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Propiverine Compared to Oxybutynin in Neurogenic Detrusor Overactivity – Results of a Randomized, Double-blind, Multicenter Clinical Study

Manfred Stöhrer [a], *Gerd Mürtz* [b,*], *Guus Kramer* [c], *Frieder Schnabel* [b], *Edwin P. Arnold* [d], *Jean-Jaques Wyndaele* [e] *and the Propiverine Investigator Group*

[a] *Department of Urology, Traumatological Hospital, Murnau, Germany*
[b] *Apogepha, Dresden, Germany*
[c] *Bennebroek, The Netherlands*
[d] *Department of Urology, Christchurch, New Zealand*
[e] *Department of Urology, University Hospital Antwerpen, Edegem, Belgium*

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FVC, frequency volume chart
ITT, intention to treat
PP, per protocol

Abstract

Objectives: To compare the efficacy and tolerability of propiverine and oxybutynin in patients with neurogenic detrusor overactivity.
Methods: Patients were eligible, if at least 18 years of age and suffering from neurogenic detrusor overactivity. Eligibility also required a maximum cystometric capacity less than 300 ml. After a one-week run-in period, propiverine 15 mg t.i.d. or oxybutynin 5 mg t.i.d. were administered for 21 days. As primary efficacy outcomes urodynamic parameters were assessed. As tolerability outcome the percentage of patients with newly manifesting anticholinergic adverse events was taken.
Results: 131 patients were recruited at 20 study centers. The maximum cystometric capacity (ml) was increased significantly in the propiverine group from 198 (±110) to 309 (±166), and in the oxybutynin group from 164 (±64) to 298 (±125). Similarly, maximum detrusor pressure during the filling phase (cm H_2O) was lowered significantly in the propiverine group from 56.8 (±36.2) to 37.8 (±31.6), and in the oxybutynin group from 68.6 (±34.5) to 43.1 (±29.2). No significant differences resulted between treatment groups.

Anticholinergic adverse events were reported less frequently in the propiverine compared to the oxybutynin group (63.0% versus 77.8%). Dryness of the mouth, the most frequent adverse event, was reported significantly less (47.1% versus 67.2%; $p = 0.02$) in the propiverine compared to the oxybutynin group.
Conclusion: Propiverine and oxybutynin are equally effective in increasing bladder capacity and lowering bladder pressure in patients with neurogenic detrusor overactivity. The trend for better tolerability of propiverine compared to oxybutynin achieved significance for dryness of the mouth.

* Corresponding author. Tel. +493513363435; Fax: +493513363440.
E-mail address: gmuertz@apogepha.de (G. Mürtz).

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1. Introduction

The efficacy of oxybutynin has been well established over almost three decades of clinical experience, both in idiopathic [1,2] and neurogenic detrusor overactivity [3]. However, therapeutic efficacy is associated with a high incidence of adverse events, up to 80% with oral administration [4], typically anticholinergic in nature (e.g. dry mouth, constipation, drowsiness, blurred vision), often dose-limiting, in some cases necessitating premature treatment discontinuation. A recent review and metaanalysis of anticholinergics by Chapple et al. [5] concluded oxybutynin immediate release was not well tolerated. Despite being an efficacious drug of first choice in patients suffering from this condition, the poor tolerability of oxybutynin necessitated the search for alternative drugs. This applies especially to neurogenic detrusor overactivity, which often requires higher dosages [6] for suppressing involuntary detrusor contractions during the filling phase. Tolterodine is also of proven efficacy, but it too is not freely available in some countries, notably Australia and NZ.

