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PROSTAGLANDINS: AN OVERVIEW

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ABSTRACT

Prostaglandins are bioactive lipid compounds derived from fatty acids and are important signalling molecules in the human body. They exert their effects by binding to specific receptors known as prostaglandin receptors. These receptors are integral to a wide range of physiological processes, including inflammation, pain perception, blood flow regulation, and reproductive functions. There are several types of prostaglandin receptors, classified into various families, including EP, FP, DP, IP, and TP receptors. Each type of receptor responds to specific prostaglandin subtypes. The activation of prostaglandin receptors triggers intracellular signalling cascades, ultimately leading to diverse effects, such as vasodilation, vasoconstriction, inflammation, and pain perception. In inflammation, prostaglandins promote vasodilation, making blood vessels wider to allow immune cells to reach the affected area, resulting in redness and swelling. They also contribute to pain perception by sensitizing nerve endings. Prostaglandins are crucial for regulating blood pressure and blood clotting. Some types cause vasoconstriction, while others cause vasodilation. This balance affects blood pressure. In reproductive health, prostaglandins play a key role in uterine contractions during menstruation and labour. Understanding the interactions between prostaglandins and their receptors is essential for developing targeted therapies and medications. Medications that either stimulate or inhibit specific prostaglandin receptors can be used to treat various medical conditions. Many research had been carried out to develop and make use of prostaglandin analogues to treat various diseases. But with the changing era and advancement in technology, more emphasis on research and development is required for the benefit of health care system.

KEYWORDS: Prostaglandins, eicosanoids, biosynthetic pathways, Prostanoid Receptors.

INTRODUCTION

Prostaglandins (PG) is the generic name for a group of closely related, cyclic, oxygenated 20 C-atom containing unsaturated fatty acids. These are considered to be derived from a hypothetical parent acid called prostanoic acid which is a 20 C-atom containing fatty acid with a five-membered cyclopentane ring.[1-3]

PG is not just one substance, but a whole family of compounds (PGA, B, C, D, E and F) and are formed in most of the tissues.[4] Prostaglandin was first isolated from seminal fluid present in the prostate gland, in 1935 by the Swedish physiologist Ulf von Euler[5] and independently by the Irish-English physiologist Maurice Walter Goldblatt (1895–1967) and hence the name prostaglandins was given to those compounds which is a misnomer.[6-8] The inflammatory mediators derived from the membrane phospholipids are called "eicosanoids", which include PGs, thromboxanes, leukotrienes and platelet-activating factor (PAF). The eicosanoids are derived from arachidonic acid which is also called eicosa tetraenoic acid.[9] It is a 20 C-atom containing unsaturated fatty acid having four double bonds (eicosa 20 C-atom; tetraenoic 4 double bonds). The term prostanoids includes only PGs and thromboxanes.[10,11]

NOMENCLATURE

The nomenclature of eicosanoids (particularly of PGs) is a bit confusing. These are the derivatives of arachidonic acid. All prostaglandins have a cyclopentane ring with a double bond between C-13 and C-14 and an OH group at C-15. The subscript "2" denotes that the PG has a total number of two double bonds in the side chain (inclusive of that between C13-C14). The subscript "α" denotes that the orientation of the OH group at the 9-position of the cyclopentane ring is above the plane of that ring.

The names of the first two PGs were assigned on their method of separation: PGE from Ether and PGF from phosphate buffer (Fosfat in Swedish language). PGA and PGB were so named because the former was stable in Acid while the latter in Base. The alphabets like D, H and I were later suffixed to PGs in a random manner. PGE_2 has a C=O group at position 9 and an OH group at

position 11 of the cyclopentane ring while $PGF_{2\alpha}$ has OH groups at both of these positions.[12,13]

BIOSYNTHESIS OF EICOSANOIDS

The flow chart outlines the biosynthetic pathways of various eicosanoids as well as the exact steps where clinically useful drugs block these pathways. With suitable stimuli (physical, chemical. neurological or humoral, e.g., bradykinin), the enzyme phospholipase A_2 (PLA_2) is activated which liberates arachidonic acid from the membrane phospholipids. At least three PLA_2 (cardiac PLA_2, cytosolic PLA_2 and secretory PLA_2) mediate arachidonic acid release from membrane lipids.[14]

