveness of these injectables is very high, close to zero failures, as long as they are used correctly. The risk of pregnancy is greatest when a woman takes a long time to get an injection or fails to give it. Users may experience alterations in the menstrual cycle, such as lower intensity or fewer days of bleeding, irregular, occasional, prolonged menstruation and amenorrhea (FINOTTI, 2015).

Among the detectable benefits, we can highlight the decrease in the frequency and intensity of menstrual cramps and help to prevent ectopic pregnancy, endometrial and ovarian cancer, ovarian cysts, PID and benign breast diseases. Complaints related to its use are also reported, the most frequent being: breast pain, headache, dizziness and weight gain. They are contraindicated in cases of arterial hypertension, thromboembolistic diseases, valvular heart diseases, family history of cerebrovascular accident (CVA), exclusive breastfeeding less than six weeks after delivery or less than six months. The return of ovulation after interruption of the applications, is on average 60 days after the last injection (FARIAS *et al.*, 2017).

QUARTERLY ISOLATED

The quarterly injectable contraceptive has only slow-release progestogen in its composition. It is commercialized in Brazil with the formulation of depot medroxyprogesterone acetate (DMPA), because the hormone present is in the form of micro crystals in suspension and, when injected into the muscle, it is deposited there and absorbed slowly. It is presented at a dose

of 150 mg, with intramuscular application, under the trade names Depo-Provera® and Contracep®. The mechanism of action of DMPA is the inhibition of the LH surge with consequent anovulation, thickening of the cervical mucus preventing sperm ascension, thinning of the endometrium preventing the adherence of an unlikely blastocyst formation and reduction of ciliary movements of the tube inhibiting oocyte uptake (PANISSET et al., 2015).

DMPA must be started within the first five to seven days of the menstrual cycle. The onset of drug action occurs within 24 hours after application and is maintained for up to 14 weeks, being a margin of protection if there is a delay in the application, which is usually applied every 12 weeks. It is very effective as it requires little user participation and has a lower failure rate in the first year associated with correct use (0.3-3.0%). Most women using DMPA develop amenorrhea according to the time of use (LOPEZ et al., 2016).

It has benefits such as a significant decrease in endometrial and ovarian cancer, reduction of pelvic inflammatory disease, ectopic pregnancy and endometriosis symptoms, in addition to bringing benefits to disorders related to the menstrual cycle, such as menorrhagia, dysmenorrhea, iron deficiency anemia, pre-menstrual syndrome. menstrual and premenstrual migraines. As for the side effects that can happen, there are bleeding, irregularities in the form of spottings (breakouts) or abundant bleeding, weight gain, headaches, breast tenderness, abdominal pain, mood swings, depression and decreased libido. In addition, the use of quarterly contraceptives reduces bone mineral density in women who have reached peak bone mass, and impairs the mineral bone acquisition among those who have not yet reached this peak (VEISI; ZANGENEH, 2013).

The drug can be used in women who have contraindications to estrogen, such as smokers over 35 years old, hypertensive or diabetic. It can also be used by women with iron deficiency anaemia, seizure disorders, congenital heart disease, migraine with aura and a previous history of thromboembolism. It has an absolute contraindication (WHO category 4), when there is current breast cancer, whereas relative contraindications (WHO category 3) are: less than six weeks postpartum, high blood pressure levels, multiple risk factors for cardiovascular disease arterial disease, deep vein thrombosis, pulmonary embolism, heart disease, unexplained vaginal bleeding, stroke, nephropathy, retinopathy or neuropathy, systemic lupus erythematosus, active viral hepatitis, and liver tumors (PANISSET *et al.*, 2015).

Most women who discontinue DMPA use return to menstrual cycles within six months of the last injection, but in some cases this period can extend for up to a year, taking longer when the user is overweight. In the case of lactating women, the first injection must be administered from the sixth week postpartum (JACOBSTEIN; POLIS, 2014).

TRANSDERMAL ADHESIVE

Contraceptive transdermal patches are small patches with a surface area of 20 cm^2, which contain 750 μg of ethinylestradiol and 6 mg of norelgestromin. These patches glued to the skin daily release 20 μg of the estrogenic component and 150 μg of the progestin, which is converted into levonorgestrel through hepatic metabolism. The transdermal contraceptive presents a practical and simple dosing scheme and is used once a week, alternating the application location weekly (lower abdomen, outer part of the arm, upper part of the buttocks, upper back) for three consecutive weeks and, in the fourth week, free of the patch, hormone withdrawal bleeding occurs. Continuous use can also be

performed (FINOTTI, 2015).

The mechanism of action of this method is similar to other combined hormonal contraceptives, as the combination of estrogen and progesterone acts by preventing the secretion of gonadotropins, which prevents ovulation. Furthermore, it produces changes in the cervical mucus, which becomes thick and unsuitable for spermatozoa, causes atrophy in the endometrium, and alters the secretion and tubal motility, causing the ovule transport to be impaired (BRITTON et al., 2020).

This method has the same efficacy (Pearl index 0.7), contraindications and adverse event profile similar to those of CHO, with the exception of a higher incidence of application site reactions. In addition to these local reactions, users often experience spotting, intermittent bleeding, nausea, breast symptoms, headache, upper respiratory tract infection, and dysmenorrhea.

The transdermal contraceptive patch has benefits over CHO due to the absence of first-pass metabolism in the liver, more stable plasma levels and ease of use for patients with swallowing difficulties and patients with absorptive syndromes. In addition, it is likely that patients who opt for this method will experience the same benefits as users of CHOs, such as reduced iron deficiency anemia and the risk of ovarian and endometrial cancer (COLQUITT; MARTIN, 2016).

Opposing this fact, it is known that the main risk attributed to the use of combined hormonal contraceptives is the risk of venous thromboembolism (VTE), this fact does not differ in the transdermal route. In this sense, it is worth remembering that VTE is a known risk of all combined hormonal contraceptives, but that it is a relatively rare event with low absolute risk (ROSS; HARDEE, 2012).

VAGINAL CONTRACEPTIVES

The contraceptive vaginal ring is another combined hormonal method, its action involves a flexible and transparent ring, made of evatane. In its composition there are 2.7 mg of ethinyl estradiol and 11.7 mg of etonogestrel evenly distributed, an ethylene vinyl acetate copolymer. Placement is simple. The patient herself introduces it into the vagina between the first and fifth day of menstruation, and it is important to associate it with other non-hormonal methods (barrier methods) until the seventh day. Thus, it must be withdrawn after 21 days, lasting only one cycle. It is an easy-to-adhere method, as there is only need to make a monthly placement (LEE, 2020).

