



HOW NON PHARMACOLOGICAL PROCEDURES CAN HELP TO REDUCE DRUGS NEED AND HEALTHCARE COSTS IN OVB - URGENCY MICTURITION

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ABSTRACT

Aim of this work is to verify the efficacy of the KEGEL procedure used in the micturition urge dysfunction and the contribution that this can provide in reducing-avoiding pharmacological therapy. This approach can be useful to reduce healthcare costs (direct and indirect) and in order to increase the patient's quality of life. The social implications are relevant. The complexity in physiology and pathology in this condition needs an adequate treatment: Not only pharmacological approach or physiotherapeutic but also psychological and of lifestyle modification. This multidisciplinary approach can produce global benefit. The more severe cases are not considered in this work because required treatment like Botulin toxin injection or surgery procedure.

KEYWORDS: Overactive bladder.anatomy.physiology. nervous control, muscle.pelvic floor dysfunctions. Non pharmacological actions, KEGEL EXERCISE (KE), bladder training. psychology. pharmacology, drug need. avoided costs, quality of life Urology. micturition urgency. coffeine, Pharmacoeconomy.

INTRODUCTION

Overactive bladder is a condition whit specificf symphoms like minctionary urgency, increase of minctionary frequency, incontinency, nicturia.

Other imply bladder involuntary detrusor contractions.

This condition imply great quality of life reduction:

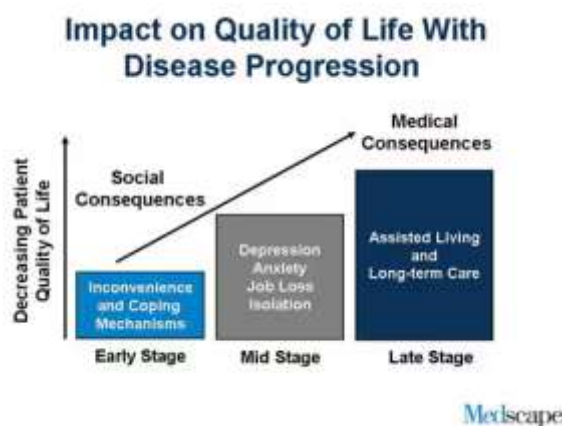


Fig No. 1: From Diane K. Newman, Mescape Urology 2024.

Variuos condition are involved like diabetes, reduced renal function, bladder cancers,IPB, increase bladder wall sensibility, weakened of pelvic musculature. pregnancy – birth, neurological condition like Parkinson disease, ICTUS, Multiple sclerosis. CNS or spinal cord or nerve damages. urological surgery or radiotherapy.

According Tammyris Helena Rebecchi Silveira et al

“It is now recognized that DM causes tissue damage by altering redox signaling in target organs. NADPH oxidase. whose sole function is the production of reactive oxygen species. plays a pivotal role in other well-known and bothersome diabetic complications”



Fig. No. 2: From <https://doi.org/10.3390/antiox13101155>

Also the ageing is a factor involved.

Other iatrogenic factors can be diuretics, high amount of coffee, alcoholic drinks, wine, IVU, high body weight, Menopausa with low estrogen level.

The diagnosis: general physicians or urologic evaluation anamnesi. imaging, laboratory test PSA test in men, fluxometry, cisto- retrograde uretrography, cystoscopy Urine analysis and uroculture to exclude infections, blood traces Neurological exam to detect sensorial or anomalous reflex.

Test urodynamic: the bladder functionality and its capacity to fill in right way. If not correctly empty during the urination the residual urine can produce similar symptoms like OVB.

In order to measure the amount of urine not emitted the physician can carry out an bladder ecographic analysis or to put a catheter through uretra in order to drain and measure the post. Mictional Residue still in bladder.

Uroflusometry, functional test to measure the volume and velocity of urinary flux.

Cistometry: to search involuntary contraction or if the bladder is not able to store urine correctly.

Uretrocistoscopy: to exclude cancers and kidney stones.

Various are the possibility of intervention:

behavioral: reducing body weight, normalize idric intake. avoid dietetic irritants like spieces, alcool. coffeina, artificial sweeteners et other.

Stop smoking, because irritant bladder and due by the fact that cough can produce urine loose.

Pelvic flor rehabilitation, KEGEL EXERCISE (KE), double mintion, bladder training.

Other imply intermittent urologic catheterism

Use of absorbent presidia for social life, good diabete control.

Related the drugs: anticholinergic for the detrusor iperactivity (controindacted if IPB. Glaucoma. Miatenia gravis). agonists of beta 3 adrenoceptor (Mirabegron), botulinic toxin A injection in refractory cases(MS and spinal cord lesions).

Sacran neruomodulation with pacemaker. surgery in particular patiens.

The specialist involved : urologist. ginecologist, neurologists. physioterapist, geriatriy. general physicians. nurse. pharmacist. pscyologist. Nutrition specialist. radiologists and laboratory medicine.

Systematic Review 10 November 2022

Healthcare and economic burden of anticholinergic use in adults with overactive bladder: a systematic literature review

Corinne Duperrouzel, Coby Martin, Ari Mendell, M. Bourque, Adam Carrera, Alicia Mack. and Jeffrey Nesheim

Journal of Comparative Effectiveness Research

<https://doi.org/10.2217/cer-2022-0160>

“Overactive bladder OAB is associated with increased incidence of various comorbidities, including depression, anxiety. falls, and reduced health-related quality of life. OAB is also associated with an high economic burden EB. including medical costs, lost productivity and healthcare resource utilization ; average healthcare costs (including inpatient, emergency

room, outpatient, pharmacy and other costs) for patients with OAB have been estimated about at \$3003 per patient per month vs \$1123 per patient per month for a matched control group without OAB”

In this works are analized the Pelvic floor (PF) dysfunction in men expecially related the micturition urgency.

This situation imply heavy socially implication related the high frequency in the micturition with Reduction of the quality of life of the patiens.

In the physiology of this fucntion various muscle are involved and related nervous system: sympatic, parasympatic and also somatic- voluntary.

Micturition is thus under cortical control. mediated by the spinal reflex arc, which inhibits the pontine center until it is deemed appropriate to void.

The motor cortex controls the voluntary muscle of the external urethral sphincter.

According article : Auton Neurosci. 2016 Oct

Role of pelvic floor (PF) in lower urinary tract function

Christopher J Chermansky. P. A Moalli

DOI: 10.1016/j.autneu.2015.06.003

“The pelvic floor (PF) plays an integral part in lower urinary tract storage and evacuation. Normal urine storage necessitates that continence be maintained with normal urethral closure and with urethral support. The endopelvic fascia of the anterior vaginal wall, its connections to the arcus tendineous fascia pelvis. and the medial portion of the levator ani muscles must remain intact to provide a normal urethral support. Normal pelvic floor (PF) function PFF is required for urine storage. Normal urine evacuation involves a series of coordinated events, the first of which involves complete relaxation of the external urethral sphincter EUS and levator ani muscles. Acquired dysfunction of these muscles will initially result in an sensory urgency and detrusor overactivity; With time the acquired voiding dysfunction can result in intermittent urine flow and incomplete bladder emptying, progressing to urinary retention in the severe cases. “

Anatomy, Abdomen and Pelvis, Sphincter Urethrae

Peter Sam; Jay Jiang; S. W. Leslie; Chad A. LaGrange.

June 4, 2023.