Following its release, the arachidonic acid is oxygenated and cyclised by the cyclo-oxygenase pathway. Pathways through which PGs are synthesized are shown in **Fig. 1.**[15-22]

BIOSYNTHESIS OF PGS AND THROMBOXANE A_2

(Cyclo-oxygenase Pathway)

Two unique cyclo-oxygenase (COX) enzymes (COX- I and COX-2; also known as PGH synthase-1 and -2, respectively), convert arachidonic acid into different prostanoids (i.e., PGs and thromboxanes).[22] COX-1 is constitutively expressed (i.e., it is always present in most of the cells); while COX-2 is inducible in inflammatory cells by an inflammatory stimulus (e.g., endotoxins, cytokines and tumour promoters).[23] The two isozymes also differ in their functions. COX- I have "housekeeping" functions, e.g. gastric cytoprotection and regulation of vascular responses. COX-2 is involved in normal renal development and vascular prostacyclin (PGL) production.[24] COX-2 is the predominant cyclo-oxygenase at the sites of inflammation but not at sites such as GIT and platelets.

A new COX isozyme (COX-3) has also been identified recently. In humans, COX-3 mRNA is expressed most abundantly in the cerebral cortex and the heart. It is selectively inhibited by paracetamol. It is involved in pain perception and fever but not in inflammation.[25-26]

Both the COX_S promote oxygenation and cyclisation of arachidonic acid to yield PGG_2 which is then rapidly modified by peroxidase moiety of COX to PGH_2.[27] PGH_2 being highly unstable gets quickly converted to prostaglandins (PGE_2, $PGF_{2\alpha}$ and PGD_2), prostacyclin (PGI_2) and thromboxane A_2 by separate pathways as shown in **Fig.1**. In platelets, the pathway leads to thromboxane A_2 (TXA_2), in vascular endothelium it leads to prostacyclin (PGI_2) and in mast cells to PGD_2, while in vasculature, GIT, lungs and other tissues to PGE_2 (PGF is formed mainly in smooth muscles of GIT, bronchi, uterus and blood vessels).[27,28]

All prostanoids, then rapidly undergo oxidative metabolism to their corresponding inactive metabolites. The half-life of most PGs in circulation is less than one minute.[29]

BASIC PHARMACOLOGY OF PROSTANOIDS (PGS & TXA_2)

Prostanoid Receptors

Based on the five classes of natural prostanoids (PGD_2, PGE_2, $PGF_{2\alpha}$, PGI_2, and TXA_2) there are five main classes of prostanoid receptors which are termed as DP, EP, FP, IP and TP receptors, respectively.[30] The EP receptors are further subdivided into four subgroups as EP_1, EP_2, EP_3, and EP_4.[31] All of these receptors are G-protein coupled receptors, which utilise IP_3/DAG or cAMP transducer mechanisms.[32] Their characteristics are summarised in **Table. 1**

Table 1.

Receptor type[30]	Endogenous ligand	G- protein II Messenger	Function
DP[1]	PGD2	GS; ↑Camp	Inhibits platelet aggregation, Vasodilatation, Relaxation of GIT, bronchial and uterine muscle[33-36]
EP1[37,38]	PGE2 (also PGF2α)	Gq; ↑ IP3 ↑ DAG	Bronchoconstriction, GIT smooth muscle contraction[37,38]
EP2[37,38]	PGE2	Gs; ↑ CAMP	Bronchodilatation, Vasodilatation; GIT smooth muscle relaxation, Stimulation of intestinal fluid secretion[39-41]
EP3[37,38]	PGE2	Gi; Gs; Gq ↑ or ↓ cAMP ↑ IP3, DAG	Inhibition of gastric acid secretion; Increased gastric mucus secretion (cytoprotective action), Contraction of the pregnant uterus and GIT smooth muscle, Inhibition of lipolysis and of Autonomic neurotransmitter release[42]
EP4[37,38]	PGE2	Gs; ↑cAMP	Vasodilatation, Maintenance of patent ductus[37,38]
FP[1]	PGF2α	Gq; ↑ IP3 ↑ DAG	Contraction of the uterus and GIT smooth muscle, ↓ intraocular pressure[27]
IP[37]	PGI2	Gs; ↑ cAMP	Inhibits platelet aggregation; Vasodilatation; Renin release, Natriuresis[37]
TP[1,43]	TXA2	Gq; ↑ IP3 ↑ DAG	Causes platelet aggregation, Vasoconstriction; Bronchoconstriction, smooth muscle cell mitogenic[43]

