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Authors: CR Chapple1, H Madersbacher2, K Dreikorn3, W Dorschner4, G Mürtz5
Institution: 1Urological Unit, Royal Hallamshire Hospital, Sheffield, UK; 2Neurourology, University Innsbruck, Austria; 3 Urological Unit, St. Jürgens Hospital, Bremen, 4 Urological Unit, University Leipzig, 5Apogepha, Dresden, Germany

Title: URODYNAMICS AND FREQUENCY/VOLUME CHART - DO THEY CORRELATE? TREATMENT ANALYSIS OF PROPIVERINE IN COMPARISON TO OXYBUTYNIN AND PLACEBO IN URGE INCONTINENCE

Aims of Study:

Three placebo-controlled clinical studies evaluating efficacy and tolerability of propiverine (prop.) vs. placebo (plac.) in patients suffering from urge incontinence are presented. In this analysis urodynamics and frequency/volume charts are contrasted and the results of prop. compared to oxybutynin (oxy.).

Methods: The presentation summarises three placebo-controlled multicentre studies comprising data from 598 patients suffering from urge incontinence. 15 mg prop. t.i.d. or plac. or 5 mg oxy. b.i.d. were applied for treatment periods lasting 14 [2] or 28 [1, 3] days. For proof of efficacy the maximal cystometric bladder capacity as defined by ICS criteria and results from frequency/volume charts were evaluated comparing prop. with plac. [1, 2, 3] and oxy. [1].

Results:

	[1] Prop.	Plac.	Oxy.	[2] Prop.	Plac.	[3] Prop.	Plac.
patients [n]	149	72	145	72	62	49	49
age [years]	49.6	47.6	50.3	44.5	41.2	68.4	66.5
Max. cystometric bladder capacity*							
pre [ml]	222	211	226	243	269	186	207
post [ml]	311	263	322	313	305	233	226
change [ml]	89	52	96	70	36	47	19
	+ 40 %	+ 25 %	+ 43 %	+ 29 %	+ 13 %	+ 25 %	+ 9 %
Frequency/d				n.a.	n.a.		
pre	10.4	11.5	12.6			8.7	7.4
post	8.5	10.5	10.2			6.5	6.7
change	- 1.9	- 1.0	- 2.4			- 2.1	- 0.7
	- 16 %	- 9 %	- 19 %			- 22 %	- 8 %
Incontinence/d				n.a.	n.a.		
pre	1.7	1.4	1.8			0.9	0.4
post	0.6	0.7	1.2			0.3	0.2
change	- 1.1	- 0.7	- 0.6			- 0.6	- 0.2
	- 65 %	- 50 %	- 33 %			- 67 %	- 50 %
Dry mouth [n]	78	20	95	37	16	1	0
	53.4 %	27.8 %	66.9 %	51.4 %	22 %	2.0 %	0 %

n.a.= not applied * data of [3] derived from uroflow

1. Efficacy: In all cited studies, the maximal cystometric bladder capacity increased significantly with prop. by 40 [1], 29 [2], and 25 % [3] achieving significance in comparison with plac. as well ($p=0.0105$, $p=0.046$, $p<0.01$) (table). Frequency and incontinence decreased significantly with prop. in comparison to plac. The

efficacy results with prop. were comparable to oxy.
2. Tolerability: Prompting patients for adverse events resulted in a high incidence rate for dryness of the mouth [1, 2]. In the study focusing on elderly a lower rate of adverse events was achieved with spontaneous reporting [3].

Conclusions: (1) The analysis reveals a good correlation between parameters derived from urodynamics and frequency/volume charts: The increase of max. cystometric bladder capacity is reflected by a significant decrease in frequency approxamating to the normal range.
(2) Efficacy parameters shows prop. and oxy. to be equally effective drugs.
(3) Prop. achieved favourable results for the most discerning tolerability parameter in this indication, namely dryness of the mouth, considering a high incidence rate with plac. and an even higher incidence rate for oxy.
(4) Incidence rates for adverse events are highly dependent on methodological aspects, e. g. prompting for adverse events versus spontaneous reporting.
(5) High placebo effects concerning efficacy and tolerability are due to study population characteristics, especially a high percentage of patients suffering from sensory urge.
(6) Pharmacological properties of prop. comprise its dual mode of action, its half-life-time of 20 hours and its high bioavailability and represent distinctive differences to oxy. [4]. However, data on clinical efficacy is mainly published in the German and Japanese literature. Recently, prop. was internationally acknowledged to be acceptable treatment by the WHO consensus conference on incontinence as one of the few drugs with pharmacological, physiological and clinical evidence in support of its use for the treatment of bladder overactivity [5].

[1] Madersbacher et al. Brit J Urol 1999; 84: 646-651
[2] Dreikorn et al. Data on file
[3] Dorschner et al. Eur Urol 2000; 37: 702-708
[4] Wada et al. Arch int Pharmacodyn 1995; 330: 76-89
[5] Andersson KE et al. in Abrams et al. Incontinence. 1999; 447-486

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