Each cycle requires a seven-day break, then a new ring must be inserted at the same time as the previous one was removed. Thus, like the other hormonal methods, the ring also has its release of daily doses, in this the dosage is 120 μg of etonogestrel and 15 μg of ethinylestradiol distributed in three weeks (LETE, 2013).

The main mechanism of action is blocking ovulation, as etonogestrel prevents follicular maturation and ovulation, also inhibiting the hypothalamic-pituitary-ovarian axis. Furthermore, secondary to this mechanism, there is thickening of the cervical mucus, making sperm transit difficult (BRITTON et al., 2020).

The adverse effects and complications are similar to those that occur in CHOs, therefore, there are incidences of thromboembolic diseases. Therefore, they are contraindicated in cases of severe vaginal atrophy, vaginal stenosis, uterine prolapse, significant cystocele or rectocele. Because, during the use of the ring, it becomes more conducive to irritating and infectious processes and brings more chances of expelling from the ring. In addition, the method is not indicated in cases of pregnancy or suspicion, lactating women

(six months after delivery), smokers who smoke 15 or more cigarettes a day, aged over 35 years, previous history of hypertension, risk factors for heart disease, liver cirrhosis, hyperlipidemia, bleeding of unknown cause and breast cancer (STIFANI et al., 2018)

UTERINE CONTRACEPTIVE

According to Finotti (2015), the IUD consists of a solid object of variable shape that is inserted through the uterine cervix into the uterine cavity, with the aim of preventing pregnancy. IUDs are presented in three main groups: non-medicated (Lipps Loop), medicated (or copper) and hormonal (levonorgestrel). This method has different mechanism of action. The unmedicated IUD is still present in some countries. An example of this is the polyethylene device impregnated with barium sulfate, called the Lipps Loop. It depends on a foreign body reaction for its contraceptive action, as it promotes a sterile inflammatory response that produces minimal tissue damage and functions as a spermicide.

The copper IUD consists of a copper-colored silver wire that promotes biochemical and morphological changes in the endometrium and alters the cervical mucus. Furthermore, copper increases the production of prostaglandins and inhibits endometrial enzymes, which affect sperm movement, thus preventing pregnancy. Copper ions also have a direct action on sperm motility, inhibiting their ability to penetrate cervical mucus. This option is approved for contraceptive use for up to 10 years (LANZOLA; KETVERTIS, 2021).

The hormonal IUD, on the other hand, has a reserve with 52 mg of levonorgestrel and releases 20 μg of levonorgestrel per day, with a duration of 5 years. Its mechanism of action also alters the cervical mucus, making it thick and inappropriate for sperm penetration, preventing its motility in the cervix, endometrium and fallopian tubes. Furthermore, the high concentration of levonorgestrel in the endometrium prevents the response to circulating estradiol, causing an antiproliferative effect on the endometrium and inhibiting its mitotic activity (CREININ; HSIA, 2016).

When there are no contraindications for the method, the IUD is an alternative for any woman who wants a reliable and prolonged contraceptive method. Therefore, women who have estrogen contraindications or women who are breastfeeding are good candidates for the use of IUDs. Regarding the choice of type, a decisive factor is the menstrual flow. Thus, women on anticoagulation or with coagulation disorders may be better candidates for the hormone than for the copper IUD (JATLAOUI et al., 2017).

This method can be used in young people and adolescents (even if they are nulliparous), if carefully selected. It can be used in postpartum women at the time of delivery after delivery of the placenta, in post-abortion women, lactating women and perimenopausal women. Despite being a good method, it presents some risks, such as uterine perforation at the time of insertion, infections (in the first 20 days there are more chances), expulsion and contraceptive failure. Possible side effects of hormonal IUDs include headaches, nausea, hair loss, breast tenderness, depression, decreased libido, ovarian cysts, oligomenorrhea, and amenorrhea. The main side effect of the copper IUD is increased menstrual bleeding, which can continue even with long-term use(HARDEMAN; WEISS, 2014).

Among the contraindications for the method are: pregnancy or suspected pregnancy, acute pelvic inflammatory disease, current, recurrent or recent STD, immediately after septic abortion, benign and malignant trophoblastic disease, unexplained vaginal bleeding, risk factor for STDs and HIV,

sepsis puerperal, compromised immunity, cervical or endometrial cancer, 48 hours to four weeks postpartum, ovarian cancer and hypersensitivity to any component of the device. For the levonorgestrel IUD, additional contraindications are: confirmed or suspected breast malignancy or other progestogen-sensitive cancer, liver tumors (benign or malignant), and liver disease. For the copper IUD, additional ones include Wilson's disease and copper sensitivity (LANZOLA; KETVERTIS, 2021).

In addition, there are also indications for IUD removal. The main indication for removal is the patient's preference for whatever reason, whether it be desire for pregnancy, irregular bleeding pattern, heavy vaginal bleeding, and discomfort or pain, which may represent displacement of the device. Bleeding changes, especially heavier bleeding, are more likely to occur with copper-containing IUDs than with levonorgestrel IUDs, leading the patient to desire removal. Another indication for removal is an intrauterine pregnancy. Leaving the IUD in place increases the risk of miscarriage by 40% to 50% (KUMAR et al., 2014).

SUBDERMAL CONTRACEPTIVE IMPLANT

Subdermal implants emerged as a great option to solve any forgetfulness, since for a better effectiveness of the pill it needs to be ingested every day at the same time. In this sense, the implants still have other advantages, bypassing the first hepatic passage, and providing a constant release of steroids. Thus, it can be defined that in contraception by implants, a release of progestogen is maintained with daily doses much lower than when administered orally or injected, for years. Furthermore, the method offers a contraceptive option for women who have contraindications to combined hormonal methods and want reversible long-term pregnancy protection (ROCCA et al., 2021).

The regularity of the amount of hormone released by the implant does not depend on the concentration inside it, but on the solubility in the capsule wall, so the progestogen is soluble in polymerized silicone, that is, despite the internal volume decreasing, the release remains constant. Another factor analyzed is the formation of a fibrous capsule around the silicone tube, which causes a drop in release occurring naturally (MANICA; NUCCI, 2017).