“The urethral sphincter US is a muscular structure that regulates the outflow of urine from the bladder into the urethra. There are 2 urethral sphincters, the external and internal urethral sphincters IUS. When these muscles contract, the urethra narrows, and urination stops or slows.

The urethral sphincter US is critical for the maintenance of urinary continence. Urinary incontinence is often associated with the pathology of the urethral sphincter and is a very common problem worldwide.

The urethral sphincter muscles are located within the deep perineal pouch.”

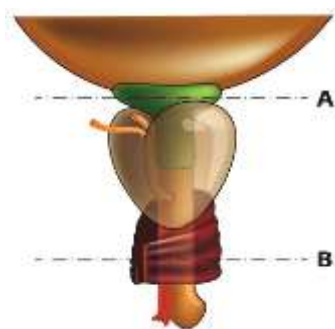


Fig. No. 3: Male urethral sphincter image showing: A) the internal urethral sphincter. B) the external urethral sphincter. From DOI: 10.15537/smj.2017.1.15293

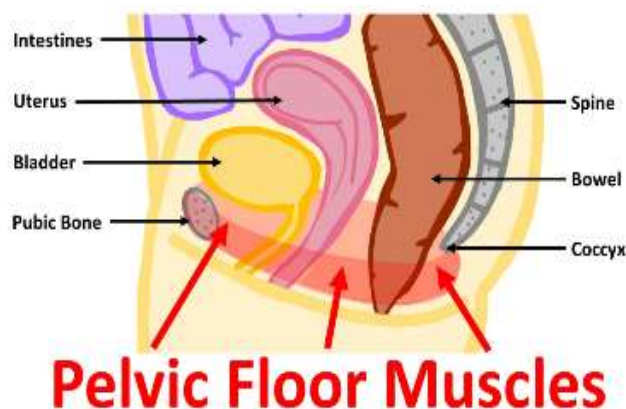


Fig. No. 4: From <https://cioffredi.com/belly-care-overview/>

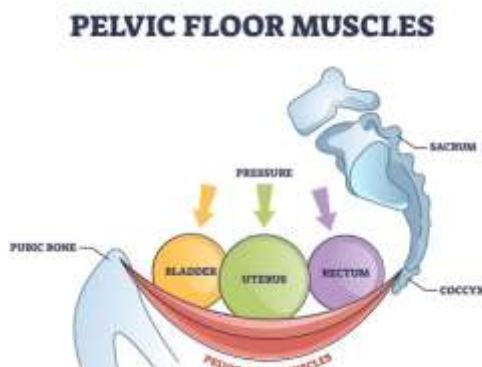


Fig. No. 5: From The Pelvic Clinic.

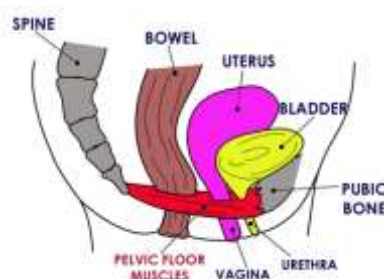


Fig. No. 6: <https://norfolkandwaveneycommunityhealth.nhs.uk/msk/self-help/women-s-men-s-health-pregnancy/the-pelvic-floor/>

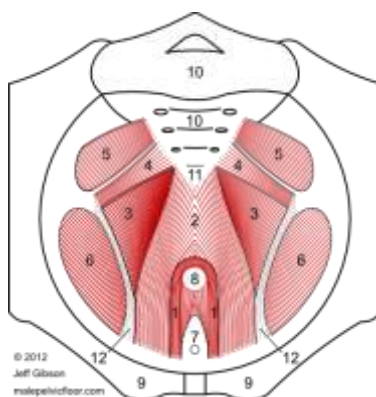


Fig. No. 7: The pelvic diaphragm viewed from above. From <http://www.malepelvicfloor.com/anatomy.html>

1. Puborectalis muscle, 2. Pubococcygeus muscle, 3. Iliococcygeus muscle, 4. Coccygeus muscle Other muscles, 5. Piriformis, 6. Obturator Internus, Other landmarks, 7. Urethral opening, 8. Anal opening, 9. The paired pubic bones in the front of the pelvis, 10. The sacrum, 11. Coccyx (tail bone), 12. Tendinous arch.

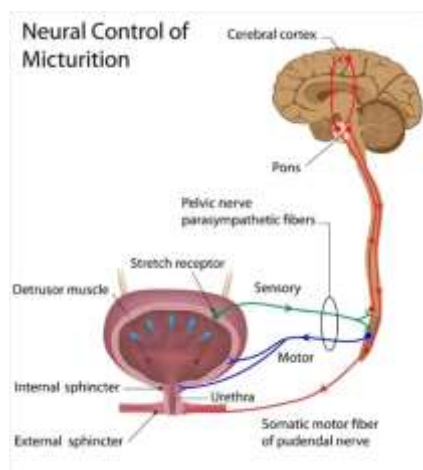


Fig. No. 8: From <https://www.news-medical.net/health/Micturition-Reflex-Neural-Control-of-Urination.aspx>

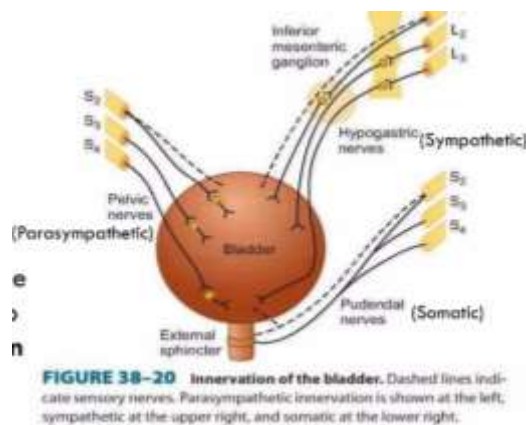
In article <https://www.news-medical.net/health/Micturition-Reflex-Neural-Control-of-Urination.aspx>

By Dr. Liji Thomas, MD

“The act of micturition is an autonomic reflex at the level of the spinal cord SC. This reflex also helps to complete micturition when the act is voluntarily initiated, or when it follows a period of inhibition by the brain, by relaxing external sphincter ES.

The control of this process is mediated via afferent signals AS from stretch and volume receptors in the bladder, as well as from the muscles of the pelvic floor (PF), the vagina/penis, and the rectum, which informs the brain about the extent of filling, initiating several spinal reflexes. These serve to inhibit micturition until filling is complete while activating the voluntary external urethral sphincter EUS via the pudendal nerve. At the same time, detrusor activity is inhibited and the internal urethral sphincter is stimulated via sympathetic activity. Impulses from the filling bladder are carried to the spinal cord SC via the pelvic and hypogastric nerves, whereas the pudendal and hypogastric nerves carry impulses from the neck of bladder and urethra.”

Micturition is a SPINAL REFLEX facilitated or inhibited by higher brain centre, subjected to voluntary/involuntary facilitation.

**Fig. No. 9**

The parasympathetic nerve (pelvic) are motor to the detrusor and inhibitory to the internal urethral sphincter (IUS)

The somatic nerve (pudendal) involved in the voluntary control of the external urethral sphincter

Sensory nerve : involved in cortical sensation

The detrusor muscle is mainly responsible for emptying the bladder during micturition.

The internal urethral sphincter is a smooth muscle. the external sphincter is a skeletal muscle.

