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REVIEW ARTICLE

Drug Considerations in Dental Clinic for Patients with Benign Prostatic Enlargement

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Abstract

Benign prostatic enlargement (BPE) is an extremely common condition among males across the globe. Half of the people suffering from this condition will have lower urinary tract symp- toms (LUTS). Benign prostatic hyperplasia (BPH) is the histopathological abnormality seen underneath this condition. Drugs that dentists prescribe in clinics especially NSAIDs can have severe side effects in such patients. This article discusses such drugs and their effects in patients with benign prostatic enlargement. (2020, Vol. 04; Issue 01: Page 7 - 12)

Keywords: BPE, LUTS, BPH, NSAIDs, Urinary retention.

Introduction

Prostate gland increases in volume by 2.4cm^3 per year on average from 40 years of age. Benign prostatic enlargement is the non- malignant growth of prostate in age- ing men around the globe. The enlarge- ment begins in the peri- urethral zone and gradually involves both the glandular and stromal tissues to a variable degree. The clinical features of BPE include difficulty in voiding urine due to obstruction of ure- thra by prostate, hesitation, poor urinary flow, sensation of incomplete emptying, urge of incontinence (1). All of these symp- toms constitute the LUTS.

The histologic prevalence of BPH across the globe is 10% in men of 30 years of age, 20% in their 40s, 50-60% in their 60s and 80-90% in their 70s and 80s (2). Not all men with BPH will develop BPE and not all patients with LUTS will develop BPE. Sim- ilarly patients with enlarged prostate may show no symptoms at all. Such condition is called as 'Silent Prostatism'. Histologic BPH although identified by International Classification of Diseases (ICD) code 600; it doesn't necessarily constitute any prob- lem for the patients. The patients only start to feel any sort of discomfort if he/she develops lower urinary tract prob- lems (3).

Association with non-steroidal anti inflammatory drugs (NSAIDs)

Prostatic diseases have been said to be associated with increased activity of cyto- kines, growth factors and cyclo-oxygen- ases (COX) 1 and 2. It has been seen that increased activity of COX 1 and 2 leads to increased levels and activation of prosta- glandins which in turn causes variety of inflammatory, angiogenic and anti-apop- totic processes (4).

Inflammation has been a major source for the development and progression of BPH. Inflammatory cytokine IL-17 has been seen to be present in inflamed prostate but not in normal one (5). Also COX-1 and COX-2 have been expressed in BPH and increased COX-2 levels have been associ- ated with increased levels of Bcl-2 and cell proliferation in BPH (6, 7). NSAIDs with their COX-1 and COX-2 inhibition effects can help to reduce the inflammatory ef- fects and progression in BPH. However dif- ferent studies have shown that NSAIDs have variable effects in patients with BPH. NSAID induced inhibition of cyclo-oxyge- nease -2 and prostaglandin synthesis leads to inhibition of bladder contraction which eventually causes acute urinary re- tention in both normal patients and pa- tients with BPH (8).

A Dutch treatment study from the Harvard records focussed on 45 years and older. It included patients with BPH, kidney stone, surgery, immobility, urinary tract infec- tion etc. with detailed medical infor- mation. It was seen that acute urinary re- tention was 2.2 times higher in those tak- ing NSAIDs than those who were not tak- ing them. It was also seen that it was 3.3 times higher in those who started NSAIDs recently than in those who were taking these drugs for some time now (9).

In the study of Minnesota (1990-2002), 2,447 men were evaluated for effects of NSAIDs on prostate. The study showed that effects of BPH was reduced in many subjects but the urinary flow rates were slow meaning that some amount of uri- nary retention was present (10).

The above two studies have demonstrated the fact that NSAIDs are friends as well as foes when it comes to their usage in BPH. In 2005, silverio et al conducted a study where 46 patients with BPH and LUTS were divided into 2 groups; one was treated with finasteride and one with finasteride and rofecoxib. The patients in finasteride and rofecoxib group showed reduction of BPH symptoms (11).