The implant is usually placed on the inside of the non-dominant arm, 6 cm to 8 cm above the elbow, in a vertical direction. It is essential that the professional has specific training to reduce the risk of complications. It is essential that the physician verify the proper placement of the implant after its placement by palpating the stick in the patient's arm (BHATIA et al., 2011).

In Brazil, it was only in the 2000s that the *Implanon®* was approved by the National Health Surveillance Agency (ANVISA), among other implant models, this was the one that presented the most benefits with a smaller number of days of bleeding and amenorrhea.

Thus, with 68 mg of etonogestrel the *Implanon®* it inhibits ovulation and alters the cervical mucus for a period of three years. Thus, this is the only subdermal implant used in Brazil (BRAGA; VIEIRA, 2015).

The *Implanon®* It is highly effective and is easy to place and remove. In addition, it is possible to use it in lactation, it improves endometriosis, dysmenorrhea and chronic pelvic pain. However, like other progestins taken alone, it can cause side effects such as irregular uterine bleeding. Thus, the main mechanism of action described for implants, in general, is ovulatory dysfunction, including anovulation, with or without luteinization of the unruptured follicle, and ovulation with

luteal phase defect (JACOBSTEIN; POLIS, 2014).

There are some contraindications which include pregnancy or suspicion, active thromboembolic disease, liver disease, undiagnosed vaginal bleeding or progesterone-dependent tumors, and suspected breast cancer.

LACTATION METABOLISM

In women, the breasts begin their development and differentiation at puberty, regulated by hormones and with each menstrual cycle they undergo structural changes. However, the apex of this process occurs in pregnancy. During this period, there is the action of hormones such as prolactin and placental lactogen hormone (hPL), when the final stage of maturation and the breast differentiation process occurs. Thus, understanding the main mechanisms involved in lactation is essential for understanding possible methods of contraception during this period (CARVALHO et al., 2021).

In the mammary gland, concomitantly with fetal growth and breast development, the process of mammogenesis occurs, which consists of preparing for lactation. The breast grows under the influence of hormones such as estrogen, progesterone, glucocorticoids, prolactin, hPL, GH, IGF-I and insulin. There is an increase in adipose tissue, vascularization and the network of myoepithelial cells that surround the alveoli. The system of intramammary ducts grows and becomes arborized, the number of alveoli increases and many lobules are formed. Along with estrogens, prolactin is responsible for the development of ducts and alveoli. (CIAMPO; CIAMPO, 2018).

Thus, it is possible to identify that milk production does not occur before delivery due to the high concentrations of estrogens and progesterone, which prevent the action of prolactin in alveolar cells. During breastfeeding, there is a greater proliferation of alveoli and the duct system which, associated with the accumulation of milk in the alveoli, promote breast enlargement. At the end of breastfeeding, the gland regresses, but the alveoli persist, making the breast of a multiparous woman different from a nulliparous one (GEDDES; PERRELLA, 2019).

After the process of mammogenesis, the secretory function of the mammary gland begins with lactogenesis, a mechanism in which it develops its ability to produce milk. This process takes place in two stages. The first is called lactogenesis I, where at this stage the breast is ready to produce milk in small amounts due to the presence of high levels of progesterone produced by the placenta. After delivery, the expulsion of the placenta occurs, followed by a significant decline in progesterone levels, consequently, serum prolactin levels rise. Between 24 and 48 hours, the breast becomes voluminous due to dilation of the alveoli and ducts. At this moment, lactogenesis II begins, being the second stage, this is characterized by the most voluminous secretion of milk (LOPEZ; JUNIOR, 2017).

From that moment on, the regulation of milk secretion becomes autocrine. At that moment, in galactopoiesis, the volume of secreted milk is determined by the stimulus produced by emptying and sucking the breasts. Suction, in addition to inducing the release of prolactin ensuring lactogenesis, is the most important stimulus for the release of oxytocin, responsible for milk ejection. If there is no suction, hormones reduce their plasma concentrations, thus reducing production. Contrary to this, with constant suction, prolactin concentrations remain high between 8 and 12 weeks, after which period basal secretion decreases physiologically (ANDREAS et al., 2015).

The process of oxytocin release is mediated by the neuroendocrine reflex of ejection, which is triggered by the depolarization of neurons in the paraventricular and supraoptic nuclei, with suction being one of the stimuli. In the myoepithelial cells that surround the mammary alveoli, oxytocin binds to its membrane receptors inducing the contraction of these cells, expelling milk from the alveoli and increasing intramammary pressure, causing the ejection of milk from the nipples. Although sucking is the primary stimulus to activate milk ejection, its neuroendocrine reflex can also be conditioned. Visual, auditory or psychological stimuli can induce the release of oxytocin and prolactin, evidencing the involvement of higher neural centers in the control of oxytocin and prolactin secretion. For this reason, physical and psychological stress can inhibit this process, since activation of the adrenergic system inhibits oxytocin secretion, causing vasoconstriction of breast vessels. Furthermore, there are other factors that interfere with low production such as hyperthyroidism, excessive use of antihistamines, insufficient development of alveolar tissue, excess caffeine and poor diets (TRUCHET et al., 2017).

The composition of milk also changes according to the period of breastfeeding, between the second and seventh day postpartum there is the formation of colostrum, which is a thicker yellowish secretion, secreted in small amounts, which contains greater amounts of proteins, fat-soluble vitamins A, D, E and K, IgG immunoglobulin and smaller amounts of lactose, fat and water-soluble vitamins C and B complex. Thus, colostrum offers the newborn more immunological elements. In addition, components such as growth factors, lactoferrin, anti-inflammatory cytokines, oligosaccharides, antioxidants, pre and probiotics, leukocytes and antibodies are identified. These components help to activate the newborn's immune system, boost intestinal function and seed a healthy intestinal microbiome in the first days of life (PICÓ et al., 2021).

After this initial period, there is the formation of transition milk that occurs between the seventh and 21st day, when the concentrations of IgG and proteins decrease and there is an increase in lactose and fat, increasing the caloric content of milk. Consequently, mature milk begins to be formed, its composition is a balance between macronutrients such as proteins, lipids and carbohydrates, and micronutrients such as vitamins A and C, minerals such as iron, calcium and zinc, thus being sufficient to exclusively feed the baby up to the sixth month of age in most cases (LOPEZ; JUNIOR, 2017).