Propiverine hydrochloride (referred to in the following as propiverine) is one of the few drugs recommended for the treatment of detrusor overactivity by the International Consultation on Incontinence [4]. It comprises a neurotropic and a musculotropic mode of action, thus inducing antimuscarinic effects as well as effects on the calcium-influx and calcium-homeostasis [7]. Most of the propiverine studies have focussed so far on patients suffering from idiopathic detrusor overactivity [8–10], and demonstrated the beneficial effects of its dual mode of action. In a dosage-optimizing study of spinal cord injured adults Mazur and coworkers [11] recommended 15 mg propiverine t.i.d. as adequate dosage in most patients. Subsequently, Stöhrer et al. [12] proved the efficacy of propiverine (15 mg t.i.d.) compared to placebo over a treatment period of 14 days by documenting urodynamic improvements.

Therefore the aim of this study was to compare the efficacy and tolerability of propiverine and oxybutynin in patients suffering from neurogenic detrusor overactivity.

2. Patients and methods

This multinational, double-blind, comparative trial was conducted at 20 study centers specialized in neurourology. Ethical approval was obtained at each center. All patients gave written informed consent, and the study was conducted in accordance with the declaration of Helsinki.

2.1. Patients

Patients were eligible, if at least 18 years of age and suffering from a known neurological disorder and had demonstrable detrusor overactivity at urodynamic assessment. Maximum cystometric capacity was restricted to 300 ml. Patients were excluded if they had other genitourinary tract anomalies (e.g. infravesical obstruction, ectopic ureters, hypospadias, fistulas, anomalies of the urethra, epispadias), a post void residual >15% of the bladder capacity, acute infections of the genitourinary tract, or clinically relevant diseases of the kidneys. Further exclusion criteria were abnormal liver, gastrointestinal tract or cardiovascular system function, metabolism disorders (e.g. diabetes mellitus, diabetes insipidus), pre-existing medical contraindications for anticholinergics (e.g. megacolon, achalasia, respective cardiac or ocular disorders like tachyarrhythmias of hemodynamic significance, angina pectoris, glaucoma, myasthenia gravis). Patients were also not eligible, if having participated in any other study with an investigational drug within at least one month prior to inclusion in this study, or if concomitant treatment, possibly interfering with the trial medication, was applied.

2.2. Study design

After a one-week run-in period patients were randomized (1:1) using random permuted blocks with a computer-generated randomization list prepared by a trial-independent statistician. Patients received either oral propiverine 15 mg t.i.d. or oxybutynin 5 mg t.i.d. (double-dummy technique with matching placebos) for 21 days. No dose adjustment of the trial medication was allowed during the study. Oxybutynin immediate release was chosen, because oxybutynin extended release was not yet commonly available at the planning for this study. Trial drugs of identical appearance covered 28 days, thus guaranteeing sufficient medication even in those cases with possibly prolonged treatment periods. Medication was pre-packaged according to the randomization list, and a multiple of the block size was distributed to each study center. The investigators at each center had to allocate individual treatment by assigning subject numbers in consecutive order.

Efficacy assessment, conducted prior to and after 21 days of treatment, comprised maximum cystometric capacity, maximum detrusor pressure during filling phase, and detrusor compliance as urodynamic parameters. Residual urine was assessed after having performed urodynamics, either by catheterization or by ultrasound. All methods, definitions and units of this study conform to the standards recommended by the International Continence Society, except when specifically noted [13].

Furthermore, the patients completed 5-day bladder diaries prior to treatment and at treatment termination. Secondary efficacy outcomes were 24-h micturition frequency, 24-h incontinence episodes and mean volume voided/micturition in the per-protocol-population.

The primary tolerability outcome was the percentage of patients with newly manifesting typical anticholinergic adverse events in both treatment groups.

Table 1 – Demographic characteristics (safety population)

		Propiverine	Oxybutynin	Total Population
N		70	61	131
Gender				
Male	*n* (%)	54 (77.1)	45 (73.8)	99 (75.6)
Female	*n* (%)	16 (22.9)	16 (26.2)	32 (24.4)
Age [years]	$x \pm$ s.d.	38.8 ± 13.9	37.7 ± 15.1	38.3 ± 14.4
Range		18–67	18–76	18–76
Height [cm]	$x \pm$ s.d.	175.8 ± 9.2	173.9 ± 9.8	174.4 ± 9.5
Weight [kg]	$x \pm$ s.d.	74.5 ± 13.6	72.1 ± 11.2	73.4 ± 12.5

$x \pm$ s.d.: arithmetic mean ± standard deviation.