So it is possible to see in the nervous control of micturition various centers:

- 1) cortical center involved: inhibitory to the pontine center
- 2) brain stem center (pons) facilitatory micturition
- 3) sacral spinal cord -parasympathetic (reflex evacuation)

The cortical center controls the pontine in order to have a socially acceptable micturition frequency.

The pontine is a coordination center : involved in synchronization for a complete evacuation

The spinal center : involved in the reflex. An inefficient contraction of the detrusor produces incomplete evacuation

By Dr. Liji Thomas, MD

“Micturition is thus under cortical control CC as well as mediated by the spinal reflex arc SRA, which inhibits the pontine center until it is deemed appropriate to void. The motor cortex controls the voluntary muscle of the external urethral sphincter EUS.”

Related the lifestyle and medication involved:

Pelvic floor (PF) Dysfunction

W R. Grimes; Michael Stratton.

June 26, 2023.

“Therapeutic interventions for patients with pelvic floor (PF) dysfunction PFD should be tailored to their specific needs. A multidisciplinary approach is many times necessary. Patients with a history of sexual, physical, remotional abuse should have the information relayed to the entire treatment team to facilitate modifications of therapy to accommodate patient’s needs.

From medline website:

How to do Kegel Exercises

Once you know what the movement feels like, do KEGEL EXERCISES (KE)3 times a day:

“Make sure your bladder is empty, then sit or lie down.

Tighten your pelvic floor (PF) muscles. Hold tight and count 3 to 5 seconds.

Relax the muscles and count 3 to 5 seconds.

Repeat 10 times, 3 times a day (morning, afternoon, and night).

Breathe deeply and relax your body when you are doing these exercises.

KEGEL EXERCISES (KE)can be done any time you are sitting or lying down. You can do them when you are eating, sitting at your desk, driving, and when you are resting or watching television”.

Lifestyle Modifications

Diet: avoidance of alcohol, caffeine (cola, tea, coffee), acidic foods/beverages, including citrus and tomatoes, concentrated sugar, artificial sweeteners, like aspartame, spicy foods, and cigarettes for urinary frequency and incontinence. These changes have overlapping benefits for anorectal symptoms, including incontinence.

Weight loss: a 3% to 5% weight reduction can decrease urinary incontinence episodes by about 50%.

Pelvic floor (PF) exercises (Kegel): to strengthen the pelvic floor (PF) PF.

Core exercises: to strengthen the pelvic floor (PF) and support.

Medications

Topical vaginal estrogen for overactive bladder, vaginal thinning, and dyspareunia.

Anticholinergics (fesoterodine, tolterodine) for OVB.

Beta3 agonists (mirabegron) for OVB.”

MATERIAL AND METHODS

With an observational point of view various relevant literature is reported related th scope of this work

The reported figure helps to better explain the concepts.

An experimental project is submitted

After evalutaion of all this a global conclusion is provided.

RESULTS

From literature

According Yi-Chen Huang et al

“In 1948, KEGEL EXERCISES (KE)were first described by A. Kegel for pelvic floor (PF) muscle PFM strengthening. The perineometer, also called the vaginal manometer, has been designed to record the contraction strength of pelvic floor (PF) muscles and can be used to

guide the participants to conduct the exercises correctly. Dr. Kegel's study showed that the exercises could help to prevent cystocele, rectocele, or urinary stress incontinence.” (1)

(Arnold Kegel was an USA professor of gynecology introduced this practice exercise in 1948.)

Sonia R Adams et al

“ We conducted a prospective cohort work STUDY of women with urinary urgency and frequency symptoms. Participants underwent PFPT once or twice per week for 10 weeks. Symptom improvement was assessed using validated questionnaires, voiding diaries, subjective measures.

57 participants enrolled; 21 (36.8%) withdrew or completed less than 5 weeks of PFPT. 31 (54.4%) of the remaining 36 participants completed 10 weeks of PFPT. The mean age of the study group (n = 36) was 48.9 ± 15.0 years. The primary diagnoses were OB syndrome (n = 24, 66.7%) and painful bladder syndrome PBS (n = 12, 33.3%). Women attended a median of 14.0 (interquartile range. 8.0-16.0) PFPT visits over a median of 11.9 weeks (IQR, 10.0-18.1). At baseline, the median Pelvic floor (PF) Distress PFD Inventory-Short Form 20 score was 79.2 (IQR, 53.1-122.9), and decreased to 50.0 (IQR, 25.0-88.5; $P < 0.001$) after PFPT; the urinary and prolapse symptom subscales both decreased significantly. Participants reported a decrease from a median of 10.0 voids per day to 8.0 ($P < 0.001$).

On the Patient Global Impression of Improvement, 62.5% of women reported : they were "much better" or "very much better."

The PFPT with myofasical release techniques improves urinary symptoms while avoiding the medications and more invasive therapies. The high dropout rates suggest that the motivation or logistic factors may play a significant role in utilization and success of this treatment option.” (2)

Ilaria Soave et al

“Pelvic floor (PF) muscle training consists in the repetition of 1 or more sets of voluntary contractions of the pelvic muscles. By building muscles volume, PFMT elevates the pelvic

floor (PF) PF and pelvic organs, closes the levator hiatus, reduces pubovisceral length and elevates the resting position of the bladder.”(3)

Related the pharmacology involved:

https://www.rxlist.com/how_do_urinary_antispasmodic_agents_work/drug-class.htm

“Urinary antispasmodic agents UAA are medications prescribed to treat bladder overactivity BO which can cause urinary urgency and incontinence. Urinary antispasmodic agents increase bladder capacity, delay the desire to void, decrease the frequency and urgency to urinate, and reduce pain caused by difficulty in the urination.

UAA relax the detrusor smooth muscle which contracts to release urine and prevent spasms of the muscles around the urinary tract. Urinary antispasmodic agents work in the following ways to decrease uninhibited the bladder contractions:

Block acetylcholine (ach) from stimulating muscarinic receptors, which are protein molecules on smooth muscle cells in the bladder lining. ACH is a natural chemical (neurotransmitter) that nerve endings secrete to make the muscles contract.

Block the activity phosphodiesterase, an enzyme that breaks down signaling molecules known as cyclic adenosine monophosphate. An increase in cAMP concentration results in the relaxation of the smooth muscles.

Urinary antispasmodic agents include:

oxibutinin oral, topical, transdermal.flavoxate”

OTHER

Tolterodin DETRUSITOL antimuscarinic

Genurin flavoxate: anticholinergic-parasympatholytic action reduces the tonus of smooth muscle in the bladder

Solifenacin antagonizes the M2 and M3 muscarinic receptors in the bladder to treat an overactive bladder

Trospio clorure: antimuscarinic

Evgenyi I Kreydin et al

“OVB is a symptom complex consisting of bothersome storage urinary symptoms that is highly prevalent among both sexes and has a significant impact on the quality of life. Various antimuscarinic agents and the beta-3 agonists mirabegron and vibegron BETMIGA are currently available for the treatment of OAB” (4)

Omar Dawood et al

“ The human bladder expresses various sympathetic and parasympathetic receptors to help regulate The micturition. Activation of the parasympathetic system will result in bladder contraction. Receptors positively affecting bladder contraction and micturition include the M2 and M3 rec. subtypes, which function via the parasympathetic nervous system PNS. These receptors work to increase intracellular calcium ICA and down-regulate cyclic-adenosine, which will increase muscle contraction. Negatively affecting micturition predominantly includes the sympathetic beta-3 adrenergic receptors. Mirabegron is a beta-3 rec. agonist which will cause detrusor muscle relaxation. Animal studies have shown that the beta-3 receptor agonists exhibit a dose-dependent detrusor relaxation DR (mediated via up-regulation of cyclic-adenosine) during the storage phase of micturition. Mirabegron can aid in the symptomatic relief of OAB and symptoms of urge urinary incontinence, urgency, urinary frequency.

