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An Overview on Misoprostol and Its Use in Myomectomy

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Abstract:

Background: Misoprostol is a synthetic prostaglandin E1 analog widely used in obstetrics and gynecology due to its uterotonic and cervical-ripening properties. It has established roles in medical termination of pregnancy, induction of labor, treatment and prevention of postpartum hemorrhage, and management of incomplete abortion. In addition, it is used in gastroenterology to prevent gastric ulcers in patients receiving nonsteroidal anti-inflammatory drugs (NSAIDs). Its low cost, ease of administration (oral, vaginal, sublingual, buccal, rectal), and stability at room temperature make it particularly valuable in resource-limited settings. However, its use requires careful dosing due to risks of hyperstimulation, uterine rupture, gastrointestinal side effects, and teratogenicity if pregnancy continues.

Keywords: Misoprostol, prostaglandin E1 analog, uterotonic, induction of labor, abortion, postpartum hemorrhage, gastric ulcer prevention.

Introduction:

Misoprostol, a methyl ester analog of prostaglandin E1, has become one of the most versatile drugs in obstetrics, gynecology, and gastroenterology. Originally marketed for gastric ulcer prevention, its ability to induce uterine contractions and promote cervical ripening led to its extensive off-label use in reproductive health **(1).**

The drug can be administered through various routes—oral, vaginal, sublingual, buccal, or rectal—offering flexibility in clinical practice. In obstetrics, misoprostol is used for cervical ripening before labor induction, management of missed or incomplete abortion, and prevention/treatment of postpartum hemorrhage. It is currently included in WHO guidelines as a core medicine for safe abortion and maternal care **(2).**

Despite its wide use, misoprostol carries safety concerns, including uterine hyperstimulation, risk of uterine rupture (particularly in scarred uteri), and gastrointestinal side effects. Nevertheless, systematic reviews continue to confirm its effectiveness and cost–benefit role, particularly in resource-limited settings where alternatives are scarce **(3).**

Many techniques had been used to decrease bleeding in open, laparoscopic or hysteroscopic myomectomy; they include preoperative measures as preoperative use of GnRH agonists for at least 3 months to reduce the size of myoma or the preoperative administration of local prostaglandins and intraoperative measures as uterine artery ligation, intermittent uterine arteries closure using tourniquet, intraoperative infusion of uterotonic agents such as oxytocin or ergometrine, direct infiltration of the myoma with vasoconstrictive agents such as adrenaline or vasopressin **(4).**

One such strategy under investigation is the administration of preoperative sublingual misoprostol, a synthetic prostaglandin E1 analogue. Misoprostol has been widely used in obstetrics and gynecology for its uterotonic properties, the prevention of postpartum hemorrhage, and cervical ripening prior to labor induction. It stimulates uterine contractions and this increase in myometrial contraction will lead to contraction of the vessels supplying blood to the leiomyomas. Misoprostol has also been shown to increase uterine artery resistance and reduce blood flow to leiomyomas **(5).**

Recent studies have explored its potential benefits in hysteroscopic myomectomy, focusing on its ability to reduce intraoperative bleeding, minimize the risk of complications, and enhance postoperative recovery. Misoprostol can stimulate uterine contraction and reduce uterine blood flow, based on the hypothesis that pre-operative misoprostol may redistribute the blood from the diseased uterus back to the circulation, hence reducing operative blood loss **(6).**

Synthesis and Secretion

In terms of its synthesis, misoprostol is not naturally occurring. It is chemically synthesized through the modification of naturally occurring prostaglandins. The specific synthetic process involves the chemical modification of prostaglandin E1 to create the structure of misoprostol **(7).**

Misoprostol receptors

The main receptors targeted by misoprostol are known as prostaglandin E receptors (EP receptors). These receptors are part of the larger family of G protein-coupled receptors (GPCRs), and they mediate the cellular responses triggered by prostaglandin E1 (PGE1) and its analogs. There are four subtypes of EP receptors, designated as EP1, EP2, EP3, and EP4. Each subtype has different tissue distribution and signaling pathways, leading to diverse physiological effects:

EP1 receptor: Activation of EP1 receptors leads to smooth muscle contraction and vasoconstriction. In the context of misoprostol, EP1 receptor activation is believed to contribute to its uterotonic effects, such as inducing uterine contractions **(8).**

EP2 receptor: Activation of EP2 receptors results in smooth muscle relaxation, vasodilation, and an anti-inflammatory response. Misoprostol's binding to EP2 receptors may contribute to its cervical ripening effects and inhibition of gastric acid secretion **(9).**

EP3 receptor: EP3 receptors have multiple isoforms and can have varied effects depending on the isoform expressed. Activation of certain EP3 receptor isoforms can lead to smooth muscle contraction, vasoconstriction, and inhibition of gastric acid secretion. Other isoforms can mediate inhibitory effects on adenylate cyclase and contribute to anti-inflammatory actions **(10).**

