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BLADDER OUTLET OBSTRUCTION AND SYMPTOMATIC OVERACTIVE BLADDER – CONTRAINDICATION FOR ANTIMUSCARINICS ? A STUDY REVIEW ON PROPIVERINE

Hypothesis / aims of study
50% of males with bladder outlet obstruction (BOO) suffer from symptoms of the overactive bladder (OAB), being even more bothersome than voiding symptoms. This study review evaluates possible improvements of the efficacy profile, especially in regards to symptoms of the OAB by combining alpha-blocker (AB) and propiverine. Furthermore, it is analyzed, whether the administration of additional antimuscarinics presents a possible risk for post void residual (PVR) and urinary retention.
Study design, materials and methods
Four studies in patients with OAB, concomitant either with symptomatic benign prostatic enlargement (BPE) (1,3) or proven BOO (2), undertaken in Japan and Korea, were analyzed: Study 1 (1) compared tamsulosin with a combination of tamsulosin and propiverine, study 2 (2) compared doxazosin with a combination of doxazosin and propiverine, study 3 (3) and 4 evaluated the combination of AB and propiverine in patients unresponsive to previous AB monotherapy.
Results
Demographic and patients` characteristics (tab.1) and results (tab. 2) are presented.

Table 1: Demographic and patients characteristics

	Study 1	**Study 2**	**Study 3**	**Study 4**[1]
Patient Population	134 men ≥50 years	228 men ≥50 years	35 men unresponsive to AB	35 men unresponsive to AB
Symptoms	Pollakiuria or urinary incontinence due to detrusor overactivity	Urgency + frequency (> 8 /24 h)	Storage symptoms according to IPSS	Storage Symptoms according to IPSS
Urodynamic assessment	No pressure-flow study	Urodynamic assessment (Abrams-Griffiths-Score>20)	no pressure-flow study	no pressure-flow study
PVR	-	Restricted to <30% of max. cystometric bladder capacity	-	-

[1]Japanese Neurogenic Bladder Society, 2004, 15: 192-197

Table 2: Results

	Study 1		**Study 2**		**Study 3**	**Study 4**
Medication	Tamsulosin (0.2 mg/day)	Propiverine (20 mg/day) + Tamsulosin (0.2 mg/day)	Doxazosin (4 mg/day)	Propiverine (20 mg/day) + Doxazosin (4 mg/day)	Propiverine + Doxazosin[1)]	Propiverine + Tamsulosin / Naftopidil[1)]
Patient Number (N)	59	75	67	131	35	35
Treatment duration (weeks)	4	4	8	8	12	4
Storage symptoms: -IPSS	-	-	-	-	20.4 ∏15.8	15.3 ∏ 13.0
-Daytime	Improve-	Improve-	8.5∏7.6	8.8 ∏6.9	-	-

frequency[4)]	Ment rates : 29.6%	ment rates: 44.7%				
-Nocturia[4)]	Improve-Ment Rates : 22.5%	Improve-ment rates : 44.4%	2.2∏1.6	2.2 ∏1.5	-	-
-Urgency	Improve-ment rates : 18.2%	Improve-ment rates : 22.2%	-	-	-	-
Quality of life score or „Patient´s Global Satisfaction Questionnaire“	-	-	Signific. lower satis-faction rates for AB monother.	Significantly higher satisfaction rates in the combination group	Quality of life score 3.0∏2.2	Quality of life score 4.5∏3.6
Voided volume/ micturition (ml)	220∏247	163∏168	164∏196	170∏224	98 ∏130	-
Post void Residual (ml)	45.4∏35.9	41.4∏65.4[2)]	30.8∏26.1	28.8∏49.6	Not sign. Increased.	29.5∏42.6
Maximum flow rate (ml/sec)	11.5∏14.4	11.3∏11.8	10.5∏12.2	10.4∏11.4	8.7∏9.5	10.4∏9.6
Urinary retention (N)	0	2[3)]	0	0	0	0

1) Dosages not reported
2) mostly after 14 – 30 days
3) after 6 – 8 days
4) arithmetic means in study 2

Interpretation of results

Symptoms of the OAB: A combination of AB and propiverine for symptomatic BPE / BOO demonstrated advantages compared to AB monotherapy. Urgency was only evaluated in study 1. However, significant differences did not result.

Quality of life or patient satisfaction reflect the improvements of storage symptoms.

Urinary retention: Urinary retention occurrred in 2 / 241 patients of the combination treatment, but in none of 126 patients taking AB only.

Effectiveness of voiding: The additional administration of propiverine did not impair voiding function. The increase in voided volume by antimuscarinics towards normal values obviously results in more effective detrusor contractions, thus proving the concept of optimum bladder capacity for minimum bladder work. Moreover, antimuscarinics with an additional calcium-channel modulating effect, e.g. propiverine, may be superior to antimuscarinics with a solitary mode of action.

Concluding message

Based on the results of these four studies, for daily practice the following procedure can be recommended: If AB do not adequately improve the symptoms of OAB patients with concomitant BOO, the added administration of propiverine is effective and safe. Combination treatment with AB and propiverine may be more useful in patients with maximum flow rates of at least 10 ml/sec or PVR of 50 ml or less.

References:

(1) A comparative study of the efficacy and safety of Tamsulosin (Harnal capsules) alone and in combination with propiverine hydrochloride (BUP-4 tablets) in patients with prostatic hypertrophy associated with pollakiuria and/or urinary incontinence. Japanese Journal Urol Surg 1999, 12 (4): 525–536

(2) Combination treatment with propiverine hydrochloride plus doxazosin GITS in men with overactive bladder coexisting benign prostatic obstruction: a prospective, randomized, controlled, multicenter study. Joint Meeting of the International Continence Society and the International UroGynecological Association. 34th Annual Meeting, Paris France, 25th – 27th August 2004, Abstract 207. Journal Urology accepted

(3) Propiverine hydrochloride relieves irritative symptoms of benign prostatic hyperplasia. Journal Urology 2004, 171 (4, suppl.), 357-358, Annual Meeting of AUA, May 8-13, San Francisco, USA, Abstract 1358