Contraindications : Previous hypersensitivity reaction to mirabegron or any excipients of tablet or the oral suspension. Mirabegron use correlates with hypertension, and its contraindication includes severe un-controlled hypertension. Blood pressure BP optimization should be considered before initiating mirabegron therapy.”(5)

Kris R. Brown et al

“Pelvic floor (PF) exercises PFE are also known as Kegel, or childbirth, exercises. KEGEL EXERCISES (KE)are commonly used and have a 30% to 90% success rate in women with stress incontinence.” (6)

Generally for iperreflexia are more used anticholinergic drugs instead the alfa -litics if functional obstruction.

RELATED Oxibutinin

“ Oxibutinina tablets XL is contraindicated in the patients with urinary retention, gastric retention and other severe decreased gastrointestinal motility conditions, uncontrolled narrow-angle glaucoma.”

From <https://go.drugbank.com/drugs/DB00706>

“Tamsulosin is a alpha-1A and alpha -1D blocker. 70% of the alpha-1 adrenoceptors in the prostate are of the alpha-1A subtype. Label By blocking these adrenoceptors, smooth muscle in the prostate is relaxed, urinary flow is improved. Label The blocking of alpha-1D adrenoceptors relaxes the detrusor muscles of the bladder which prevents storage symptoms. The specificity of tamsulosin focuses the effects to the target area while minimizing effects in other areas. “

Buscopan HYOSCINE N-Butylbromide (antimuscarinic and anticholinergic) is a muscle relaxant prescribed by physicians to reduce spasms of the gastrointestinal tract, and/or urinary-genital tract

SILODYX silodosin : alfa 1 A adrenoceptor, indication for IPB symptoms. Blockade of these α 1A-adrenoreceptors causes smooth muscle in these tissues to relax, thus decreasing bladder outlet resistance BOR, without affecting detrusor smooth muscle contractility. This causes an improvement of both storage (irritative) and voiding (obstructive) symptoms (Lower urinary tract symptoms, LUTS) associated with benign prostatic hyperplasia.

OTHER useful DRUGS used : duloxetine (CYMBALTA), TCA, SSRI.

Relevant are also the effect played by stress, anxiety and depression of the overactive bladder.

Third line treatments for Overactive Bladder:

Botulinum toxin injections into the bladder

Neuromodulation – altering nerve messages or signals to the bladder using electrical stimulation by:

Posterior tibial nerve stimulation (PTNS) or

Sacral neuromodulation using InterStim®

Between other kind of factor to be taken in consideration

Related alimentar behaviour : drink at least 1000-1500 ml water die (if physician allow) day in order to diluite urine : too much concentrated irritate the bladder mucose. It is necessary not to take in a single way by refracted durign the day.

Not drink water the two hour before to go to sleep in order to reduce the need to wake up to go in bath.

Not intake irritant food like caffeine and etilic alcool or species because irritate the bladder. No smoke to avoid smoke (nicotin and the chemical substantie inhaled can irritate the bladder).

Related psychological aspects : When there is an episode of bludder urgency it is useful also to think to other things in order to heve distraction (Mindfulness or other technique).

Jan Baker et al

“The objective of this work was to evaluate if a mindfulness-based stress reduction program is a viable treatment worthy of further evaluation for the treatment of the urinary urge incontinence.

This was a single-arm pilot study of 7 women who participated in an 8-week mindfulness-based stress reduction program MSRP to evaluate its effectiveness in reducing urinary leakage episodes. Improvement was measured by 3-day bladder diary, OVB Symptom and Quality of Life-Short Form, Health-Related Quality of Life, and Patient Global Impression of Improvement.

Mean incontinence episodes per day decreased from 4.14 (SD, 1.96; range, 2.67-7.67) at baseline to 1.23 (SD, 0.93; range, 0.33-2.67) after the treatment (P = 0.0005 for change). After the treatment, 5 of 7 women were improved based on the Patient Global Impression of Improvement PGII. and 2 were unchanged.

Significant improvements on both Health-Related Quality of Life and OVB Symptom and Quality of Life-Short Form were reported after treatment. Results were sustained at 1 year in 4 of 7 women. Two women sought treatment, and 1 was lost to follow-up at 12 months.”(7)

Fátima Fitz et al

“Pelvic floor (PF) muscle training involves the contraction of the puborectal, anal sphincter and external urethral muscles, inhibiting the detrusor contraction, what justify its use in the treatment of OAB symptoms.

Prospective clinical trial with 27 women with mixed urinary incontinence. with predominance of OAB symptoms and loss ≥ 2 g in the pad test. It was evaluated: pelvic floor (PF) muscles function (digital palpation and manometry); urinary symptoms (nocturia, frequency and urinary loss); degree of discomfort of OAB symptoms; and quality of life (Incontinence Quality-of-Life Questionnaire). The PFMT program consisted of 24 outpatient sessions (2x/week + home PFMT).

There was a significant improvement of the urinary symptoms to the pad test (5.8 ± 9.7 , $p < 0.001$), urinary loss (0.7 ± 1.1 , $p = 0.005$), nocturia (0.8 ± 0.9 , $p = 0.011$). Reduction in the degree of discomfort of urinary symptoms was observed according to OAB-V8 questionnaire (10.0 ± 7.7 , $p = 0.001$). There were significant results in PFMs function: Oxford (3.6 ± 0.9 , $p = 0.001$), endurance (5.2 ± 1.8 , $p < 0.001$), fast (8.9 ± 1.5 , $p < 0.001$) and manometry (26.6 ± 15.8 , $p = 0.003$). Quality of life had a significant improvement in the 3 domains evaluated by I-QoL. The PFMT without any additional guidelines improves the symptomatology, the function of PFMs and the quality of life of women with OAB symptoms. “(8)

Marcella G Willis-Gray et al

“Lifestyle and behavioral factors play a role in OAB as well. A body mass index (BMI) of >30 kg/m² is another risk factor for the OAB symptoms. Studies have found smoking to be risk factor for increased urgency, but this has not been consistent with other research studies. High caffeine intake (>400 mg/d) has also been associated with OAB There are also behaviors that can increase the likelihood of OAB. These include both inadequate / excessive fluid intake, caffeine, carbonated beverages, spicy food, artificial sweeteners, and alcohol. Identifying modifiable risk factors earlier on can aid in the treatment of OAB.”(9)

Young-Sam Cho et al

“**Caffeine may promote incontinence** through its diuretic effect, particularly in individuals with underlying detrusor overactivity DO. in addition to the increasing muscle contraction of the bladder smooth muscle. Caffeine may affect bladder function via central micturition

centers, including medial preoptic area, ventrolateral periaqueductal gray, pontine micturition center. The results indicated that caffeine consumption increased contraction pressure CP and time significantly ($P < 0.05$, vs. control).

c-Fos expression levels in the central micturition areas were increased by the caffeine administration ($P < 0.05$, vs. control), and the lowest dose of caffeine (10 mg/kg) enhanced c-Fos expression to the greatest extent ($P < 0.05$, 50 and 100 mg/kg vs. 10 mg/kg).