2.3. *Statistical analysis*

All confirmatory analyses for non-inferior, equivalent efficacy and tolerability of propiverine compared to oxybutynin were planned to be performed in the per-protocol-population (pp). As primary efficacy outcomes maximum cystometric capacity (1st primary parameter) and maximum detrusor pressure during filling phase (2nd primary parameter) were selected. As primary tolerability outcome (3rd primary parameter) the number of patients with anticholinergic adverse events, excluding pre-existing and events unrelated to study medication, was chosen. For each of these 3 hypotheses an one-sided *t*-test with Bonferroni-adjusted alpha of 0.0167 was performed. Relevant differences for non-inferiority testing were defined prior to study conduct: 68% of the standard deviation of the reference treatment oxybutynin for the 1st and 2nd primary parameter, 32% of the patients for the 3rd parameter.

Additionally, secondary to confirmatory analyses descriptive analyses were conducted with two-sided *t*-tests: for each of the primary parameters as well as for clinically relevant parameters derived from the frequency volume chart (24-h micturition frequency, 24-h incontinence episodes, mean volume voided/micturition) in the pp-population. In order to further validate these urodynamic and clinical results descriptive analyses were also planned to be conducted in the intention-to-treat-population (itt).

Additional analyses in regards to secondary binary tolerability parameters were conducted using Fisher's exact test in the safety population.

3. Results

3.1. *Patient population*

All 131 enrolled patients (safety population) suffered from neurogenic detrusor overactivity as defined by the ICS [13]. Most had had a traumatic spinal cord injury ($n = 122$) with complete or incomplete lesions located above the sacral micturition center. Other causes were myelitis ($n = 1$), multiple sclerosis ($n = 2$), myelodysplasia ($n = 4$), and spinal tumours ($n = 2$).

The demographic characteristics of the safety population were comparable between both treatment groups (Table 1). Due to premature treatment terminations (propiverine $n = 16$, oxybutynin $n = 9$) the itt-population consisted of 107 patients. Premature treatment terminations occurred to a comparable extent in both groups, the reasons therefore are given in Table 2.

Due to 16 patients being considered to violate the trial protocol (inadequate diagnosis, no urodynamic assessment at study termination, insufficient compliance, etc.) the pp-population comprised 91 patients. Twenty study centers, all specialised in neurourology, participated.

3.2. *Primary efficacy – urodynamic parameters on filling cystometry*

The maximum cystometric capacity, increased significantly both in the propiverine group ($n = 46$) from 198 ml (±110) to 309 ml (±166), and in the oxybutynin group ($n = 45$) from 164 ml (± 64) to 298 ml (±125). According to the confirmatory analysis ($p = 0.011$) non-inferior, equivalent efficacy of propiverine compared to oxybutynin could be shown. The descriptive analysis revealed no significant difference between both treatment groups (Fig. 1).

The maximum detrusor pressure during filling phase, was lowered significantly in the propiverine group from 56.8 cm H_2O (±36.2) to 37.8 cm H_2O (±31.6), and in the oxybutynin group from 68.6 cm

Table 2 – Premature treatment terminations (*N*)

	Propiverine	Oxybutynin	*p*-value
Lack of efficacy	1	0	n.s.
Adverse events	11	4	n.s.
Non-compliance	1	3	n.s.
Other reasons	3	2	n.s.
Overall	16	9	n.s.

n.s.: not significant.