Prostaglandins biosynthesis

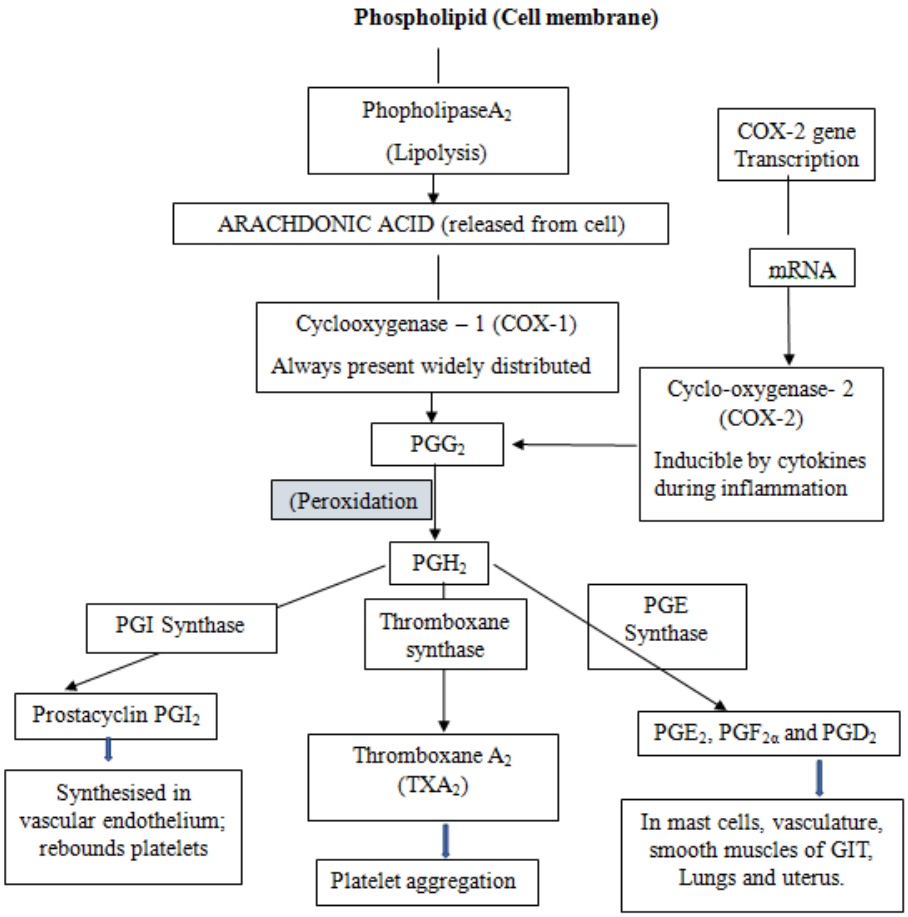


Fig. 1.

PHARMACOLOGICAL EFFECTS OF PROSTANOIDS

The PG_S, PGI_2, and TXA_2 have a vast variety of effects on vascular, gastrointestinal, reproductive and bronchial smooth muscles. Other targets include platelets, kidneys, endocrine organs, adipose tissue and CNS.

1) Cardiovascular System

$PGF_{2\alpha}$: Potent vasoconstrictor for large arteries and veins. It has little effect on BP, heart rate, cardiac contractility or capillary permeability. It is not a smooth muscle cell mitogen.