A study by Kang et al. (2004) has found out that Aspirin, Ibuprofen were associ- ated with moderate risk of nocturia, tran- surethral resection of the prostate (TURP) and aggravates the symptoms of BPH (12).

Association of BPH with usage of amitriptyline

It is a first generation tricyclic antidepres- sant with prominent anticholinergic ef- fects. Tricyclic antidepressants (TCAs) are the class of drugs that selectively benefits depressed without agitating psychotics (13). This drug is frequently used in dental clinics in treatment of oro-facial neuro- pathic pain and even sometimes used plainly as an anti-depressant in depressed patients. It has been seen that the anti- cholinergic effects of Amitriptyline occur within 24 hours of admission and at a lower dose than its anti-depressant effects (14).

Being an anticholinergic it blocks the parasympathetic pathway which in turns ef- fects the contraction of detrusor muscle and which is necessary for voiding of

urine, also it causes the urinary trigone to constrict thus causing relaxation of uri- nary bladder resulting in urinary reten- tion. It mainly occurs due to Muscarinic 3 (M3) receptor blockade (13, 15). As a result use of Amitriptyline is contraindicated in cases of BPH.

Association of BPH with adrena-line

Adrenaline is a commonly used direct sympathomimetic adrenergic group of drug. It is most commonly used in cases of cardiac arrest as it is a powerful cardiac stimulant and anaphylactic shock. In the field of dentistry adrenaline is most com- monly used as a vasoconstrictor with local anaesthesia which is used in different nerve blocks. This drug acts via the beta receptors present in urinary bladder; re-laxes the detrusor muscle and contracts the urinary trigone thus causing urinary retention especially in elderly cases with BPH (13).

However no cases have been reported of urinary retention in BPH patients who have undergone dental nerve blocks but few cases of post-operative urinary reten- tion has been reported in BPH patients who have undergone regional anaesthesia in the sacral region for vascular surgeries especially carotid endarterectomy (16).

Association of BPH with antihis-taminics

Antihistaminics are group of drugs that antagonize the actions of Histamine at H1 and H2 receptors. H1 receptor antagonists are mainly used to treat allergy, utricaria, rhinitis etc. and H2 receptor antagonists are used for treatment of peptic ulcers and gastric reflux. First generation H1 receptor antagonists like diphenyhydramine, chlorpheneramine, promethazine etc have the ability to cross the blood brain barrier and additionally they bind to muscarinic receptors leading to anticholinergic effect which causes urinary retention. However no cases of urinary retention have been re- ported upon systemic administration of antihistaminics. Moreover second genera- tion H2 receptor antagonists like cetiriz- ine, levocetrizine, acrivstine etc. does not cross blood brain barrier and no binding to muscarinic receptors are seen so the adverse anticholinergic effects including urinary retention is not seen (13, 15).

Su Ling et al. (1996) in their study have reported that antihistaminics have a 24%- 28% attributed risk to cause moderate to severe urinary retention in elderly patients (17).

Association of BPH with benzodi-azepines

In 1960 with the advent of Chlordiazepox- ide and Diazepam a brighter area of treat- ment was seen in the field of sedative-hyp- notics. These drugs were introduced as anti-anxiety drugs and were better than the barbiturates because of their high therapeutic index and the hypnotic doses didn't affect the cardiovascular and respir-atory functions.

In dental offices diazepam is mainly used as a centrally acting muscle relaxant in a dose of 5-10 mg in cases of spasm of mus- cles of mastication and limited mouth opening and in cases where peripheral muscle relaxants have failed to act reason- ably. Moreover alprazolam and clonazepam in doses of 0.25mg and 0.5mg has also been used as anti- anxiety medi- cations in very apprehensive patients.

Different authors have suggested that due to the muscle relaxant properties of ben- zodiazepenes especially diazepam; it can lead to urinary retention which is seen more in elderly patients with problems like BPH (15). Few authors have contradicted this fact stating that the muscle relaxant and anxiolytic properties of this group of drugs can treat acute urinary retention (18).