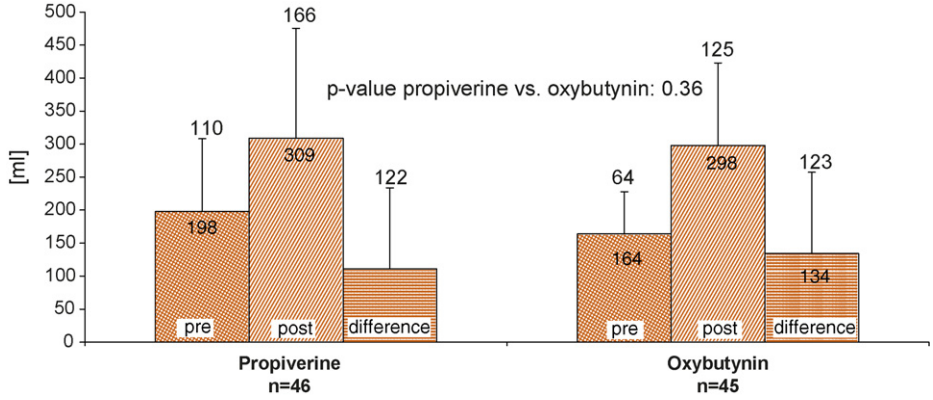

Fig. 1 – Maximum cystometric capacity.

H_2O (±34.5) to 43.1 cm H_2O (±29.2). According to the confirmatory analysis ($p < 0.0001$) non-inferior, equivalent efficacy of propiverine compared to oxybutynin could be shown. No significant differences between propiverine and oxybutynin resulted (Fig. 2).

As a secondary efficacy outcome, detrusor compliance, assessed during filling cystometry, demonstrated significant improvements: in the propiverine group from 10.8 ml/cm H_2O (±13.8) to 22.7 ml/cm H_2O (±24.3), and in the oxybutynin group from 12.7 ml/cm H_2O (±12.1) to 37.8 ml/cm H_2O (±48.3), no significant ($p = 0.11$) inter-group-differences resulted (Fig. 3).

Residual urine was increased for propiverine from 72.6 ml (±115) to 140.9 ml (±167) and for oxybutynin from 65.3 ml (±78) to 149 ml (±133) which indicated no significant ($p = 0.13$) differences between the two groups. 14 patients in the propiverine and 17 patients in the oxybutynin groups were not able to void during urodynamics, and there were no significant differences between the two groups ($p = 0.31$).

3.3. *Secondary efficacy – clinical data: frequency volume chart (FVC)*

The 24-h micturition frequency, 24-h incontinence episodes and mean volume voided/micturition in the pp-population are given in Table 3. All these outcomes improved significantly within both groups, but no significant differences between both treatment groups resulted.

The results of the reported pp- and the itt-population are almost identical, both for the urodynamic and the parameters derived from FVC.

3.4. *Tolerability and safety*

The 3rd primary outcome was the number of patients with typical anticholinergic adverse events,

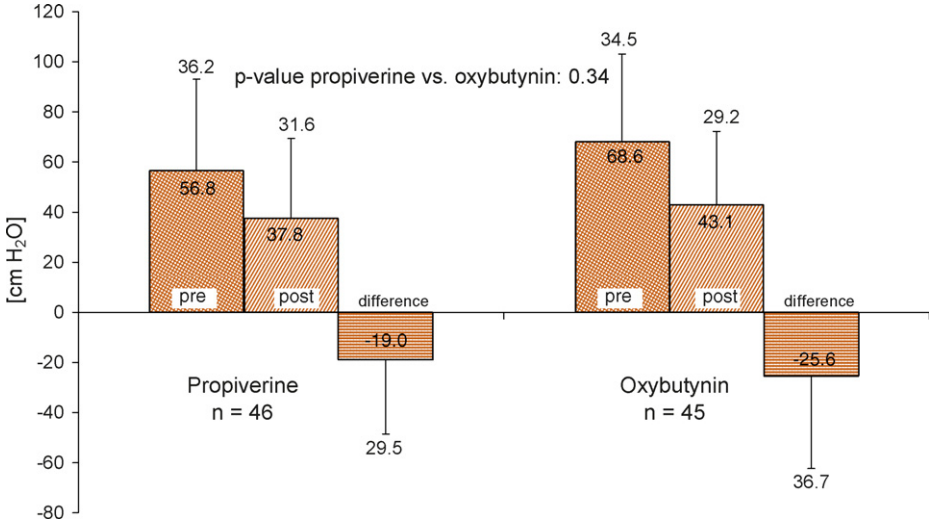

Fig. 2 – Maximum detrusor pressure during filling phase.