Mature milk is composed of: 1% protein (casein, lactalbumin and lactoglobulin), 7% lactose, 3.5% fat, 88.5% water and large amounts of calcium, phosphorus and hormones. This composition represents 70Kcal/100ml. Initial production is 550ml/day and later up to 2000ml/day (BRAVI et al., 2016).

From maturation, changes become slower than initially, varying according to the needs of the infant. During this entire period of breastfeeding, the lactating woman enters the process of postpartum amenorrhea, but this mechanism is directly associated with the duration, frequency and intensity of breastfeeding, this association is established by the capacity of prolactin to inhibit ovulation, therefore, mothers who do not breastfeeding women return to normal menstrual cycles 6 weeks postpartum (TRUCHET et al., 2017).

Breastfeeding is the result of a complex physiological mechanism that occurs since pregnancy, presenting several properties that help in the nutrition and development of the infant. Thus, it has an immunological and nutritional function, which makes it

essential for maintaining the homeostasis of the newborn. (BRAZIL, 2015).

DEVELOPMENT OF THE INFANT'S LIVER AND RENAL FUNCTIONS

HEPATIC DEVELOPMENT

Liver emergence occurs midway through the third week of embryologic development as a bulge from the endodermal epithelium in the distal part of the foregut. The protuberance corresponds to the hepatic bud, which are rapidly proliferating cells that enter the transverse septum, which is the mesodermal plate that lies between the pericardial cavity and the yolk sac pedicle (Figure 1). When liver cells penetrate the septum, the connection between the hepatic diverticulum and the foregut narrows and forms the bile duct, where there is formation of a ventral bulge that gives rise to the gallbladder and cystic duct (LUNA *et al.*, 2013).

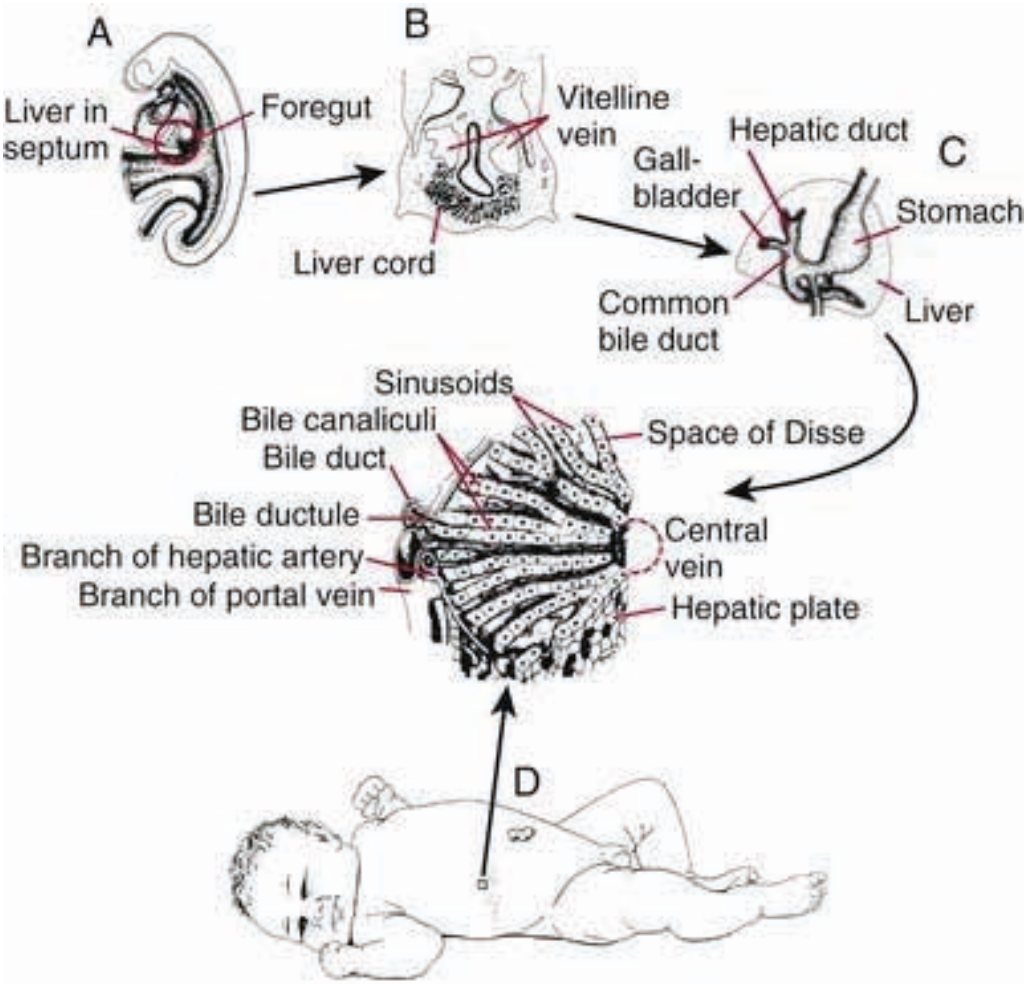

Figure 1. Liver morphogenesis. (Adapted from NELSON, 2009).

By the tenth week of development, the weight of the liver is approximately 10% of the total body weight of the fetus. And this is partially attributed to the large amount of sinusoids and the hematopoietic function. However, this activity gradually decreases during the last two months of uterine life, leaving only a few small hematopoietic islets. At this time, the weight of the liver is only 5%. From the tenth second week, there is formation of bile by hepatocytes. From there, since the gallbladder and cystic duct have already formed, and the cystic duct has joined the hepatic duct to form the bile duct, bile can enter the digestive system, imparting a dark green color to the meconium (content intestinal tract of the fetus) (LANGMAN, 2016).

