

Research Article

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Misoprostol Intoxication in the Third Trimester in Pregnant Patients

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Abstract:

Background: Misoprostol is an analog of Prostaglandin (PG) E1, which initially began to be marketed in pharmacies in many places since the end of the 1980s under the trade name of Cytotec.

Methodology: A bibliographic review was carried out through various databases from 2012 to 2021; The search and selection of articles was carried out in journals indexed in English and Spanish. The following keywords were used: intoxication, misoprostol, pregnant patients.

Results: Exposure to misoprostol has been associated with a number of defects including arthrogryposis and limb reduction, brain anomalies, gastroschisis, and Moebius syndrome.

Conclusion: For the gynecological, misoprostol is a very useful drug for the interruption of pregnancy at any stage of this, not only for this, it also helps to expel a missed abortion, it is effective for the induction of labor, and it also acts as a treatment for postpartum hemorrhage.

Keywords: Intoxication, misoprostol, pregnant patients.

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Introduction

It should be noted that misoprostol is a medication widely used by gynecologists, its objective is to generate anatomical and functional modifications in the cervix and the evacuation of the gravid uterus, these drugs are used both for the preparation of the cervix for the induction of labor, the ripening of the cervix and is also used on many occasions for abortions. (1)

Now, misoprostol is a prostaglandin analog that is mainly indicated for the treatment of peptic ulcers, however, its effectiveness in producing cervical contractions has been demonstrated in multiple studies. We know that the success of a birth revolves around the reduction of risks for both the mother and the fetus, this includes the rapid and uncomplicated recovery of both, within the parameters that we can evaluate to know the

Misoprostol Intoxication in the Third Trimester in Pregnant Patients

maternal well-being, we have the following; coagulation times, blood count, in addition to endless physiological and physical parameters such as the evaluation of vital signs, such as blood pressure, heart rate, also the amount of postpartum bleeding, skin color among many others. Since the early detection of some of these risks can allow a series of therapeutic actions to try to reduce maternal mortality associated with postpartum. (2)

However, due to the lack of control over misoprostol, intoxications can be generated due to the lack of information that many patients have, given that this information can be acquired very easily and even anonymously, the patients who receive it take at home and without medical supervision, most of the time they believe that the higher the dosage of medication they take, the more effective it will be. (3)

The purpose of this article is to explore in the existing literature the most important and up-to-date aspects of possible misoprostol poisoning during the third trimester in pregnant patients.

Materials and Methods

A bibliographic review was carried out, in which the PubMed, Scielo and ScienceDirect databases, among others, were searched. The compilation and selection of articles was carried out in journals indexed in English and Spanish from 2012 to 2021. As keywords, the following terms were used in the databases according to the DeCS and MeSH methodology: intoxication, misoprostol, patients pregnant women In this review, 30 original and review publications related to the subject studied were identified, of which 24 articles met the specified inclusion requirements, such as articles that were in a range not less than the year 2007, that were articles of full text and reporting on misoprostol intoxication in the third trimester in pregnant patients. As exclusion criteria, it was taken into account that the articles did not have sufficient information and that they did not present the full text at the time of review.

Resultados

Misoprostol

Misoprostol is an analog of Prostaglandin E1, which initially began to be marketed in pharmacies in many places since the late 1980s

under the trade name of Cytotec, mainly as a treatment for peptic ulcers, usually in children. cases caused by the excessive use of non-steroidal anti-inflammatory drugs. (4) PGE, as we already know, represses gastric secretion stimulated by the food we eat, histamine by direct action on the secretory cells. Its use for this purpose is contraindicated in pregnant women, because PGE1 generates uterine contractions during the gestation period, which can cause the interruption of pregnancy, it also produces the maturation of the uterine cervix, as well as the induction of labor with a live fetus, taking advantage of its characteristics of being cheap, easily accessible, stable and suitable for any environmental temperature. Misoprostol is constituted and is active for oral administration, although it can be used by other routes of administration such as vaginal, sublingual, rectal. (5)

Among the functions that this drug fulfills, it has been considered that misoprostol is more effective than oxytocin and dinoprostone, which are the drugs legally indicated for labor induction, and it is cheaper than the aforementioned drugs. Bearing in mind that the bladder catheter is used for labor induction, as well as a two-balloon catheter, it is introduced through the cervical canal to reach the extra-amniotic space. (6) The balloon is then inflated to hold the catheter in place to increase the diameter of the cervix due to hydrophilic properties and produce cervical dilation. (7)

Due to the advantages that misoprostol presents, it is widely used in gynecology and obstetrics services, however, it has not yet been approved for such use due to the possible serious risks evidenced, such as uterine rupture, increasing the possibility of maternal death, also due to the little information that is known about the contraindications of this drug. Even so, the advantages continue to be many, as we had already mentioned, this medication increases the intensity and frequency of the uterine muscle contractions, which generates the expulsion of the uterine content, it also helps in the induction of labor and works as a treatment for postpartum hemorrhage. (8)

Nowadays, the secondary effect that misoprostol has on pregnant women is already known, that is why in the population around the world, this medicine is being used for out-of-hospital

Misoprostol Intoxication in the Third Trimester in Pregnant Patients

purposes in women for the interruption of pregnancy in any period of this same (9). Being even more, the little information they know about the repercussions that the use of this medicine can have during the third trimester of pregnancy, however, cases have been reported that ensure its teratogenicity in this period. (10)

It should be noted that, like any marketed medication, endless studies and tests have also been carried out on it, but its toxicity has not been determined, however, according to evidence from studies conducted on animals, it has been shown that misoprostol does not have an irrelevant potency as an acute toxicant. (11) In other words, acute oral toxicity after a single dose made it possible to establish a safety margin of at least 500 to 1,000 times between the lethal dose in experimental animals and the therapeutic dose in humans. (12)

First of all, we can note that the use of misoprostol has made it possible to avoid labor induction failures and also to avoid the complications that usually occur due to cesarean sections, lowering the rate of performing them. (13)

In the investigation carried out, there were not many reported cases of misoprostol intoxication during the third trimester of pregnancy.