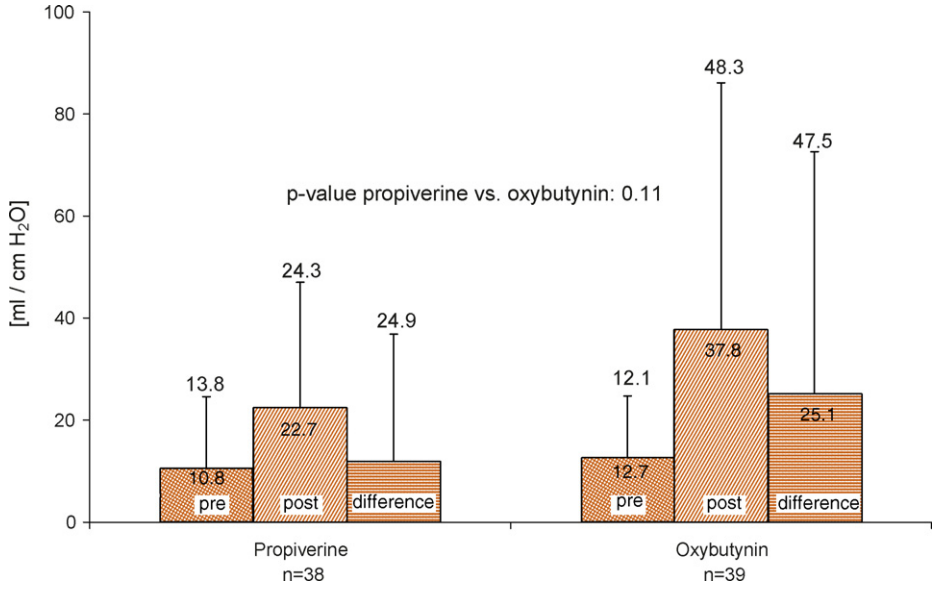

Fig. 3 – Detrusor compliance.

excluding pre-existing events and events considered unrelated to study medication, manifesting during the treatment period in the pp-population: in the propiverine group 29/46 patients (63.0%) presented with anticholinergic adverse events compared to 35/45 patients (77.8%) in the oxybutynin group. According to the confirmatory analysis ($p < 0.0001$) non-inferior, equivalent tolerability of propiverine compared to oxybutynin can be assumed. The descriptive analysis showed no significant difference ($p = 0.17$) between both groups.

Secondary tolerability outcomes, all assessed in the safety population, comprised:

1. The number of patients experiencing adverse events, excluding pre-existing and adverse events considered unrelated to study medication. Adverse events occurred in 48/70 patients (68.6%) of the propiverine, and in 48/61 (78.7%) patients of the oxybutynin group, respectively.
2. Dryness of the mouth was the most frequently reported adverse event. It occurred significantly less often ($p = 0.02$) in the propiverine (33/70; 47.1%) compared to the oxybutynin (41/61; 67.2%) group (Fig. 4).
3. All other anticholinergic adverse events showed no significant differences between both treatment groups, the respective p-values are therefore not reported (Table 4).

