Drugs for Erectile Dysfunction

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OVERVIEW

- Erectile dysfunction(ED) and benign prostatic hyperplasia(BPH) are the common urological disorders in male.ED is the inabilty to maintain penile erection for the successful performance of sexual activity. Cause of ED has many causes but someone them are vasscular disease, diabetes, medication, depression and sequelae to prostatic surgery. BPH is nonmalignant enlargement of prostate, which occure naturally as men age.

Drugs used for erectile dysfunction

a) Alprostadil$_{(muse, caverject, edex)}$

b) Avanafil$_{(stendra)}$

c) Sildenafil$_{(viagra)}$

d) Tadalafil$_{(cialis)}$

e) Vardenafil$_{(levitra, staxyn)}$

All the above drugs are phosphodiesterase-5 inhibitors. But Alporstadil$_{(muse, caverject, edex)}$ are synthetic prostaglandin E1(PGE1) and its mechanism of action is unknown and its available in

phosphodiesterase-5 inhibitors

a) All four PDE5 inhibitors, Avanafil$_{(stendra)}$, sildenafil$_{(viagra)}$, tdalaafil$_{(cialis)}$, vardenafil$_{(levitra, staxyn)}$ are equally effective in treating of ED and advers effect profile are simillar. However, these agent differ in the duration of action and the effect of food on drug absorption. [Note:sildenafil$_{(viagra)}$ and Tdalaafil$_{(cialis)}$ are also indicated to treat pulmonary ypertension, although the dosage regimen differ for this indication.

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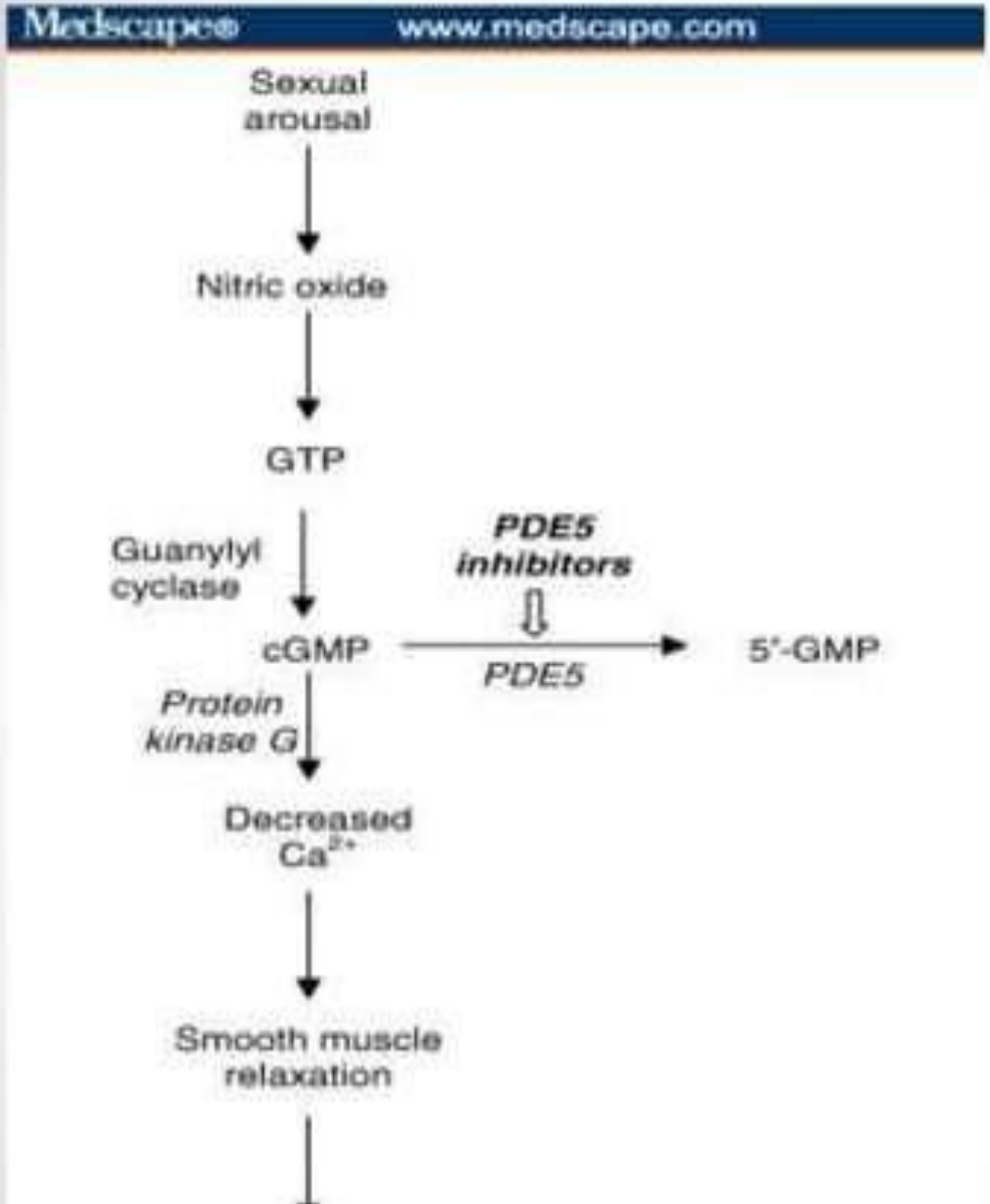
- Taking one of these tablets will not automatically produce an erection. Sexual stimulation is needed first to cause the release of nitric oxide from your penile nerves. These medications amplify that signal, allowing some men to function normally. Oral erectile dysfunction medications are not aphrodisiacs, will not cause excitement and are not needed in men who get normal erection.