PGI_2: It is uniformly vasodilator and is more potent hypotensive than PGE_2. It keeps the patency of ductus arteriosus.[44]

PGE_2: Causes vasodilatation in most vascular beds. When injected with I.V. it produces a fall in BP. It has a weak positive inotropic effect on the heart and increases cardiac output slightly. It also increases capillary permeability. It is continually produced in ductus arteriosus during foetal life and keeps it patent.[45,46]

TXA_2: It is a consistent vasoconstrictor and a smooth muscle cell mitogen. It is the only eicosanoid to have a mitogenic effect. This effect is potentiated by testosterone which upregulates TP-receptors.[47]

2) Platelets

PGI_2 effectively inhibits platelet aggregation. PGD_2 and PGE_2 also have antiaggregatory actions but PGE_2 has inconsistent effects. TXA_2 is a potent platelet aggregator. Working together with PGI_2, it maintains the integrity of the vascular endothelium, preventing platelets to aggregate and stick to the arteriolar walls. Because platelets lack nuclei (and hence DNA), they cannot continually synthesise COX-1 and therefore a limited amount of COX-1 and TXA_2 persists only up to the lifetime of platelet (approx. 7 days). This contrasts with the vascular endothelial cells, which have nuclei and therefore can produce new COX-1 (and therefore PGI_2) on a regular basis. This property of platelets has been exploited by using low doses of aspirin for the prevention of coronary thrombosis.[48]

3) Uterus

Both PGE_2 and $PGF_{2\alpha}$ uniformly contract pregnant as well as nonpregnant uterus in vivo, but $PGF_{2\alpha}$ is 20 times more potent than PGE_2. In vitro, however, PGE_2 relaxes nonpregnant but contracts the pregnant uterus while $PGF_{2\alpha}$ consistently contracts both. At term, PGs, in low doses, soften the cervix and make it more yielding. PGs produced by the foetus, at term, may be involved in the initiation and progression of labour. Primary

dysmenorrhoea is attributable to the increased endometrial synthesis of PGE_2 and $PGF_{2\alpha}$ during menstruation, with uterine contractions which lead to ischaemic pain. Aspirin group of drugs, therefore, are highly effective in relieving dysmenorrhoea in most women.[49]

4) Bronchial Muscle

PGE_2 and $PGI_{2\alpha}$ cause relaxation of bronchial smooth muscle. $PGF_{2\alpha}$ and TXA_2 (also PGD_2 through a TP receptor) induce contractions of respiratory muscles. Asthma may also be attributed to an imbalance between bronchoconstrictor PGs ($PGF_{2\alpha}$, TXA, and LTs) on one hand and bronchodilator PGs (PGE_2, PGI_2 and PGE_1) on the other. The dilator PGs also inhibit histamine release. In some individuals, aspirin induces asthma because of the shift in arachidonic acid metabolism from the COX-pathway (blocked by aspirin) to the leukotriene pathway. Leukotrienes are very powerful broncho- constrictors.[50-52]

5) Gastrointestinal Tract

PGE_2 markedly reduces acid secretion in the stomach. PGI_2 also inhibits acid secretion but to a lesser extent. Both PGE_2 and PGI_2 also increase mucus production and mucosal blood flow, i.e., PGE_2 and PGI_2 are antiulcerogenic. The ulcerogenic action of the aspirin group of drugs is probably due to the loss of this cytoprotective influence.

The longitudinal muscle of the gut is contracted by PGE_2 (via EP_3 effect) and by $PGF_{2\alpha}$ (via FP effect). PGE_2 also increases water and electrolyte secretions in the intestines. Hence colic with watery diarrhoea are important side effects of PGE_2. PGI_2 opposes the propulsive activity of PGE_2 and does not produce diarrhoea. PGs seem to play some important role in colonic cancer and regular intake of aspirin, therefore, reduces the risk of colonic cancer.[53-55]

6) Kidney

The renal medulla produces substantially more PG_S compared to the renal cortex. Both PGE_2 and PGI_2 cause natriuresis and renal vasodilatation and inhibit ADH action to promote water clearance. In addition, PGE_2 decreases Cl reabsorption. Both facilitate $ß_1$ adrenoceptor stimulated renin release. TXA_2, however, causes renal vasoconstriction, and perhaps an ADH-like effect (but kidneys synthesise very little TXA_2). Loop diuretics, e.g., furosemide, produce a part of their effect through stimulation of COX activity to produce vasodilator PGE_2 and PGI_2. That is why, the patient's response to a loop diuretic diminishes if a COX-inhibitor like indomethacin is administered concurrently.[56-58]

7) Male Reproductive System

There is about 20 times more PGE (PGE_1 and PGE_2) than $PGF_{2\alpha}$ in fertile semen. TXA_2 and LT_S are not found in semen. Testosterone promotes prostaglandin production while large doses of aspirin decrease PG contents of seminal fluid. PGE_2, due to its smooth muscle relaxing effect, enhances penile erection. It increases sperm motility from the vagina to uterus.[59-62]