Association of BPH with atropine It is the classical anticholinergic drug. It is the prototype drug of this class and highly selective for muscarinic receptors. It comes under the natural alkaloids group of anticholinergics. These drugs are mainly used to treat narrow angle glau- coma in a dose of 1% atropine sulphate eye drop and 5% atropine sulphate eye ointment.

In dentistry it is mainly used as an anti – sialagogue as it decreases salivary secre- tion via the M3 blockage. Mainly used in dental offices if sialorrhoea / ptyalism (ex- cessive salivary secretion) is present. Sometimes excessive salivary secretions can result in problems in retention of cer- tain orthodontic and prosthodontics appli- ances in such cases a controlled, well monitored dose of atropine is used to de- crease the salivary secretion.

Being the prototype anticholinergic it has a relaxing action on the ureter and urinary bladder which further leads to urinary re- tention in patients especially in elderly people with BPH (13, 15).

Association of BPH with calcium channel blockers (CCBs)

These are one of the first line anti hyper- tensives used all around the world. All the subgroups of CCBs namely dihydro- pyridines (amlodipine), phenylalkylamine (verapamil), benzothiazepine (diltiazem) are all potent anti hypertensives. They re- duce blood pressure by reducing periph- eral resistance without affecting the car- diac output.

Due to its smooth muscle relaxation activ- ity due to inhibition of calcium influx it has been found to causes urinary reten- tion and LUTS in elderly patients with or without BPH.

Elhebir SE et al. (2013) found that the in- cidence of urinary retention and moderate to severe LUTS is higher in elderly patients with or without BPH who are on calcium channel blockers than the non users (19). In a health professional cohort study the incidence of LUTS and urinary retention is

2.2 folds higher in elderly patients on CCBs than the non users (20).

Lots of patients coming to the dental clin- ics are on these drugs and a dental sur- geon should always be aware about its side effects.

Association of BPH with nasal de-congestants

These are the group of drugs that are used in cases of nasal congestion. These are al- pha agonists which upon dilute applica- tion (0.5-1%) causes local vasocon- striction. One of the most common drugs of this family is pseudoephedrine which is a stereoisomer of ephedrine. It is widely used as a nasal decongestant especially in cases of acute rhinitis.

One of its adverse effects is urinary reten- tion especially in elder patients and those who have BPH. This action is mainly due to its systemic action on alpha 1A and beta adrenoceptors. The alpha 1A subtype promotes contraction of bladder neck,

urethra and prostate which further en- hances bladder outlet resistance espe- cially in elderly patients with enlarged prostate (21).

Association of BPH with antiparkinsonian agents

In his original essay on Parkinsonism, Dr. James Parkinson has mentioned bladder dysfunction as one of the non-motor symptoms of Parkinsonism which eventu- ally causes urinary retention (22). Patients with Parkinsonism are treated with certain drugs such as anticholinergics, amantadine, monoamine oxidase B inhib- itors, levodopa and dopamine agonists. Anticholinergic drugs are used in Parkin- son patients who are less than 70 years of age with disabling resting tremor and pre- served cognitive function (15).

The anticholinergic action of these drugs causes the ureter and urinary bladder to relax causing urinary retention. These symptoms further add up with bladder dysfunction symptom of Parkinsonism thus complicating the condition even more (16).

Conclusion

Benign prostatic hyperplasia is a very common condition seen mainly in old aged patients. The above discussed drugs are very commonly used by medical profes- sionals all around the globe. As dental di- agnosticians it is our prime duty to take a thorough history of the patients to search for conditions like BPH and give them drugs that do not cause any adverse reac- tion. Any mistakes in identification of the condition can lead to unwanted problems for both the patients and the doctor. A thorough knowledge of BPH along with the adverse drug reactions related to it is a must for us dentists so that we can even- tually plan and give the suitable drugs as because someone has rightly said that; 'failing to plan is planning to fail'.

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