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MECHANISMS OF ACTION AND CLINICAL APPLICATIONS OF PHARMACOLOGICAL AGENTS AFFECTING UTERINE MUSCLES

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Abstract. The contractile activity of the uterus is an important physiological process involved in pregnancy, labor, and the postpartum period. Myometrial contraction is primarily regulated by changes in intracellular calcium concentration and the interaction between actin and myosin filaments. Pharmacological agents affecting uterine muscles are widely used in obstetric practice to stimulate or suppress myometrial activity. According to their pharmacological effects, these drugs are generally divided into two major groups: uterotonics, which increase uterine contractions, and tocolytics, which decrease myometrial contractility. The aim of this thesis is to summarize the main mechanisms of action and clinical applications of the most important pharmacological agents affecting uterine muscle activity.

Keywords: myometrium, uterotonics, tocolytics, oxytocin, prostaglandins, ergometrine, nifedipine, atosiban, uterine contraction, postpartum hemorrhage.

Introduction

The myometrium is composed predominantly of smooth muscle cells whose coordinated contraction is essential for normal labor and effective uterine involution after delivery. Myometrial contraction is closely associated with an increase in intracellular Ca^{2+} concentration. Calcium binds to calmodulin and activates myosin light-chain kinase, resulting in phosphorylation of myosin and interaction between actin and myosin filaments. This process generates smooth muscle contraction.

During pregnancy, the functional properties of the myometrium gradually change. Toward the end of pregnancy, the expression and sensitivity of oxytocin receptors increase, while prostaglandins contribute to cervical ripening and stimulation of uterine contractions. These physiological mechanisms provide the basis for pharmacological regulation of uterine activity.

Uterotonic Agents

Uterotonics are pharmacological agents that increase uterine tone and contractility. They have an important role in labor induction and augmentation and in the prevention and management of postpartum hemorrhage.

Oxytocin is one of the most important uterotonic agents used in clinical practice. It binds to specific oxytocin receptors located on myometrial cells. Activation of these Gq/11-coupled receptors stimulates phospholipase C, resulting in the formation of inositol-1,4,5-trisphosphate and an increase in intracellular Ca^{2+} concentration. Increased calcium activates the contractile apparatus and produces rhythmic uterine contractions. Oxytocin is commonly used for induction and augmentation of labor and for the prevention and treatment of postpartum hemorrhage associated with uterine atony.

Prostaglandins are important endogenous mediators of uterine activity. They participate in cervical ripening and stimulate myometrial contractions. Misoprostol, a prostaglandin E1 analogue, increases uterine contractility and promotes cervical changes. It is used in several obstetric indications, including labor induction and management of postpartum hemorrhage. Dinoprostone, a prostaglandin E2 preparation, is primarily used for cervical ripening and induction of labor. The

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choice of a prostaglandin depends on the clinical indication, gestational age, route of administration, and maternal and fetal conditions.

Ergometrine is an ergot alkaloid that produces powerful and relatively prolonged uterine contractions. It can be used in selected cases of postpartum hemorrhage caused by uterine atony. However, because it can also cause vasoconstriction and increase arterial blood pressure, its use requires particular caution in patients with hypertension or hypertensive disorders of pregnancy.

Tocolytic Agents

Tocolytics are drugs that reduce myometrial contractility. Their principal clinical role is the temporary delay of preterm labor rather than complete or prolonged prevention of delivery. This short-term delay can provide time for antenatal corticosteroid administration, maternal transfer to a specialized perinatal center, or other appropriate obstetric interventions.

Nifedipine is a calcium-channel blocker that inhibits L-type calcium channels in smooth muscle cells. By reducing Ca^{2+} influx into myometrial cells, it decreases the activation of the contractile apparatus and consequently reduces uterine contractions. Nifedipine is commonly considered in the management of threatened preterm labor when tocolysis is clinically appropriate. Hypotension and other cardiovascular effects should be considered during treatment.

Atosiban is an oxytocin receptor antagonist. By competitively inhibiting the action of oxytocin on myometrial receptors, it reduces intracellular signaling responsible for uterine contraction. This mechanism makes atosiban a specific pharmacological approach to reducing oxytocin-mediated myometrial activity.

Clinical Importance and Safety

The clinical effectiveness of uterine-active drugs must always be considered together with their safety profiles. Excessive stimulation of the uterus with oxytocin or prostaglandins may result in excessively frequent or prolonged contractions and may compromise fetal well-being. Prostaglandins can also cause gastrointestinal adverse effects such as nausea, vomiting, and diarrhea, as well as fever or chills depending on the preparation and dose.

Ergometrine may produce hypertension because of its vasoconstrictor activity and therefore requires careful patient selection. Tocolytic agents may cause cardiovascular adverse effects, with hypotension being particularly relevant for calcium-channel blockers such as nifedipine. Therefore, appropriate monitoring of maternal vital signs and fetal condition is important when clinically indicated.

The choice of a uterine-active pharmacological agent should be individualized according to the clinical objective. Factors such as gestational age, cervical status, uterine activity, maternal blood pressure, comorbidities, contraindications, and potential adverse reactions should be taken into account.

Conclusion

Pharmacological agents affecting uterine muscles play an essential role in modern obstetric practice. Uterotonics such as oxytocin, prostaglandins, and ergometrine increase myometrial contractility and are mainly used for labor induction, augmentation, cervical ripening, and prevention or treatment of postpartum hemorrhage. In contrast, tocolytics such as nifedipine and atosiban reduce uterine contractility and may be used to temporarily delay preterm labor in selected clinical situations.

A clear understanding of the molecular mechanisms of these drugs, particularly their effects on intracellular Ca^{2+} signaling, oxytocin receptors, prostaglandin pathways, and smooth muscle contraction, contributes to their rational clinical use. Appropriate selection of the drug, dose, route of administration, and duration of treatment, together with careful maternal and fetal monitoring, is essential for achieving therapeutic effectiveness while minimizing potential risks.