Neither lethal nor other serious adverse events were documented during the study. Haematology,

Table 3 – Frequency volume chart (pp-population)

		Propiverine	Oxybutynin	Propiverine vs. Oxybutynin*
24-h micturition frequency	Pre	10.9 ± 6.9	12.0 ± 12.7	$p = 0.84$
	Post	7.9 ± 5.7	9.5 ± 10.4	
	Difference	−2.9 ± 2.9	−2.5 ± 3.3	
	p-value+	$p < 0.05$	$p < 0.05$	
24-h incontinence episodes	Pre	3.9 ± 4.5	3.3 ± 3.4	$p = 0.54$
	Post	2.3 ± 4.6	2.0 ± 3.2	
	Difference	−1.6 ± 2.3	−1.3 ± 2.0	
	p-value+	$p < 0.05$	$p < 0.05$	
Mean voided volume/micturition (ml)	Pre	182 ± 115	206 ± 127	$p = 0.59$
	Post	209 ± 136	242 ± 126	
	Difference	+27 ± 55	+37 ± 72	
	p-value+	$p < 0.05$	$p < 0.05$	

Arithmetic means ± standard error of the arithmetic mean.
* p-value of 2-sided t-test for two independent groups.
+ p-values of pre-post comparisons.

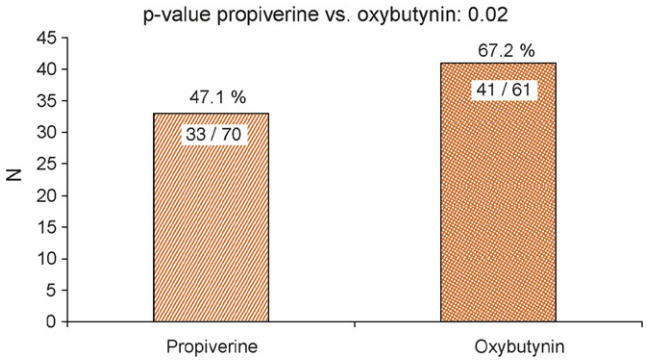

Fig. 4 – Dryness of the mouth.

clinical chemistry and urinalysis did not indicate any differences between both treatment groups.

4. Discussion

In the management of patients with neurogenic detrusor overactivity the key medical objective is to protect the upper urinary tract by achieving a low pressure bladder reservoir [14,15]. This study confirms that both propiverine and oxybutynin achieved significantly lower bladder pressures.

In contrast to idiopathic detrusor overactivity, video-urodynamic assessment still presents the mainstay for verifying the diagnosis of neurogenic detrusor overactivity before drug treatment. The urodynamic and clinical data are complementary. Our approach of focussing on cystometric findings is supported by results of Ockrim et al. [16] who reported consistent cystometric findings (e.g. detrusor overactivity) over sequential studies in spinal cord injured men, whereas in men with lower urinary tract symptoms but with no neurological disease, the number and pressure of involuntary detrusor contractions in consecutive cystometries significantly decreased.

Few clinical trials of oxybutynin [3] and propiverine [12] have focussed on neurogenic detrusor overactivity. Furthermore, in patients with neurogenic detrusor overactivity a dose optimizing study has been conducted only for propiverine [11], however, none for oxybutynin. The increase in maximum cystometric capacity, paralleled by a decrease in maximum detrusor pressure during filling phase confirm previous reports for propiverine [12], oxybutynin [17] and trospium chloride [17,18], the three anticholinergics most thoroughly investigated in this condition. Only in cases of treatment failures of oral anticholinergic medication Botulinum-A toxin [19] might be considered as another option in the treatment cascade of neurogenic detrusor overatcivity.

A treatment period of 3 weeks was considered to be sufficient, because another study conducted in neurogenic detrusor overactivity [12], restricted to 2 weeks of treatment, demonstrated rapid onset of action for propiverine. In regard to long-term efficacy it is known from clinical practice that propiverine and oxybutynin are efficacious in conditions requiring life-long medication.

The major patient objective is to achieve continence, and thus to improve quality of life. There were significant improvements in 24-h micturition frequency, in incontinence episodes, in mean voided volume per micturition in both treatment groups without relevant inter-group differences. However, in our patients these parameters are of comparatively minor importance, because most of them are practising intermittent catheterization, and / or using diapers to avoid incontinence in case of insufficient micturition control.