NGF expression in the central micturition areas CMA increased with caffeine administration ($P < 0.05$, vs. control), and the lowest dose of caffeine (10 mg/kg) enhanced NGF expression to the greatest extent ($P < 0.05$, 50 and 100 mg/kg vs. 10 mg/kg).”(10)

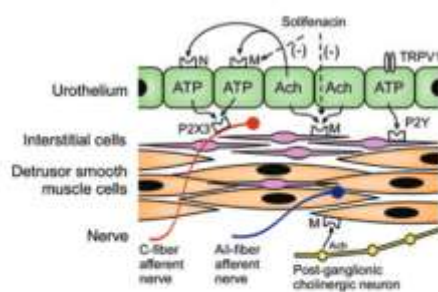


Fig. 2 Urothelium may synthesize and release multiple neurotransmitters which consequently affect the excitability of afferent nerves and affect the detrusor muscle contractility. ACh, acetylcholine; ATP, adenosine triphosphate; M, muscarinic receptors (M_1 , M_2); N, nicotinic receptors; TRPV1, transient receptor potential vanilloid 1.

Fig n 10 from Pathophysiology of Overactive Bladder February 2012 Lower Urinary Tract Symptoms 4(s1) En Meng et al

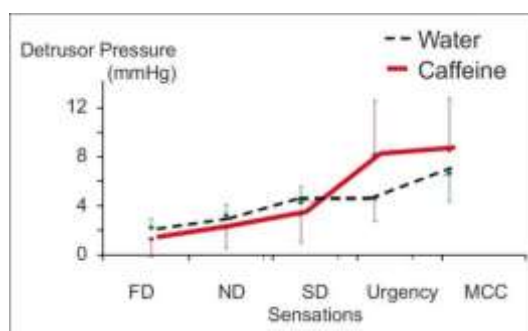


Fig n 11 Detrusor pressure at filling phase (mean \pm SE) in mmHg after water and caffeine ingestions (FD=first desire to void, ND=normal desire to void, SD=strong desire to void, MCC=maximal cystometric capacity). From DOI: 10.4103/0974-7796.75862

Supatra Lohsiriwat et al

“Caffeine at 4.5 mg/kg caused diuresis and decreased the threshold of sensation at filling phase, with an increase in flow rate and voided volume. So, **caffeine can promote early urgency and frequency of urination**. Individuals with LUTS should avoid or be cautious in consuming the caffeine containing foodstuffs. “

Seiji Matsumoto et al

“OVB and IBS are pathologically characterized by overactivity (irritability) of the bladder and bowel, respectively, previous work studies have shown that they frequently occur concurrently “(11)

Glícia Estevam de Abreu et al

“Functional constipation is associated with OVB and its dry subtype, particularly in the younger population. This association is responsible for lower quality of life scores, especially when urinary incontinence is present.”(12)

Nancy E RINGEL et al

“When compared to never to <1 serving/week, women consuming ≥ 1 serving/day of artificially sweetened beverages had 10% greater odds of reporting mixed urinary incontinence MUI after adjustments. Amount of artificially sweetened beverage consumption was not associated with the stress or urgency urinary incontinence symptoms.” (13)

Saeid Golbidi et al

“Diabetic cystopathy DC is a well-recognized complication of DM, which usually develops in middle-aged or elderly patients with long-standing and poorly controlled disease. It may have broad spectrum clinical presentations. Patients may be asymptomatic, or have a wide variety of voiding complaints from OVB and urge incontinence to decreased bladder sensation and overflow incontinence.”(14)

Between the mechanism involved in polyuria : osmotic property of glucose, oxidative stress. nerve damages (neurogenic bladder), diabetes cause excessive thirst with increase water intake. Diabete and methabolic syndrome increase body weight and this increase intraabdominal pressure.

J. Patrick Mershon et al

“Sodium glucose cotransporter 2 inhibitors SGLT2i are the newest class of drugs for the

treatment of DM type II and off-label use for heart failure and other diagnoses has been expanding. SGLT2i use results in glucosuria which has a diuretic effect. Diuresis and glucosuria together may provoke / exacerbate OVB symptoms such as urinary frequency, urgency, and urgency incontinence. Additionally, higher rates of infection may be seen with glucosuria. (15)

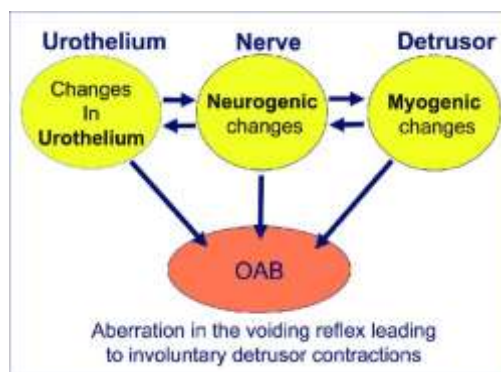


Fig. n 12 Mechanisms underlying overactive bladder. From DOI: 10.5489/cuaj.11181.

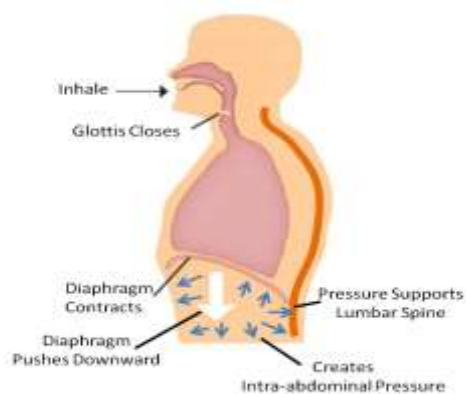


Fig. n 13 From Pinfree Health clinic.

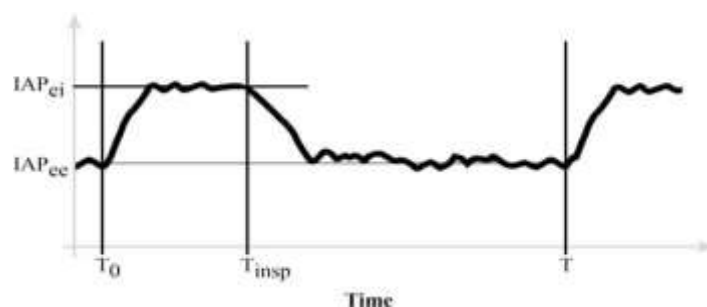


Fig. n 14 Effect of respiration on intra-abdominal pressure (IAP). T_0 , start of inspiration; T_{insp} , inspiratory time; T , total respiration time; IAP_{ee} , end-expiratory IAP; IAP_{ei} , end-inspiratory IAP. From DOI: 10.1186/2110-5820-2-S1-S18

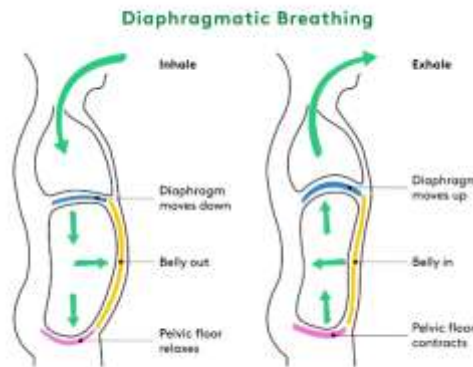


Fig n 15 From Hinge Health Breathing in stretches your pelvic floor (PF). Breathing out contracts your pelvic floor (PF).