Many metabolic processes are immature in a newborn, due to fetal patterns of activity of various enzyme processes. Many of the fetal liver functions are performed by the maternal liver, which supplies nutrients and serves as a pathway for the elimination of metabolic products and toxins. Fetal liver metabolism is devoted to the production of proteins necessary for growth. After birth, production and storage of essential nutrients, bile excretion and elimination processes become major functions. Thus, adaptation outside the womb requires synthesis of new enzymes. However, the modulation of these processes depends on the supply of placental hormones, dietary intake and hormones in the postnatal period (SIMOPOULOU et al., 2020)

The liver after birth is extremely important for metabolic functions. Among them, the metabolism of carbohydrates stands out, since it is responsible for strictly controlling the serum levels of glucose, since to maintain blood glucose, hepatocytes produce free glucose by glycogenolysis (immediately after birth, infants are dependent on it) or gluconeogenesis. It is also important for protein metabolism, since in the postnatal period protein synthesis varies according to the protein class, there is an increase in lipoproteins, there is a low concentration of albumin that grows from development and transferrin levels are similar. to that of an adult, which after 3 to 5 months decline and then rise again to reach the final concentration. The liver is important in lipid metabolism, as fatty acid oxidation provides a source of energy in early life. Breast milk provides the main source of calories and is rich in fat and low in carbohydrates, which requires gluconeogenesis to maintain blood glucose. When this supply of glucose is low, there is the production of ketone cups from fatty acids that can provide energy for hepatic gluconeogenesis and fuel for brain metabolism. Liver functioning is also essential in biotransformation, liver excretory function and bile flow (CASIMIRO, 2013).

RENAL DEVELOPMENT

The urinary system begins to develop before the genital system and is formed by the kidneys, ureters, urinary bladder and urethra. In the development of the kidneys and ureters, there are three sets of excretory organs in the embryos. The first is the pronephros, which is a rudimentary, non-functional structure that appears early in the fourth week of development. The second is the mesonephros, which appear at the end of the fourth week caudally to the pronephros and function as temporary kidneys until the permanent kidneys develop. The third is the metanephros, which begins to develop at the beginning of the fifth week and begins to function about four weeks later, which will become the kidneys proper from two sources of mesodermal origin, the ureteric bud - ureter primordia., from the renal pelvis, calyces and collecting tubules (Figure 2) - and the metanephric blastema - forms the nephrons (CARDOSO; PALMA, 2009).

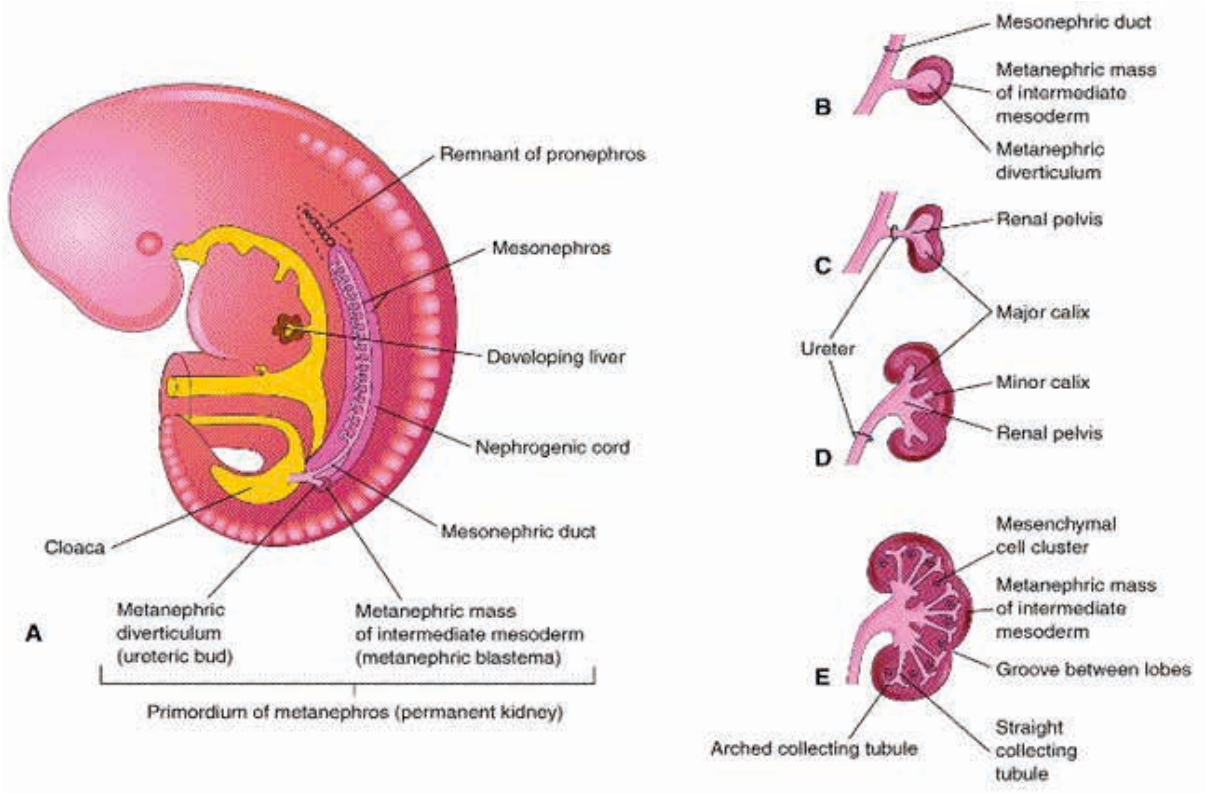

Figure 2. Permanent kidney development. The image demonstrates the development of the ureter, renal pelvis, calyces and collecting tubules (Adapted from: MOORE, 2008).

In this context, the metanephric kidneys are found close to each other in the pelvis and as the abdomen and pelvis grow, the kidneys move away from each other. And around the ninth week the kidneys come into contact with the adrenal glands, when they reach their adult position. This rise results from the growth of the body of the embryo, in the region located caudally to the kidneys. The caudal part of the embryo grows in the opposite direction to the kidneys, as a result, they progressively occupy more cranial levels. Initially, the hilum of the kidney, through which vessels and nerves enter and exit, is located ventrally. However, as the kidney "ascends", it medially rotates nearly 90 degrees. Thus, normally, the kidneys assume a retroperitoneal position (external to the peritoneum), in the posterior wall of the abdomen (ROSENBLUM et al., 2017).

The definitive kidney becomes functional around the twelfth week. The fetal kidneys are subdivided into lobes and these lobulations disappear during childhood as the nephrons enlarge and grow. By the end of term gestation, nephron formation is complete and functional maturation of the kidneys occurs after birth(SIMOPOULOU *et al.*, 2020).