8) Central Nervous System

No clear cut physiological role of PGs in CNS has yet been established. Nonetheless, PGE_1 and PGE_2 are pyrogenic (via EP_3 receptor action). Their synthesis is blocked by aspirin. In some animal species, PGD_2 induces sleep. $PGF_{2\alpha}$ is not pyrogenic (unless given exogenously). PGD_2 and TXA_2 are also not pyrogenic. PGs probably function as neuro-modulators in the brain as they inhibit the release of NE from postganglionic sympathetic nerve endings.[63,64]

9) Peripheral Nerve Endings

Both PGE_2 and PGI_2 sensitise pain receptors at afferent nerve endings to mediators of pain (histamine, 5-HT and bradykinins) at the inflammatory site and amplify algesia.[65]

10) Endocrine System

PGE_2 facilitates the release of growth hormone, TSH, ACTH, FSH, LH and prolactin. However, PGE_2 analogues, per se have no significant effect on the release of these hormones. It also has insulin-like effects on carbohydrate metabolism.[66,67]

11) Bone Metabolism

PGE_2 plays some role in osteoporosis that occurs at menopause as it stimulates bone resorption. PGE_2 plays an important role in osteoporosis which occurs at menopause as it stimulates bone resorption. PGE2 secreted by osteoblasts increases when bone density decreases. It has been seen in various studies that the use of NSAIDs contributes like ibuprofen treatment being able to improve trabecular bone quality by Inhibition of prostaglandin synthesis contributing to the limitation of pathological bone growth and the formation of heterotopic ossification reducing osteoclasts and bone inflammatory cytokines (IL-1β and TNF-α).[68]

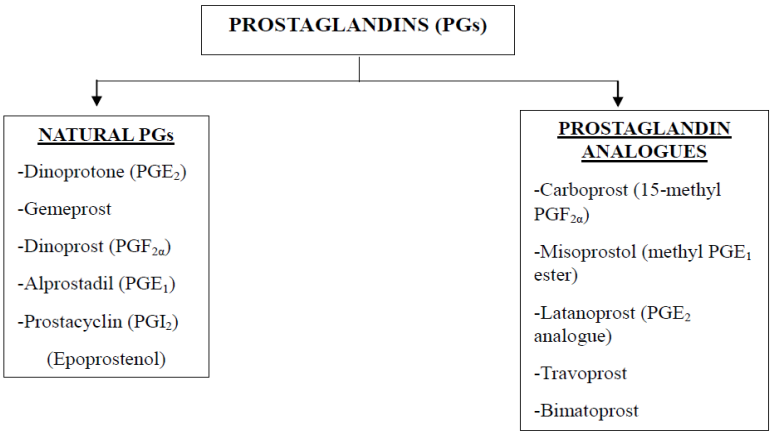
12) Eye

$PGF_{2\alpha}$ (via FP receptor action) and PGE_2 lower the intraocular pressure by increasing the outflow of aqueous humour from the anterior chamber via the uveoscleral pathway.[69]

13) Cancer

PGE_2 is considered to be the principal pro-oncogenic prostanoid, which promotes polyp formation (colon carcinogenic). TXA_2 is another likely pro-carcinogenic mediator.[70,71]

PROSTAGLANDINS AND THEIR ANALOGUES[72]



THERAPEUTIC USES OF PROSTANOIDS

PGs are not popular drugs in clinical practice because of their limited availability, instability, shorter half-life, cost, adverse effects and parenteral route of administration. Yet, some analogues are gaining popularity for the following indications:

1) Abortion

PGE_2 and $PGF_{2\alpha}$ and their analogues are used to terminate pregnancy and to induce cervical ripening in pregnancy. These prostaglandins are used for first and second-trimester abortion and appear to soften the cervix, before abortion, by increasing proteoglycan content and changing the collagen characteristics.[73,74] PGs or its derivatives in current practice are:

Dinoprostone: It is a synthetic derivative of PGE_2 which is administered vaginally for inducing abortion in the second trimester of pregnancy and for ripening of the cervix for induction of labour at full term. Its plasma half-life is 2.5-5 min. Its use for menstrual regulation or for early abortions (1-2 weeks after the last menstrual period) is usually avoided because of the chances of prolonged vaginal bleeding and severe menstrual cramps.[75]