Mechanism of action

- Sexual stimulation result in smooth muscle relaxation of the corpus cavernosum(penile tissues), increasing the inflow of blood. The mediator of this reponse is nitric oxide(NO). NO activates guanylyl cyclase, which form cyclic guanosine monophosphate($_c$GMP) from guanosine triphosphate produced smooth muscle relaxation through a reduction in the intracellular (Ca^{2+}) concentration. PDE-5 enzyme responsable fro the degradation of ($_c$GMP) in the corpus cavernosum. The duration of action of cyclic nucleotide is controlled by the action of phosphodiesterase(PDE).



Schematic diagram illustrating the mechanism of action of the phosphodiesterase type 5 (PDE5) inhibitors. Following sexual arousal, nitric oxide is released from the synapses of neurones in the corpus cavernosum of the penis. This results in accumulation of cyclic guanosine monophosphate (cGMP), produced from Guanosine triphosphate (GTP), which causes smooth muscle relaxation leading to an erection. By preventing cGMP breakdown, PDE5

Pharmacokinetics

- Sildenafil$_{(viagra)}$ and vardenafil$_{(levitra, staxyn)}$ have similar pharmacokinetic properties. Both drugs should be taken apporximately 1 houre before sexul activity, with erectile enhencement observed for up to 4 houres after administration. Thus the administration of both of drugs must be timed appopriately with regard to anticipated sexual activity. The obsorption of both durgs is delayed by consumption of high-fat meal. Tadalafil$_{(cialis)}$ has solwer onset of action than sildenafil$_{(viagra)}$ and vardenafil$_{(levitra, staxyn)}$, but a significantly longer half-life of approximately 18 hours, so its approved for once-daily dosing. The obsorption of Tadalafil$_{(cialis)}$ is not clinicly infulenced by food. Avanafil$_{(stendra)}$ has the quickest onset of action. It shoukd be taken 30 minutes prior to sexual activity. All the PDE5 inhibitors are metabolized by

Advers effects

I. The most frequent advers effeect of PDE5 inhibitors are headaceh, flushing, dyspepsia and nasal congestion.

II. Dsiturbances of color vision(loss of bule/green discrimination) may occour with PDE5 inhibitors. Probably because of inhibition of PDE-6(PDE found in the retina that important in color vision).

III. Tadalafil has been associatd with back pain and myalgias, likely because of inhibition of PDE11(An enzyme found in skeletal muscles).

IV. PDE5 inhibitors should be used with caution in patients with a history of cardiovasscular disease or those with storng risk factor of cardiovasscular disease.

V. PDE5 inhibitors should not be used more than once per day.

Alprostadil

- Alporstadil(muse, caverject, edex) are synthetic prostaglandin E1(PGE1). In penile tissue, PGE1 allow for relaxation of the smooth musclein the corpus cornosum and its mechanism of action is unknown and its available in intraurethral suppository and injectable formulation. Alporstadil(muse, caverject, edex) may be used for patients who are not candidate for oral therapies. Alporstadil(muse, caverject, edex) acts locally, which may reduce the occurance of advers effects.

Alprostadil self-injection

- With this method, you use a fine needle to inject alprostadil (Caverject Impulse, Edex) into the base or side of your penis. In some cases, medications generally used for other conditions are used for penile injections on their own or in combination. Examples include papaverine, alprostadil and phentolamine. Often these combination medications are known as bimix (if two medications are included) or trimix (if three are included).

Alprostadil urethral suppository

- Alprostadil$_{(Muse)}$ intraurethral therapy involves placing a tiny alprostadil suppository inside your penis in the penile urethra. You use a special applicator to insert the suppository into your penile urethra.

Mechanism of Action

- Alporstadil$_{(muse, caverject, edex)}$ causes smooth muscle relaxation by an unknown mechanism of action. Its belived that Alporstadil$_{(muse, caverject, edex)}$ increase concentration of cyclic AMP(cAMP) within te cavernosum tissue. As result, protent kinase is activited, allowing trabecular smooth muscle relaxation and dilation of cavernossl arteries, increase blood flow to the erection chamber compress venous outflow, so that blood entrapped and erection may occur.

Parmacokinetics

Systemic absorption of Alporstadil(muse, caverject, edex) is minimal, its quickly metabolized. The onset of action of Alporstadil(muse, caverject, edex) is 5 to 10 minutes when given as urethral suppository and 2 to 25 minutes when administrated by injection. The resulting erection may last for 30 to 60 minutes, longer, depending upon the particular patient.

Advers effects

I. Hypotension or headeach is possibility due to PGE1-induced vasodilation.

II. Locally, advers effect of Alporstadil$_{(muse,\ caverject,\ edex)}$ include penile pain, urethral pain and testicular pain.

III. Bleeding from the insertion or injection of Alporstadil$_{(muse,\ caverject,\ edex)}$ is rare.

IV. Hematoma, ecchymosis and rash are possible from Alporstadil$_{(muse,\ caverject,\ edex)}$ injection.

·TANKO