Urine produced by the fetus is deposited in the amniotic cavity where it mixes with amniotic fluid that is swallowed by the fetus and recycled by the kidneys. During fetal life, the kidneys are not responsible for the excretion of metabolic wastes, since the placenta performs this function (LANGMAN, 2016).

INJECTABLE CONTRACEPTIONAL AS A PROGRAMMER OF THE INFANT'S METABOLISM

For guidance on the use of contraceptive methods in the postpartum period, the possibility of exclusive breastfeeding with breast milk must be considered as an alternative contraception that consists of the method of lactation and amenorrhea (LAM). This is a natural method of inhibiting fertility. During the first six postpartum months, exclusive breastfeeding, on demand, with amenorrhea, is associated with a decrease in fertility, being used as a behavioral method. However, this contraceptive effect ceases to be efficient when menstruation returns and when breast milk ceases to be the only food for the infant. For these reasons, it is common to associate it with another contraceptive method that does not interfere with the infant's metabolism (NUNES et al., 2021).

The quarterly injectable is a very effective contraceptive option that can be used during this period. Its use can be started after six weeks of delivery, due to the return of the menstrual cycle in the absence of exclusive breastfeeding. Combined monthly injectables, on the other hand, must be avoided among nursing mothers at least until the sixth month after childbirth to prevent risks to the composition, quality and quantity of breast milk, as well as adversely affecting the baby's health, as there are mechanisms that present a higher risk of passing hormones to the NB and the possibility of changes in child development (MORAES, 2015).

In this context, oral hormonal contraception is also not recommended, as it has the same mechanism of combined hormones as the monthly injectable. In addition, this drug presents another risk, pointed out by the Ministry of Health, which is the association of estrus-progestagen, which is thrombogenic, presenting a greater predisposition to venous and arterial thrombosis, 3 to 18 times more in women using CHO than in women that do not use, with a higher rate of thrombotic events in the first year of use. In these conditions, contraceptives of this nature are not indicated in the puerperium, as estrogen harms breast milk by inhibiting the prolactin axis (WEISBAND et al., 2017).

Therefore, it is evident that contraceptives with progestogen alone are a good option for use in the postpartum period. They act by inhibiting the LH surge, causing anovulation, increasing the thickness of the cervical mucus and decreasing the vascularization of the endometrium, leaving it hypotrophic. In addition, they have little or no effect on the hemostatic system, with no significant change in thrombotic risk (PISSOLATO et al., 2016).

Quarterly injectable contraceptives are composed of 150 mg of DMPA, which is derived from 17 alpha-hydroxyprogesterone. This compound has its maximum serum peak ten days after application, declining afterwards. After a dose of DMPA, 1 to 13 mcg may be transferred to the infant, within three months. However, no metabolites were found in the urine of infants of mothers who used DMPA, nor was the drug's influence on the adrenal or on the function of the NBs' gonads. On the other hand, the recommendation made for the use of quarterly injectable contraceptives is six weeks after delivery, as there is a theory that the ingestion of hormones contained in breast milk could result in high circulating levels of these, due to their non-metabolization by an immature liver and the difficulty of excretion by equally immature kidneys (FERRARI, 2015).

However, in women who have a high risk of morbidity and mortality in the event of a new pregnancy or have difficulty accessing the Unified Health System (SUS), immediate prescription is recommended

right after delivery. But, with exceptions, the recommendation is that the use of isolated injectable contraceptives be restricted to the postpartum period, with it being more effective to change the contraceptive method after the end of this period (GLASIER et al., 2019).

In this context, a study was carried out, which analyzed the use of levonorgestrel (LNG) in nursing mothers and their NBs, where it was shown that after four weeks of birth, infants do not metabolize or absorb LNG. At 12 weeks, they metabolize more than they absorb, and after 24 weeks of birth, they can absorb and metabolize the drug. Some other studies analyzed the early administration of isolated progestogen pills up to one week of delivery and DMPA after two and seven days of delivery, with no evidence of changes in the development of NBs or lactation (WEISBAND et al., 2017).

CONCLUSION

It is evident that there is a diversity of contraceptive methods offered for puerperal use. Therefore, the first line of choice for nursing mothers are non-hormonal methods, as they do not influence breastfeeding and the infant's metabolism. In this meander, the main one is the lactation and amenorrhea method (MLA), which is a behavioral method. In addition, the IUD can be placed during this period, which is an option that promotes long-term contraceptive safety and efficacy. Isolated contraceptives (only with progesterone), including the quarterly injectable and isolated progestogen pills, are second-line for breastfeeding women, as they have few adverse effects on breastfeeding and on the development of NBs. These must preferably be started after six weeks, as this early start does not interfere with the infant's growth.

The use of combined contraceptives (estrogen associated with progesterone), such as monthly injectables and combined oral hormonal contraceptives, must be discouraged among nursing mothers, as they negatively interfere with the composition, quantity and quality of breast milk, as well as adversely affect the baby's health., as there are mechanisms that present a greater risk of passing hormones to the NB and the possibility of changes in child development, due to their non-metabolization by the immature liver and the difficulty of excretion by the still-developing kidneys. Furthermore, even in puerperal women who will not go through the breastfeeding process, the most indicated is to use the progestogen-only method in the first three months, due to the higher thrombotic risk in this period.

REFERENCES

ANDREAS, Nicholas J. *et al*. Human breast milk: a review on its composition and bioactivity. **Early Human Development**, [S.L.], v. 91, n. 11, p. 629-635, nov. 2015. Elsevier BV.

BHATIA, Pushpa *et al*. Implanon: subdermal single rod contraceptive implant. **The Journal Of Obstetrics And Gynecology Of India**, [S.L.], v. 61, n. 4, p. 422-425, ago. 2011. Springer Science and Business Media LLC.

BORGES, Ana Luiza Vilela *et al*. Descontinuidades contraceptivas no uso do contraceptivo hormonal oral, injetável e do preservativo masculino. **Cadernos de Saúde Pública**, [S.L.], v. 37, n. 2, 2021. FapUNIFESP (SciELO).

BRAGA, Giordana Campos; VIEIRA, Carolina Sales. Anticoncepcionais reversíveis de longa duração: Implante Liberador de Etonogestrel (Implanon®): long-acting reversible contraceptives: etonogestrel-releasing implant (implanon®). **Femina**, São Paulo, v. 43, n. 1, p. 8-14, jun. 2015.