When you inhale, your diaphragm rises up, which allows your pelvic floor (PF) to move upward with a gentle contraction. Breathing out contracts your pelvic floor (PF).

From Hinge Health

“Slow, deep breathing allows your pelvic floor (PF) PF to relax and stretch, which helps the muscles remain strong and flexible. Quick, shallow breathing (like you might do when you’re stressed) prevents your pelvic floor (PF) from fully relaxing. This can cause tightness and weakness and, over time, may lead to issues like urinary incontinence (or leakage), pelvic pain, prolapse, other pelvic symptoms.”

Seda Yakıt Yeşilyurt et al

“the Knack maneuver KM training with vaginal palpation and verbal instruction improved MVC of PFMs.” (16)

the Knack Manoeuvre is a term coined by Prof. J. Ashton-Miller from the University of Michigan. It describes the skill of intentionally contracting the pelvic floor (PF) muscles PFM to prevent urine loss just before and throughout a sudden rise in the intra-abdominal pressure associated with forceful actions such as a cough, or sneeze.

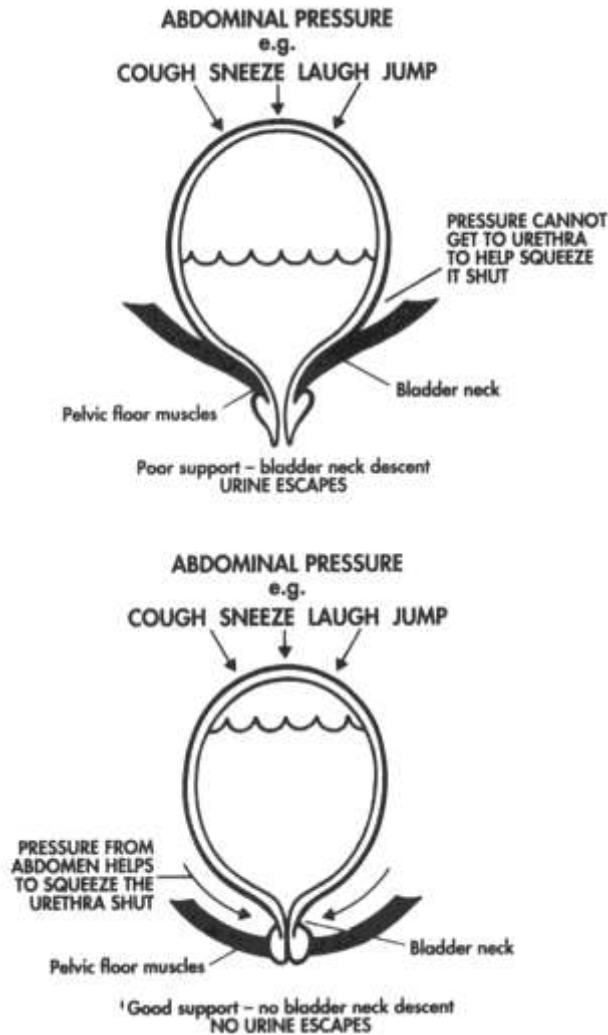


Fig n 16 from <https://i.innerstrength.com.au/pelvic-floor-dynamic-bracing-knack-female>

J F Wyman et al

“In the management of OAB symptoms, patients can be taught to control urgency by performing general relaxation techniques, including slow deep breathing exercises SDBE.to decrease the intensity of the urgency and allow the patient to delay voiding and distraction techniques in which patients get involved in tasks that involve mental concentration.”(17)

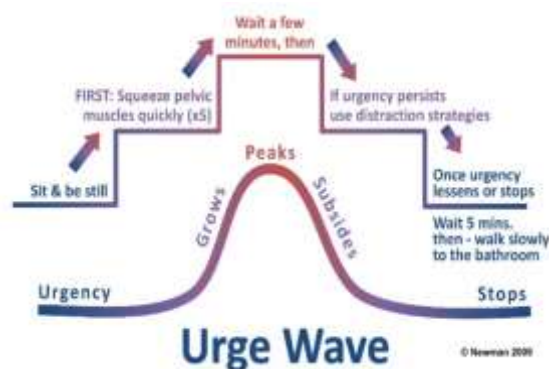


Fig. 17: from Urotoday.com

From Urotoday.com Diane Newman

“urgency follows a wave pattern; it starts, grows, peaks, and then subsides until it stops.

The key to controlling bladder urgency BU is by practicing “bladder training” BT that uses methods like “urge suppression” which are calming messages to your brain to stop you peeing so often. When you feel a sudden, urgent need to pee, do not rush or run to the bathroom. Rushing will jiggle your bladder and increase the feeling of urgency and may cause bladder leaks.

Ways to Take Control of Urgency

Focus on another body sensation. Deep breathing. Sit down and take 5 slow, deep breaths. Think about the air moving in and out of your lungs instead of how your bladder feels.

Squeeze your pelvic muscles. So when urgency comes on, sit and do a couple of gentle pelvic muscle PM squeezes, just 3 to 5 squeezes. This will calm your bladder and the urgency will go away. You can also try holding 1 strong squeeze of your pelvic muscles.

Distract yourself. If you get you mind off your bladder long enough, the feeling of urgency will often pass. One way is by focusing on a mental activity like to counting backward from 100 by 7s.

Do a task that requires a lot of thought, play a game on your phone, write a letter.

Use self-talk or good self-statements. “I am the boss, not my bladder.”

Luigino Dal Maso et al

“Compared to the lowest level of occupational PA Physical activity. the multivariate ORs for BPH for the heavy/strenuous level were 0.6 (95% CI, 0.4–0.8) at age 15–19, 0.6 (95% CI,

0.4–0.8) at age 30–39 and 0.7 (95% CI, 0.5–0.9) at age 50–59. Compared to <2 hr/week of recreational PA, the ORs for BPH for the highest level (≥ 5 hr/week) were 0.5 (95% CI, 0.4–0.7) at the age 15–19, 0.6 (95% CI, 0.5–0.8) at age 30–39, and 0.7 (95% CI, 0.5–0.8) at age 50–59. All inverse trends in risk were significant, no heterogeneity was found by reason of BPH-diagnosis, age at diagnosis, and BMI”(18).

Related the pressure in uretra

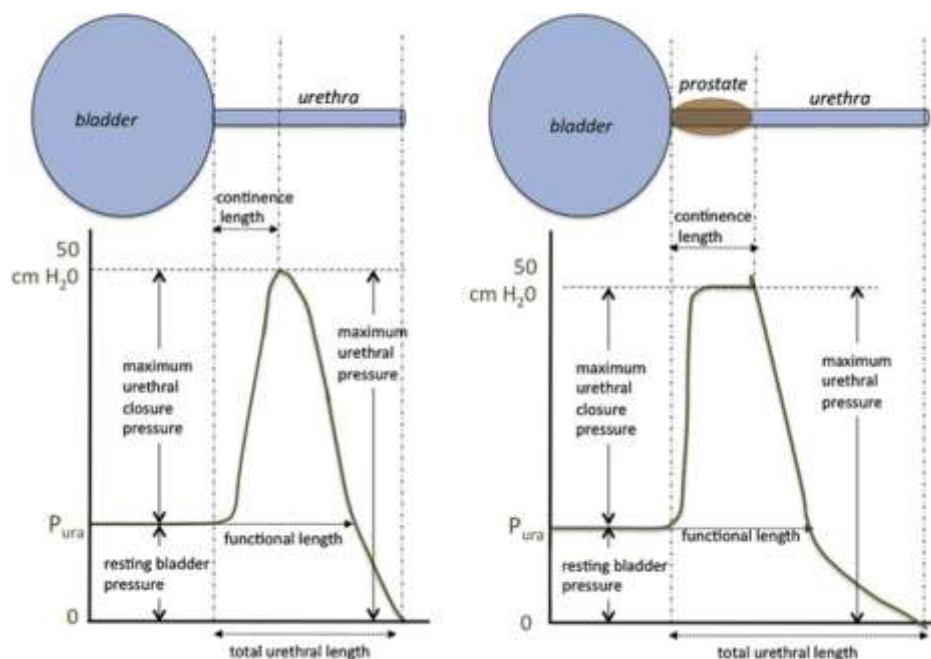


Fig.n 18 Urethral pressure profiles of the female (left) and male (right) lower urinary tract. From Animal Models of Lower Urinary Tract Dysfunction Rita I. Jabr, Christopher H. Fry, in Animal Models for the Study of Human Disease. 2013

