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Propranolol Application in Gynecological Disease: Review

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Review Article

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Abstract: Propranolol is β-adrenergic receptor blocker with reported antioxidant effect and anti-inflammatory action , is used in treatment of hypertension mainly, and the main benefit in treatment patients with angina pectoris or myocardial infarction, add to role in central nervous system diseases as migraines and anxiety disorders, and tremor but rarely used in gynecology field in spite of many action either by beta receptor block or other mechanisms it acts with, such as anti _inflammatory, anticancer, antioxidant activity, pro_poptosis, and wound healing. In this review, we have discussed the various aspects of propranolol that can be applied in clinical gynecology in number of ways such as local contraceptive, in the treatment of Vulovaginitis by affected main criteria of Trichomonas and Guardia lamblia ,which is motility ,propranolol inhibited motility of both organism and consequence inhibition of the growth of both organism, for the treatment of genital hemangioma, We have also shed some light on experimental studies _ such as its effect on polycystic ovary and endometriosis.

Keywords: Propranolol, β-adrenergic, angina pectoris, myocardial infarction, gynecology.

INTRODUCTION

Propranolol is a drug with beta blocker effect and used clinically in treated hypertension Thyrotoxicosis, and recent in capillary hemangiomas, anxiety, and essential tremors [1]. But clinical applications in gynecology is limited and route of administration oral route, injection but what about vagina route is used only as a spermicidal effect.

Function

Propranolol has an ability to crosses the blood-brain barrier Propranolol effect on blood vessel either vasoconstriction effect via beta-adrenergic antagonists or modulation function of NO either by inhibition synthesis and or release [2] or both action vasoconstriction or vasodilation according to dose in study of Sonia Maccair, demonstrated biphasic according to dose With low dose vasoconstriction effect is obvious but with high dose vasodilation effect is dominant as regards vasodilation action alone in study of Priviero, F. B *et al*., experimental on rat reported that the prolonged administration of propranolol after block of nitric oxide the vasodilation action occur by three mechanisms first mechanism agumentum of the relaxation effect of acetylcholine. Second mechanism block calcium entry into vascular smooth muscle third mechanism. Increase No bioavailability [3]. As regarded Angiogenesis the proangiogenic growth factor and proangiogenic cascade synthesis are stimulate by adrenergic agonists adds to above matrix metalloproteinase 9. Also, stimulate by adrenergic agonists thereby propranolol play role in inhibition of angiogenesis by inhibition of these proangiogenic proteins mentioned above. Others, studies mention role of propranolol in angiogenesis study of Giavazzi R1*et al.*, that expression of proangiogenic factor control by adrenergic signaling [4]. and study by Stiles *et al*., demonstrated that propranolol treated hemangioma by inhibition phosphorylation of vascular endothelium growth factor the same results in study of Lamy S, *et al*., [5, 6] study of. Hu HT *et al*., demonstrated the link between the adrenergic receptor and HIF1 α expression and the block adrenergic receptor block Angiogenesis through the down regulation of HIF1 α and VEGF [7] propranolol improve iron hemostasis by restoring bone marrow function in the study of Alamo *et al*., [8] propranolol has the ability to concentrate and raise pH of lysosomes in the study of Mak IT *et al*., so has a protective effect against iron load-mediated cytotoxicity [9]. The release and uptake of iron by macrophage is Sensitive to Propranolol study by Andrei M et al result [10]. Propranolol antioxidant effect

For example during iron overload condition for any cause antioxidant and anti-inflammatory action of Propranolol is obvious by decrease in the uptake of iron by cardiac so maintain cardiac function in iron toxicity

[11]. Another study of antioxidant action by Dimitra Taprantzi propranolol reduces systemic oxidative stress and end toxemia in cirrhotic patients with esophageal varies [12] Propranolol affect matrix metalloproteinase-2 by inhibition its activity by in study of Ftemeh Hajighasem [13] propranolol induce apoptosis [14]. Propranolol has serotonin antagonist effect [15, 16].