BRANDT, Gabriela Pinheiro *et al.* Anticoncepcionais Hormonais na atualidade: um novo paradigma para o planejamento familiar. **Revista Gestão & Saúde**, [s. l], v. 18, n. 1, p. 54-62, 2018.

BRAZIL. Ministério da Saúde. Ministério da Saúde. **Caderno de Atenção Básica: saúde da criança aleitamento materno e alimentação complementar**. Saúde da Criança Aleitamento materno e Alimentação complementar. 2015.

BRAVI, Francesca *et al.* Impact of maternal nutrition on breast-milk composition: a systematic review. **The American Journal Of Clinical Nutrition**, [S.L.], v. 104, n. 3, p. 646- 662, 17 ago. 2016. Oxford University Press (OUP).

BRITTON, Laura E. *et al*. CE: an evidence-based update on contraception. **Ajn, American Journal Of Nursing**, [S.L.], v. 120, n. 2, p. 22-33, fev. 2020. Ovid Technologies (Wolters Kluwer Health).

CARDOSO, Rui Tiago; PALMA, Isabel Mangas. Cortex Supra-Renal: **Anatomia, Embriologia e Pisiologia.** Cortex, v. 71, p. 76, 2009.

CARVALHO, Marcelo de Paula *et al.* O Aleitamento Materno. **Revista Científica Multidisciplinar Núcleo do Conhecimento**. Ano 06, Ed. 01, Vol. 03, pp. 166-177. Janeiro de 2021.

CASIMIRO, Luís Guilherme Galego. **Função hepática e gravidez**. 2013. 39 f. Dissertação (Doutorado) - Curso de Medicina, Faculdade de Medicina da Universidade do Porto (FMUP), Porto, 2013.

CIAMPO, Luiz del; CIAMPO, Ieda del. Breastfeeding and the Benefits of Lactation for Women's Health. **Revista BRAZILeira de Ginecologia e Obstetrícia / Rbgo Gynecology And Obstetrics**, [S.L.], v. 40, n. 06, p. 354-359, jun. 2018. Georg Thieme Verlag KG.

COLQUITT, Charlie W.; MARTIN, Tonya S. Contraceptive Methods. **Journal Of Pharmacy Practice,** [S.L.], v. 30, n. 1, p. 130-135, 8 jul. 2016. SAGE Publications.

CORRÊA, Daniele Aparecida Silva *et al.* Factors associated with the contraindicated use of oral contraceptives in Brazil. **Revista de Saúde Pública [online].** 2017, v. 51, n. 0, 1.

CREININ, Mitchell; HSIA, Jennifer. Intrauterine Contraception. **Seminars In Reproductive Medicine**, [S.L.], v. 34, n. 03, p. 175-182, 4 mar. 2016. Georg Thieme Verlag KG.

CUNHA, Marina Silva; VASCONCELOS, Marcos Roberto. Fecundidade e participação no mercado de trabalho BRAZILeiro. **Nova Economia**, [S.L.], v. 26, n. 1, p. 179-206, abr. 2016. FapUNIFESP (SciELO).

FARIAS, Ana Gesselena da Silva *et al*. Satisfaction of combined and exclusive injectable contraceptive users of progestogen and associated factors. **Revista da Rede de Enfermagem do Nordeste**, [S.L.], v. 18, n. 3, p. 345, 21 ago. 2017.

FARIAS, Mareni Rocha *et al*. Use of and access to oral and injectable contraceptives in Brazil. **Revista de Saúde Pública**, [S.L.], v. 50, n. 2, p. 4-8, jul. 2016. FapUNIFESP (SciELO).

FERRARI, Daniane Novais. **Efeitos do uso de contraceptivos hormonais em mulheres**. 2015. 20 f. TCC (Graduação) - Curso de Biomedicina, Centro Universitário de Brasília Faculdade de Ciências da Educação e Saúde, Brasília, 2015.

FERREIRA, Laura Fernandes. O uso da pílula anticoncepcional e as alterações das principais vias metabólicas: the use of contraceptive pill and alterations of main metabolic pathways. **Femina**, Pato de Minas, v. 7, n. 47, p. 426-432, maio 2019.

FINOTTI, Marta. **Manual de anticoncepção /** Marta Finotti. - São Paulo: Federação BRAZILeira das Associações de Ginecologia e Obstetrícia (FEBRASGO), 2015.

FIGUEIREDO, Bárbara Queiroz de *et al*. Alterações metabólicas decorrentes do uso de contraceptivos hormonais: uma revisão integrativa de literatura. **Research, Society And Development**, [S.L.], v. 10, n. 13, 19 out. 2021.

GEDDES, Donna; PERRELLA, Sharon. Breastfeeding and Human Lactation. **Nutrients**, [S.L.], v. 11, n. 4, p. 802, 9 abr. 2019. MDPI AG.

GLASIER, Anna *et al*. Contraception after pregnancy. **Acta Obstetricia Et Gynecologica Scandinavica**, [S.L.], v. 98, n. 11, p. 1378-1385, 13 maio 2019.

HAIDER, Sadia; DARNEY, Philip D. Injectable Contraception. **Clinical Obstetrics & Gynecology**, [S.L.], v. 50, n. 4, p. 898-906, dez. 2007. Ovid Technologies (Wolters Kluwer Health).

HARDEMAN, Julia; WEISS, Barry D. **"Intrauterine devices: an update."** American family physician v. 89, n. 6, p. 445-50, 2014.

JACOBSTEIN, Roy; POLIS, Chelsea B. Progestin-only contraception: injectables and implants. **Best Practice & Research Clinical Obstetrics & Gynaecology**, [S.L.], v. 28, n. 6, p. 795-806, ago. 2014. Elsevier BV.

JATLAOUI, Tara C. *et al*. The safety of intrauterine devices among young women: a systematic review. **Contraception**, [S.L.], v. 95, n. 1, p. 17-39, jan. 2017. Elsevier BV.

LANGMAN, T. W. Sadler. **Embriologia Médica**. 13. ed. Rio de Janeiro: Guanabara Koogan, 2016. 586 p.

LANZOLA, Emily L., KETVERTIS, Kari. Intrauterine Device. [Atualizado em 31 de julho de 2020]. In: StatPearls [Internet]. Treasure Island (FL): **StatPearls Publishing**; 2021.