Pathak, Satish D et al

“The patients were tested after 7 days and also after 14 days of yoga practice. In case 1, it was seen that the prostate size, on sonography SG readings, was reduced from 144 to 37 cc by just 1 month of yoga practice. Prevoid urine volume was 230 ml and postvoid was 180 ml, and after 1 month of yoga practice, it was 694 ml and 19 ml. Serum PSA initially was 25.24 ng/ml, while at the time of posttesting, it was 0.82 ng/ml. In case 2, the postvoid urine volume PVV was 50 ml initially. On the 14th day of yoga practice, it was nil. Serum PSA was 128.5 ng/ml at the time of pretesting, while on the 14th day, it was 16.35 ng/ml. The prostate size was 91 cc on sonography SG examination at pre yoga testing, while on 14th day of yoga practice, it was 23.6 cc. The yoga module, used in this study, is recommended to be employed to help the patients of enlarged prostate.”(19)

Stavros Gravas et al

“postvoid residual urine PVRU significantly decreased in the treatment arms containing dutasteride, but not with tamsulosin alone. Table 2 displays the key RCTs with 5ARIs.”(20)

S.Alan McNeilla et

“the decreases in the PVR volume were significantly ($P < 0.01$) greater with alfuzosin than with the placebo”(21)

Mohammad Reza Safarinejad

“By intention- to-treat analysis ITT. at the end of 6-month trial, 232 (81%) of 287 patients in the Urtica dioica UD group reported improved LUTS compared with 43 (16%) of 271 patients in the placebo group ($P < 0.001$). Both IPSS and Qmax showed greater improvement with drug than with the placebo. The IPSS went from 19.8 down to 11.8 with Urtica dioica and from 19.2 to 17.7 with placebo ($P = 0.002$). Peak flow rates improved by 3.4 mL/s for placebo recipients and by 8.2 mL/s for treated patients ($P < 0.05$).”(22)

Siddappa Naragatti et al

“the Lotus Pose also engages the muscles of the lower back and the pelvic floor (PF).” (23)

Experimental project hypothesis

In order to evaluate the efficacy of the KEGEL exercise it can be performed an practical experience

20 patients with simpthoms of overactive bladder – urgency

They must to be divided into 2 groups

1) group that use KEGEL EXERCISE (KE) (that can be used alone by the patients without physician intervention)

2) group using 1 cp of ioscin as antispatic (OCT over the counter) when needed.

At all it must to be subministrated a quality of life questionnaire to cover 4 hours later this two strategies

Time of observation : 30-60 days

STATISTICAL ANALISYS: to be verified if there is significative difference using this 2 strategy or not in order to to verify The effect of the KEGEL EXERCISE (KE).

DISCUSSION

In actual health care systems is needed to avoid to spend too much money or to reduce the working days lost or to increase the quality of life (good social events participations) if alternatives not pharmacological can help.

Overactive bladder and mictionary urgency are universally treated with various approach because

A complexity in muscle and nervous fiber. spinal cord and upper SNC control centers are involved.

(autonomous or voluntary), other factor can be diabetes, BPH, uretral restriction.

Pharmacological. rehabilitative or surgery approach are adopted by physicians and other healthcare professionals in relation to the severity of the pathology (urologist, physiotherapists, surgeron, geriatrics and other)

The pharmacology of the substance used is clear and also the contraindication or side effect.

It is clear the effect played by bladder irritants like spices, alcohol, and coffee and the by the BMI role.

The same the efficacy of the KEGEL procedure (see literature) and the easy way to be autosubministrated as daily practice.

The physicians and the healthcare professionals involved in this field can help the patients.

The body weight must to be controlled as well as the diabetes condition (today there are various kind of drugs that make possible under physician control to fine regulate diabetes in some population).

The right level of hydration (water drinking) and the normal functionality of the intestine (colon. rectus) as well as the right amount of physical activity are factors to be reached.

A special consideration to the stress level, anxiety or depressive status for the implication in this system and the physical activities to be performed in order to reduce symptoms.(see also literature about the specific deep breath exercise or Yoga for the prostate enlargement : in order to reduce abdominal pressure AP on the bladder).

The stress condition increases a wrong way breath (more rapid) that contribute to increase the AP that act on the bladder.

Diabete and the glicosuria acts with various mechanism in the bladder pathology.(like neuronal damage, oxidative stress. osmotic way).

To be considered the pharmacoloical effects played by the drugs in use for this condition (systemic or local): antimicrobials for bacteric prostatitis (ciprofloxacin and other). antimicotics (antifungine). NSAIDS, local cortisons.5 -alfa reduttase. alfa1- antagonista, antimuscarinics. and other.

To be considere also the effect of pytotherapy on BPH (URTICA DIOICA. SERENOA R.) and related

Suppository of Fenolmicin P3 (a poliphenol derivate from propoli) - Boisexil (Boswellia serrata Fitosom).

The psychological aspects are relevant : the distraction tecnique (think to other during and urge bladder event can be useful if addet to KEGEL EXERCISE (KE)and to the deep breath expiration).

In an evolutive point of view it is interesting to observe that umans under al evolutionary point of view was in the first Evolution not bipede (in vertical position the abdominal pressure more act on bladder) and not used to sitting in rigid chair.

The ancient Lotus Yoga position is of interest.(relaxation, breath control and for pelvic flor wellbeing).

CONCLUSION

As conclusion of this work it is possibile to say that Kegel procedure because easy to adopt also in autonomous way. added to pysical strategy and alimantar specific indication can be an interesting approach to reduce.when possible, various heathcare costs (direct or indirect like working days lost) or to imporve social life of the patiens in some pelvic flor disfunction like Minctionary urgency and OVB.

Obviously the goldens standard according literature are pharmacological. rehabilitative or surgery intervencion (in some conditions) prescribed by the phisicians but the same Kegel procedure can be added to better achieve good results as well as some YOGA and breath exercise.

It is always better if under the control a specific physicians or other helathcare professional involved.

A good use of the pharmacology (drugs) may imply to observe the efficacy also of non pharmacological intervention and in special way if this approach make possible to stop or to reduce the vicious cicle Of the. IPB, OVB, urgency. prostatitis. cystitis. flogosys, linfocite infiltration. edema and other improving the uretral flux or the plevic floor function.