Propranolol and Block Sodium Channels

Propranolol due to blocking effect on sodium channel the end result is membrane stabilizing effect and consequence of this properties it acts as a local anesthetic effect, antiarrhythmic and has central nervous system effects [17-19].

Application in Gynecology

Propranolol used in the treatment of many disease but used in gynecology diseases in clinical not mentioned in spite of many studies mentioned its multiple mechanisms of action .propranolol were considered the first line of treatment of hemangioma and genital infantile hemangioma and Food and Drug Administration approved th therapy.

Propranolol has Analgesic and Anesthetic Effect

Propranolol has analgesic and anesthetic action on local application in women with diabetic Vulovaginitis first symptom to relief is soreness of vulva and vagina after application mild burning sensation due to serotonin release follow by relief of pain in our study on the effect of propranolol on diabetic Vulovaginitis. Anter S this study agree with others study, as main complained of women with diabetic Vulovaginitis is pain and soreness [20] due to neuropathy and increase nerve growth factor in diabetic women which decrease by propranolol.

The Local Anesthetic Effect of Propranolol if Subcutaneous Injection

Produce cutaneous analgesic similar to lidocaine but more potent and prolonged action in study of Panel Yu [21, 22] the anesthetic action by decreasing Na+ influxes and also, decreased Ca2+ influxes [22, 23] propranolol decrease of neuronal excitability in nociception [24] by two mechanism first as mention above affected the channels of Ca2+ and also, activity of Na+ channels second mechanism is cyclic adenosine monophosphate by decrease cAMP intracellular [25] and consequence the activity of adenylcyclase reduce [26], third mechanism the phospholipase A activity is affected by Propranolol by decrease [27] fourth mechanism Propranolol affected interleukin-6 by decrease its activity [28] fifth mechanism Propranolol and prevent release of tumor necrosis factor [29] all the fifty actions are linked to analgesia

Propranolol and Vaginal Infection

Propranolol affected motility of sperm by inhibition and used as spermicidal [30] from this mechanism affected other motile organism as Trichomonas vaginalis and giardia. Farthing *et al*., study [31]. Adds to trichomonas and giardia infection cause vaginitis and can treatment by Propranolol also Propranolol can combat candida albican by inhibits hypha development affected the appearance of germ tubes by inhibition without decreasing growth rate by mechanism may be due to binding by propranolol of phosphatidic acid [32].

Propranolol and Defense against Bacterial Infection

Leukocyte maintain tissue homeostasis during inflammation by migration to infection site by adhesion to blood vessel wall and it found that Propranolol affected function of leukocyte by improved adhesion capacity.

In study of Michael Buckley R so, propranolol has role in defense against bacterial infection [33] other conditions of impaired adhesive function of leukocyte and may be benefit by treatment with propranolol as patients under glucocorticoid therapy [34] and patients with multiple myeloma [35].

Propranolol decrease thickness of epithelium of vagina rat on local application in study of Julie L *et al.*, found that local application of Propranolol on vagina rat thickness of epithelium decrease and the thickness increase more with each treatment of Propranolol Julie L *et al*., [36].

The impact of Propranolol on polycystic ovary in study was done by Silva *et al.*, clarified that sympathetic hyper activation play role in onset of polycystic ovary and propranolol prevent onset of polycystic cystic ovary by block beta receptor [37] as regarded propranolol and role on endometriosis as propranolol inhibition action on Angiogenesis by inhibition activity on VEGF, MMP-2, and MMP-9 so affected viability of endometriosis in study of Ozlem Uzunlar A *et al*., [38].

CONCLUSION

Propranolol is beta blocker for treatment hypertension and others away from gynecological field and by route other than vagina route in spite of its effectiveness route and less side effect but clinical applications in gynecology is limited to spermicidal and infantile genital hemangioman and my previous study was done in treatment of Trichomonas vaginalis and diabetic vulovagnitis the aim of review to open eyes on possible used of Propranolol in polycystic ovary and endometriosis and pass from animals study for more studies

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