Poisoning during the third trimester of pregnancy

Although the information collected is little about intoxication or overdose of misoprostol, it is worth mentioning the effects that can occur if it occurs, taking into account that PG receptors are very well distributed throughout the different cells of the body, these are present from the CNS, blood vessels, bronchi, digestive tract, to the uterus, among others, this means that they have an enormous variety of action, so it can hinder the diagnosis of overdose or intoxication by misoprostol, due to the diversity of the symptoms that usually occur. (14)

Among them, we must mention those described by the consulted bibliography such as hyperthermia, nausea, alterations in the level of consciousness, diarrhea, episodes of vomiting, cervical contractions, uterine hypertonia or tetany, this can cause RPM, uterine rupture also occurs, which is the spontaneous tearing of the uterus which causes the fetus to remain floating in the abdomen, especially if it is a multiparous patient and ultimately fetal death. (15) Among others we can mention limb defects, both upper and lower deformities, the one that occurs most frequently is clubfoot.

In other cases, the limb abnormalities are usually associated with arthrogyriposis, which is a set of joint contractures that often lead to muscle atrophy and buildup of fibrous tissue around the joints. (16)

Table 1. Clinical manifestations of misoprostol intoxication.

Nausea
Vomiting
Diarrhea
Dizziness
Pelvic pain
Headache
Fever
Alterations at the level of consciousness

Next, we will have the parameters established for the correct dosage of misoprostol depending on

the route of administration used for early termination of pregnancy:

Table 2. Drug dosage for early termination of pregnancy.

Via	Dose	Start of action	Duration of action
Oral	400 µg	8 min	2 hours
Sublingual	800 µg	11 min	3 hours
Vaginal	800 µg	20 min	4 hours

Misoprostol Intoxication in the Third Trimester in Pregnant Patients

The mechanism of toxicity has not yet been concisely and clearly established given the similarities that it usually presents with the hypoxia observed in children exposed to misoprostol, one of the most common arguments is that the drug tends to cause a developmental irregularity in a of the stages highly dependent on oxygen. (17) This irregularity may be caused by entrapment of fetal blood within the placenta by contractions of the cervix or also by a vasoconstrictor effect on the uterine arteries. (18)

Treatment of misoprostol poisoning

It should be remembered that misoprostol tends to be metabolized as a fatty acid, due to its main mechanism of action, so dialysis is unlikely to be an adequate treatment for overdose. In the event of an overdose, standard support measures should be used, depending on how they are required, since there is no antidote that is used as a treatment, which is why this is symptomatic, and the approach should be as in most drug intoxications. , trying to eliminate the drug in the patient through gastric lavage or vaginal lavage instead. (19)

Discussion

As we well know, there are few reported cases, therefore, there are few cases described in the literature on misoprostol intoxication during the third trimester in pregnant patients, after conducting an exhaustive search of the existing literature in the database. internationally, we found a total of 6 reported cases, of these only 2 occurred in the third trimester in pregnant patients. (twenty)

The dosage that was self-administered without medical supervision by the same patient was 4,000 mg of intravaginal misoprostol, which means a dosage well above the recommended therapeutic dose. It should be noted that the 2 self-administered doses used in both cases described in the literature were; in Randall's case, she administered 6,000 mg of misoprostol orally, still adding 2 mg of trifloperazine. In the case written by Austin, it was 600 mg orally, plus 6,000 of intravaginal misoprostol, 40% more than the recommended therapeutic dose.

According to the reports found in the biography, it describes the effects that can be produced by

misoprostol intoxication, as mentioned above, such as vomiting, diarrhea, pelvic contractions, hypertonia, which can cause fetal distress, it can also generate premature rupture of membranes (RPM), fetal death among others. It is necessary to take into account that signs such as hypotension and maternal tachycardia were present, which are not reported as effects in the bibliography, but they were presented in the same way in all cases. (twenty-one)

A strength of the current study is the implemented methodology, regarding the literature search, and steps in the selection of relevant articles, quality assessment and data extraction. However, this study has several limitations, which should be taken into account before reaching a conclusion, including the little evidence reported about misoprostol intoxication in the third trimester in pregnant patients.

Conclusion

In short, it can be concluded that for gynecology, misoprostol is a very useful drug for the interruption of pregnancy at any stage of it, not only for this, it also helps to expel a missed abortion, it is effective for the induction of childbirth, and also acts as a treatment for postpartum hemorrhage. (22)

Misoprostol has been proven to be much safer, more effective, and more accessible than other medications that share the same functionalities, in addition to allowing us better active management during the third period of pregnancy, reducing the maternal mortality rate, whether used by any route of administration, however, given the little information that is known about it, already established medications such as uterus retractors should not be changed due to proven safety. (23)

Also taking into account, as the toxicity of this drug has not been established, we must know how to identify the symptoms that occur when there is abuse of this drug, such as diarrhea, vomiting, nausea, headache, alterations in the level of consciousness, among other signs. of alarm to be able to establish the treatment, knowing well that there is no antidote for this type of poisoning, the treatment is usually symptomatic management. (24)

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Misoprostol Intoxication in the Third Trimester in Pregnant Patients

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Misoprostol Intoxication in the Third Trimester in Pregnant Patients

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