EP4 receptor: Activation of EP4 receptors generally leads to smooth muscle relaxation, vasodilation, and anti-inflammatory effects. Misoprostol's interaction with EP4 receptors may contribute to its cytoprotective effects on the gastrointestinal mucosa **(9).**

Forms and administration

Misoprostol is available in different forms and can be administered via various routes, depending on the intended use. The specific form and administration method of misoprostol are determined by factors such as the medical indication, dosage requirements, and patient preference:

Oral tablets: Misoprostol is available in tablet form for oral administration. These tablets are typically swallowed with water. The dosage and frequency of administration may vary depending on the medical indication, such as cervical ripening, medical abortion, or prevention of stomach ulcers **(11).**

Sublingual tablets: Misoprostol sublingual tablets are placed under the tongue, where they dissolve and are absorbed into the bloodstream. This route of administration allows for rapid absorption and onset of action. Sublingual administration is commonly used for medical abortion or cervical ripening **(11).**

Vaginal tablets: Misoprostol can be formulated as vaginal tablets that are inserted into the vagina. The tablets gradually dissolve, releasing the medication locally. Vaginal administration is often used for cervical ripening, inducing labor, or management of postpartum hemorrhage **(12).**

Buccal administration: In some cases, misoprostol may be administered by placing tablets against the cheek or gum (buccal administration). The tablets dissolve slowly, allowing for absorption through the oral mucosa. This method may be used for cervical ripening or medical abortion **(13).**

Rectal suppositories: Misoprostol suppositories are inserted into the rectum, where they dissolve and are absorbed. This route of administration may be used in situations where oral administration is not feasible or tolerated. Rectal administration is less commonly employed but may be utilized for certain medical indications **(13).**

Mechanism of action

Misoprostol is a synthetic prostaglandin E1 (PGE1) analog, and its pharmacological effects are primarily mediated by binding to prostaglandin E receptors (EP receptors). When misoprostol binds to EP receptors, it activates a cascade of intracellular events that lead to various physiological responses. Misoprostol stimulates the EP1 receptors in the smooth muscle of the uterus, leading to uterine contractions. This effect is utilized in medical procedures such as induction of labor and management of postpartum hemorrhage. It can also be used to facilitate the removal of uterine fibroids during hysteroscopic myomectomy **(14).**

Misoprostol can promote cervical ripening, which refers to the softening and dilation of the cervix in preparation for labor induction or other gynecological procedures. Activation of EP2 receptors leads to smooth muscle relaxation in the cervix and increased production of enzymes that facilitate cervical remodeling. Misoprostol is known to have cytoprotective effects on the gastric mucosa. By binding to EP receptors, particularly EP3 and EP4 receptors, misoprostol inhibits gastric acid secretion, increases mucus production, and enhances bicarbonate secretion. These actions help protect the stomach lining and are utilized in the prevention and treatment of gastric ulcers caused by nonsteroidal anti-inflammatory drugs **(15).**

Uses in Gynecology

Misoprostol is sometimes used as a preventive measure or as part of the management strategy for postpartum hemorrhage, which is excessive bleeding after childbirth. It can help stimulate uterine contractions and reduce blood loss. Misoprostol may be used prior to hysteroscopic procedures such as myomectomy (removal of uterine fibroids) or endometrial ablation. It helps to soften and dilate the cervix, facilitating access to the uterine cavity and improving the safety and ease of the procedure **(16).**

Misoprostol is often used to prepare the cervix for labor induction or other gynecological procedures. It helps soften and dilate the cervix, making it easier for the cervix to open and allow passage of the fetus or facilitate certain gynecological interventions. Misoprostol, in combination with another medication called mifepristone, is used for medical abortion (termination of pregnancy). It is typically administered after mifepristone to induce uterine contractions and expel the pregnancy tissue. Misoprostol can be used to manage incomplete miscarriages or missed miscarriages, where the body has not fully expelled the pregnancy tissue. It helps to initiate contractions and facilitate the expulsion of the remaining tissue **(17).**

Side effects

Misoprostol commonly causes gastrointestinal side effects, including abdominal pain, cramping, nausea, vomiting, diarrhea, and flatulence. These effects are usually transient and resolved on their own. Taking misoprostol with food or using lower doses may help reduce these symptoms. Some individuals may experience headaches while taking misoprostol. These headaches are typically mild to moderate in intensity and resolve without specific treatment **(12).**

Misoprostol can lead to excessive uterine contractions, which may result in uterine hyperstimulation. This can cause prolonged or intense contractions, leading to increased pain and potential risks to the mother and fetus. Close monitoring during the use of misoprostol is essential to avoid uterine hyperstimulation. Misoprostol can cause vaginal bleeding, which is a normal and expected side effect, especially when used for medical abortion or managing miscarriage. The bleeding is usually heavier than a regular menstrual period and can last for several days to weeks **(18).**

Rarely, individuals experience allergic or hypersensitivity reactions to misoprostol. Symptoms may include rash, itching, swelling, dizziness, or difficulty breathing. If any signs of a severe allergic reaction occur, immediate medical attention should be sought **(19).**

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