LEE, Amy L. Segesterone Acetate and Ethinyl Estradiol Vaginal Ring (Annovera) for Contraception. **Am Fam Physician**, [S.I.], v. 7, n. 9, p. 618-620, maio 2020.

LETE, Iñaki *et al*. Vaginal health in contraceptive vaginal ring users – A review. **The European Journal Of Contraception & Reproductive Health Care**, [S.L.], v. 18, n. 4, p. 234-241, 24 jun. 2013.

LOPEZ, F. A.; JUNIOR, D. C. **Tratado de Pediatria – Sociedade BRAZILeira de Pediatria.** Manole, 2017.

LOPEZ, Laureen M *et al*. Progestin-only contraceptives: effects on weight. **Cochrane Database Of Systematic Reviews**, [S.L.], v. 2016, n. 8, p. 7-9, 28 ago. 2016.

LUNA, Arthur Cássio de Lima *et al.* Caracterização histológica do desenvolvimento hepático em diferentes estágios embrionários de ratos. **Ciência Rural [online].** 2013, v. 43, n. 6, pp. 1070-1075.

KUMAR, S. *et al*. Experiência das mulheres com o uso de contraceptivo intra-uterino pós- parto na Índia. **Reprod Health** 11, 32 (2014).

MANICA, Daniela; NUCCI, Marina. Sob a pele: implantes subcutâneos, hormônios e gênero. **Horizontes Antropológicos**, [S.L.], v. 23, n. 47, p. 93-129, abr. 2017. FapUNIFESP (SciELO).

MOORE, Keith L. **Embriologia clínica /** Keith L. Moore, T. V. N. Persaud ; com a colaboração de Mark G. Torchia ; [tradução Andréa iMonte Alto Costa... et al.]. - Rio de Janeiro: Elsevier, 2008. 557 p.

MORAES, Jamile Lopes de Moraes *et al*. Conhecimento de puérperas acerca do método anticoncepcional da lactação com amenorreia. **Aquichan**, Bogotá, v. 15, n. 4, p. 475-485, Outubro 2015.

NELSON, Anita L. Transdermal contraception methods: todays patches and new options on the horizon. **Expert Opinion On Pharmacotherapy**, [S.L.], v. 16, n. 6, p. 863-873, 24 mar. 2015. Informa Healthcare.

NUNES, Iomara de Brito *et al*. Sexualidade no puerpério: uso de contraceptivos / sexuality in the puerperium. **Brazilian Journal Of Health Review**, [S.L.], v. 4, n. 1, p. 3150-3172, 2021. Brazilian Journal of Health Review.

OLIVEIRA, Ranna Priscylla Campos. O anticoncepcional hormonal via oral e seus efeitos colaterais para as mulheres. **Revista Artigos.Com**, [S.L.], v. 28, 2021.

PANISSET, Karen *et al*. Contracepção injetável trimestral. **Femina**, Rio de Janeiro, v. 43, p. 27-30, maio 2015.

PICÓ, Catalina et al. Lactation as a programming window for metabolic syndrome. **European Journal Of Clinical Investigation,** [S.L.], v. 51, n. 5, p. 8-14, 6 jan. 2021. Wiley.

PISSOLATO, L.K.B.P. et al. Amamentação e Sexualidade: uma interface na vivência do puerpério. **Rev. Fund. Care Online**. Rio de janeiro, 2016.

POLI, Marcelino Espírito Hofmeister *et al*. Manual de anticoncepção da FEBRASGO. **Femina**, v. 37, n. 9, p. 459-492, set. 2009.

ROCCA, Morena Luigia *et al*. Safety and Benefits of Contraceptives Implants: a systematic review. **Pharmaceuticals**, [S.L.], v. 14, n. 6, p. 548, 8 jun. 2021. MDPI AG.

ROSENBLUM, Stacy *et al*. Renal development in the fetus and premature infant. **Seminars In Fetal And Neonatal Medicine**, [S.L.], v. 22, n. 2, p. 58-66, abr. 2017. Elsevier BV.

ROSS, John; HARDEE, Karen. Access to Contraceptive Methods and Prevalence of Use. **Journal Of Biosocial Science**, [S.L.], v. 45, n. 6, p. 761-778, 15 nov. 2012. Cambridge University Press (CUP).

SILVEIRA, Camila Oliveira *et al*. Contracepção em mulheres com condições clínicas especiais. Critérios médicos e elegibilidade. **Reprodução & Climatério**, [S.L.], v. 29, n. 1, p. 13-20, jan. 2014. Elsevier BV. http://dx.doi.org/10.1016/j.recli.2014.06.002.

SIMOPOULOU, Mara *et al*. Assessing Clinical Embryology Research: a global bibliometric analysis. **Medicina**, [S.L.], v. 56, n. 5, p. 210, 26 abr. 2020. MDPI AG.

SOUZA, Geny Gomes de *et al.* Conhecimento e uso de anticoncepcionais hormonais: o que é certo ou errado? **Temas em Saúde**, João Pessoa, v. 16, n. 4, p. 199-211, 2016.

STIFANI, Bianca M. *et al*. Factors associated with nonadherence to instructions for using the Nestorone®/ethinyl estradiol contraceptive vaginal ring. **Contraception**, [S.L.], v. 97, n. 5, p. 415-421, maio 2018. Elsevier BV.

TRUCHET, Sandrine *et al.* Physiology of milk secretion. **Best Practice & Research Clinical Endocrinology & Metabolism,** [S.L.], v. 31, n. 4, p. 367-384, ago. 2017. Elsevier BV.

VEISI, Firoozeh; ZANGENEH, Maryam. "Comparison of Two Different Injectable Contraceptive Methods: Depo-medroxy Progesterone Acetate (DMPA) and Cyclofem." **Journal of family & reproductive health.** v. 7, n. 3, p. 109-113. 2013.

VIEIRA, Carolina Sales *et al.* Contracepção no puerpério. **Revista BRAZILeira de Ginecologia e Obstetrícia**, São Paulo, v. 30, n. 9, p. 471-481, set. 2008.

WEISBAND, Y. L. et al. Intenções pós-parto no uso de contraceptivos e escolha de métodos entre mulheres que amamentam em um hospital universitário em Ohio: um estudo transversal. **Reprod Health,** 14, 45 (2017).