Misoprostol: It is a PGE_1 derivative which is given orally for abortifacient purposes. It is used with mifepristone to induce abortion in the first few weeks of pregnancy. Vaginal, route of administration is associated with increased incidence of sepsis.[76-78]

Carboprost: It is a $PGF_{2\alpha}$ derivative which is usually administered by intra-amniotic injection for inducing second-trimester abortions.[79,80] The drug is now least preferred because of its serious toxicity such as cardiovascular collapse, chances of anaphylactic shock and pulmonary hypertension.[73,74]

2) Facilitation of labour, cervical priming and post-partum haemorrhage

Oral PGE_2 is superior to oral oxytocin analogues and is as effective as I.V. oxytocin in augmenting labour and checking postpartum haemorrhage.

Dinoprostone (PGE_2 derivative), however, is less effective than oxytocin as it is for vaginal administration. Vaginal PGE_2 or dinoprostone can also be used to soften the cervix before inducing labour. Oral $PGF_{2\alpha}$ causes more GIT toxicity than PGE_2. Though clinical benefits have not been documented, PGs can be preferred over oxytocin for inducing labour in women with pre-eclampsia, eclampsia or cardiac or renal disease as they have diuretic and natriuretic effects. In intrauterine foetal death, PGE_2 alone or with oxytocin seems to cause evacuation effectively.[80-82]

Carboprost ($PGF_{2\alpha}$ derivative) has been successfully used to control postpartum haemorrhage when oxytocin or methyl ergonovine is not available.[82]

3) Healing of peptic ulcer

PGE_1 and PGE_2 have remarkable cytoprotective effects against peptic ulcers. Misoprostol (a stable PGE_1 analogue) is orally administered in a dose of 200 µg four times daily for this purpose. This and other PGE_2 analogue (enprostil) are used for healing peptic ulcers in patients with NSAID-induced ulcers or in persons who are chronic heavy smokers.[83-87]

4) To prevent platelet aggregation

TXA_2 promotes platelet aggregation and PGI_2 inhibits it. PGI_2 derivative (epoprostenol) can be used to prevent platelet aggregation in extra-corporeal circulation such as renal dialysis and cardiopulmonary bypass. PGE_1 and PGI_2, in smaller amounts, can also be used for storage of platelets for transfusion.[89,90]

5) To treat pulmonary hypertension

A PGI_2 preparation (epoprostenol), lowers peripheral, pulmonary and coronary resistance. By providing I.V. infusion, the drug has been used to treat pulmonary hypertension. A longer-acting PGI_2 analogue, treprostinil has been approved for use in pulmonary hypertension by I.V, S.C and inhalation route.[90,91]

6) For patency of ductus arteriosus

Both PGE_2 and PGI_2 are responsible for maintaining the patency of foetal ductus arteriosus. PGE_1 being a

vasodilator and inhibitor of platelet aggregation also plays the same role. In certain types of congenital heart disease, like pulmonary artery stenosis, it becomes essential to maintain the patency of the neonate's ductus arteriosus prior to or during surgery. This is done by giving an I.V. infusion of alprostadil (PGE_1) or epoprostenol (PGI_2 preparation).[93,94]

7) Peripheral vascular disease

PGE_1 or PGI_2 infused I. V. can promote ulcer healing in acute intermittent claudication. Beraprost is a stable oral PGI_2 derivative which is given thrice a day for treating peripheral vascular disease.[95,96]

8) For treating glaucoma

Ocular drops of latanoprost (a stable, long-acting $PGF_{2\alpha}$ derivative) have shown efficacy similar to 20 timolol in reducing intraocular pressure (via FP receptor action). Other drugs in this series include bimatoprost, travoprost & unoprostone. Prostaglandin analogues are the front-line medications for the treatment of glaucoma. The currently used prostaglandin analogues (latanoprost, bimatoprost, tafluprost, and travoprost) mimic PGF2 and target one of the prostaglandin receptors (FP), though research into harnessing the other receptors using compounds like Sulprostone (EP3 receptor).[69,97]