Conflict of Interests: No

REFERENCES

1. Book Kegel Exercises Yi-Chen Huang. Ke-Vin Chang Treasure Island (FL): StatPearls 2024 Jan.2023 May
2. Female Pelvic Med Reconstr Surg. 2015 Pelvic floor (PF) Physical Therapy as Primary Treatment of Pelvic floor (PF) Disorders With Urinary Urgency and Frequency-Predominant Symptoms Sonia R Adams. Sybil G Dessie, Laura E Dodge, Jessica L Mckinney, Michele R Hacker, Eman A Elkadry DOI: 10.1097/SPV.0000000000000195
3. Arch Gynecol Obstet. 2019 Mar; doi: 10.1007/s00404-018-5036-6. Pelvic floor (PF) muscle training for prevention and treatment of urinary incontinence during pregnancy and after childbirth and its effect on urinary system and supportive structures assessed by objective measurement techniques Ilaria Soave. Simona Scarani. Maddalena Mallozzi. Flavia Nobili. Roberto Marci. Donatella Caserta
4. Int Braz J Urol. 2021 May 10;doi: 10.1590/S1677-5538.IBJU.2021.99.12 Current pharmacotherapy of overactive bladder Evgenyi I Kreydin. Cristiano M Gomes, Francisco Cruz <https://www.ncbi.nlm.nih.gov/books/NBK538513/Mirabegron> Omar Dawood; Ahmed El-Zawahry. August 28, 2023.
5. Occupational Therapy with Elders (Fourth Edition) Strategies for the COTA 2019, Chapter 17 - Strategies to Maintain Continence in Elders Kris R. Brown,Sue Byers-Connon, Jessica Hatch <https://doi.org/10.1016/B978-0-323-49846-3.00017-2>
6. Female Pelvic Med Reconstr Surg. 2012 Jan-Feb;doi: 10.1097/SPV.0b013e31824107a6. Mindfulness-based stress reduction for treatment of urinary urge incontinence: a pilot study Jan Baker. Donna Costa, Ingrid Nygaard
7. Rev Assoc Med Bras (1992). 2017 Dec;63(12):1032-1038. doi: 10.1590/1806 9282.63.12.1032. Pelvic floor (PF) muscle training for overactive bladder (OAB)

- symptoms - A prospective study Fátima Fitz. Marair Sartori. Manoel João Girão. Rodrigo Castro
8. Res Rep Urol. 2016 Jul 27;8:113–122. doi: 10.2147/RRU.S93636 Evaluation and management of overactive bladder (OAB): strategies for optimizing care Marcella G Willis-Gray. Alexis A Dieter. Elizabeth J Geller
 9. Medicine reports Caffeine enhances micturition through neuronal activation in micturition centers Authors: Young-Sam Cho Il-Gyu Ko Sung-Eun Kim Lakkyong Hwan Mal-Soon Shin Chang-Ju Kim Sang-Hoon Kim Jun-Jang Jin Jun-Young Chung Khae-Hawn Kim October 15, 2014 <https://doi.org/10.3892/mmr.2014.2646>
 10. BJU Int. 2012 Oct 26; doi: 10.1111/j.1464-410X.2012.11591.x Relationship between overactive bladder (OAB) and irritable bowel syndrome: a large-scale internet survey in Japan using the overactive bladder (OAB) symptom score and Rome III criteria Seiji Matsumoto. Kazumi Hashizume. Naoki Wada. Jyunichi Hori. Gaku Tamaki. Masafumi Kita. Tatsuya Iwata. Hidehiro Kakizaki.
 11. Arq Gastroenterol. 2018 Nov;55Suppl 1(Suppl 1):35-40. doi: 10.1590/S0004-2803.201800000-46. Epub 2018 Aug 21.FUNCTIONAL CONSTIPATION AND OVERACTIVE BLADDER (OAB) IN WOMEN: A POPULATION-BASED STUDY Glícia Estevam de Abreu. Eneida Regis Dourado. Danielle de Novais Alves. Milly Queiroz de Araujo. Natália Souza Paes Mendonça. Ubirajara Barroso Junior
 12. Menopause. 2022 Dec 13; doi: 10.1097/GME.0000000000002129 Artificially Sweetened Beverages and Urinary Incontinence- A Secondary Analysis of the Women's Health Initiative Observational Study (WHI-OS) Nancy E RINGEL. Kathleen M HOVEY. Chris A ANDREWS. Yasmin MOSSAVAR-RAHMANI. Aladdin H SHADYAB. Linda G SNETSELAAR. Barbara V HOWARD. Cheryl B IGLESIA
 13. Front Pharmacol. 2010 Nov 16;1:136. doi: 10.3389/fphar.2010.00136 Bladder Dysfunction in Diabetes Mellitus Saeid Golbidi. Ismail Laher
 14. PD12-04 SGLT2 INHIBITORS ASSOCIATE WITH OVERACTIVE BLADDER (OAB) SYMPTOMS J. Patrick Mershon, Taylor Weatherly, Erin Gill, Hafsa Asif, Dairon Denis-Diaz, Courtenay Moore, Iryna Crescenze, Columbus, OH
 15. Int Urogynecol J. 2022 May 2;33(10):2895–2903. doi: 10.1007/s00192-022-05213-6 Comparing the efficacy of the Knack maneuver on pelvic floor (PF) muscle function and urinary symptoms using different teaching methods: a prospective, nonrandomized study Seda Yakıt Yeşilyurt. Nuriye Özenin. M Ata Topçuoğlu

16. Int J Clin Pract. 2009 Aug;63(8):1177–1191. doi: 10.1111/j.1742-1241.2009.02078.x
Practical aspects of lifestyle modifications and behavioural interventions in the treatment of overactive bladder (OAB) and urgency urinary incontinence J F Wyman. K L Burgio. D K Newman
17. International Journal of Cancer Short Report Lifetime occupational and recreational physical activity and risk of benign prostatic hyperplasia Luigino Dal Maso, Antonella Zucchetto, Alessandra Tavani, Maurizio Montella, Valerio Ramazzotti, Jerry Polesel, Francesca Bravi, Renato Talamini, Carlo La Vecchia, Silvia Franceschi 28 February 2006 <https://doi.org/10.1002/ijc.21668>Citations: 37
18. CASE REPORT Effect of a yoga module on an enlarged prostate in elderly patients: Two case studies Pathak, Satish D.; Rajbhoj, Pratibha Hemant; Bhogal, Ranjeet S. Author Information Yoga Mimamsa 49(1):p 34-39, Jan–Jun 2017. | DOI: 10.4103/ym.ym_7_16
19. World Journal of Urology Article Current status of 5 α -reductase inhibitors in the management of lower urinary tract symptoms and BPH 03 December 2009 Volume 28, pages 9–15, (2010)
20. Adult urology Volume 57, Issue 3p459-465March 2001 Postvoid residual urine in patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia: pooled analysis of eleven controlled studies with alfuzosin S. Alan McNeilla · Timothy B Hargreavea · Christine Geffriaud-Ricouardb · Jean-Philippe Santonib · Claus G Roehrborc
21. J Herb Pharmacother. 2005;5(4):1-11. Urtica dioica for treatment of benign prostatic hyperplasia: a prospective, randomized, double-blind, placebo-controlled, crossover study Mohammad Reza Safarinejad
22. International Journal of Novel Research and Development (www.ijnrd.org) The Profound Influence of Padmasana (Lotus Pose) on an Individual's Life September 2023 Siddappa NaragattiSiddappa NaragattiVadiraja S HosakoteVadiraja S Hosakote.