9) Other uses

a) Male impotence: Intracavernosal injection or urethral suppository of alprostadil (PGE_1) is used to treat erectile dysfunction. Side effects include pain but priapism is less common.[98]

b) To reduce infarct size: Intravenous infusion of PGI_2 (iloprost), in the immediate post-MI period, can help reduce the infarct size but efficacy is doubtfull.[99]

c) Bronchial asthma: Aerosolised PGE_2 effectively aborts the acute attack of asthma but clinical utility is limited because of coughing as side effect.[100]

SIDE EFFECTS OF PROSTANOIDS

- Abortifacient PGs exhibit dose-related adverse effects such as vomiting, diarrhoea, fever and broncho-constriction.[101]
- Hypotension, syncope, dizziness and flushing can also occur which may be related to the vasomotor and vasovagal effects of PGE_2.[102]
- The intra-amniotic injection of carboprost ($PGF_{2\alpha}$ derivative), to induce second-trimester abortions can cause anaphylactic shock and cardiovascular collapse.[103]
- $PGF_{2\alpha}$ has a greater gastrointestinal toxicity than PGE_2. $PGF_{2\alpha}$ should be used with caution in persons having asthma.[104]
- Prolonged treatment with alprostadil (PGE_1), for maintaining the patency of ductus arteriosus, should be avoided as it may lead to ductus fragility and rupture.[93,94]
- Misoprostol (PGE_1) and enprostil (PGE_2 analogue), used for the treatment of peptic ulcer, usually cause GIT discomfort and diarrhoea. However, these side effects are dose related.[105]
- Recently, dose-dependent hyperostosis and bone pain have been reported in patients having liver disease, if these drugs are used on a long-term basis.[106]
- These results are due to a PGE-induced, EP_4-receptor mediated increase in osteoclast and osteoblast activity. Recurrent renal Ca^2 oxalate stones may be another problem due to PGE-induced hypercalciuria.[107]
- $PGF_{2\alpha}$ analogues (latanoprost and bimatoprost) used for treating glaucoma, produce blurred vision, brown pigmentation of the iris and dryness in eyes.[69]

RECENT ADVANCES IN PROSTAGLANDINS AND ITS ANALOGUE

Selexipag

Selexipag is a novel oral, selective agonist of the PGI2 (IP) receptor, undergoing phase 4 clinical trial as of 2022.[108] Activation of the IP receptor induces vasodilation in the pulmonary circulation and inhibits the proliferation of vascular smooth muscle cells and is found to be beneficial in management of pulmonary arterial hypertension.[109]

Selexipag, a PGI_2 analogue and its active metabolite are selective agonists of the IP receptor, which is administered by subcutaneous/intravenous infusion or by inhalation or orally.[110] Common side effects of Selexipag, are nausea, vomiting, headache, hypotension, and flushing, Contraindicated with strong CYP2C8 inhibitors.[111]

Treprostinil

Treprostinil, PGI_2 analogue which is undergoing a phase 4 clinical trial, is being developed to use in powder form is used in pulmonary hypertension associated with interstitial lung disease. Its common side effects are an increased risk of bleeding when used with anticoagulants or platelet inhibitors.[112]

Tafluprost

Tafluprost is a prodrug of the active substance, tafluprost acid, a structural and functional analogue of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$). Tafluprost acid is a selective agonist at the prostaglandin F receptor, increasing the outflow of aqueous fluid from the eyes and thus lowering intraocular pressure. Tafluprost, as a lipophilic ester, easily penetrates the cornea and is then activated to the carboxylic acid, tafluprost acid.[113]

Sulprostone

It is a PGE2 analogue which acts on EP3 receptor, which is under the early phase of research and has given promising results in the treatment of Glaucoma.[69]

Compound ONO-AE3–208, which is an EP_4 antagonist is under trial that inhibits growth or metastasis of breast, prostate, colon cancer cells and melanoma.[114]

CONCLUSION

As prostaglandins are vastly synthesized and have an action on most tissues of the body, it plays an important role in the physiological and pathological aspect of the body. PGs and their receptors are involved and act on most organ systems of the body, where some actions are beneficial and some are harmful and unwanted. Many research has been carried out to develop and make use of prostaglandin analogues to treat various diseases. But with the changing era and advancement in technology, more emphasis on research and development is required for the benefit of health care system.

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