Increased residual urine due to anticholinergic medication might be a theoretical problem, but was not relevant in most of our cases being on

Table 4 – Adverse events (excluding all pre-existing and unrelated adverse events; safety population)

	Propiverine ($n = 70$)	Oxybutynin ($n = 61$)	p-value
Dizziness	6	4	n.s.
Headache	2	4	n.s.
Acute urinary retention*	14	17	n.s.
Constipation	12	9	n.s.
Dryness of the mouth	33	41	0.02
Vision affected	14	6	n.s.
Nausea	4	2	n.s.
Fatigue	11	9	n.s.
Other adverse events (reported by less than 3 patients)	13	6	n.s.
All adverse events	109+	98+	n.a.

n.s.: not significant; n.a.: not applicable.
* Not to be considered as an adverse event in this patient population because it indicates complete detrusor relaxation.
+ The number of adverse events is higher than the number of patients due to multiple adverse events in some patients.

intermittent catheterization. Our results are in accordance with data presented by Stöhrer et al. [12] and complement our own clinical experience.

Officially recommended and effective dosages in clinical practice might vary widely, especially in neurogenic detrusor overactivity [6]. According to study results of Ethans et al. [20] for oxybutynin the ''average self-selected best daily dosage'' was 12.5 mg, corresponding well to the recommended dosage, whereas patients exposed to tolterodine requested on average 8.4 mg, more than two-fold of the recommended dosage. These results suggest, that efficacy in non-neurogenic conditions does not necessarily translate into efficacy in neurogenic conditions. Therefore, in some cases of neurogenic overactivity higher dosages can be recommended and adverse events appear to be tolerated. From the clinical perspective dose titration is advisable, guided by efficacy versus patient perception of side effects [6,21]. Implementing dose titration modules into clinical practice will further improve efficacy and tolerability profiles.

The overall results in regard to tolerability seem to be slightly less superior in neurogenic compared to idiopathic detrusor overactivity: Madersbacher et al. [8] proved in patients suffering from idiopathic detrusor overactivity comparatively lower incidence rates of anticholinergic adverse events for these two anticholinergics, if pre-existing adverse events were excluded. Furthermore, in Madersbacher's study severe dryness of the mouth was less frequently due to propiverine compared to oxybutynin. Our data reflect this result, because the incidence rate of dry mouth for propiverine compared to oxybutynin was lower. We assume that ''neurogenic'' patients might tolerate adverse events even better, whereas ''non-neurogenic'' patients seem to be more susceptible to adverse events [7].

Our study confirmed propiverine to be better tolerated than oxybutynin: this trend for a lower percentage of patients experiencing adverse events, if exposed to propiverine, achieved significance only for dryness of the mouth, the most frequent anticholinergic adverse event (Fig. 4): The 48% incidence rate of propiverine in our study is well in accordance with 37% reported by Stöhrer et al. [12]. Consistently, for oxybutynin higher incidence rates for dryness of the mouth are reported both in our study and the one conducted by Madersbacher et al. [17]: 67% and 56%, respectively.

5. Conclusions

In patients with neurogenic detrusor overactivity, mainly due to traumatic spinal cord injury, a randomized controlled trial, comparing propiverine and oxybutynin, showed they were equally effective, both for the medical objective of lowering detrusor pressure and for the patient objective of achieving continence.

However, patients on propiverine showed fewer anticholinergic adverse events, especially dryness of the mouth.

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References

[1] Cardozo LD, Cooper D, Versi E. Oxybutynin chloride in the management of idiopathic detrusor instability. Neurourol Urodyn 1987;6:256–7.

[2] Thuroff JW, Bunke B, Ebner A, Faber P, de Geeter P, Hannappel J, et al. Randomized, double-blind, multicenter trial on treatment of frequency, urgency and incontinence related to detrusor hyperactivity: oxybutynin versus propantheline versus placebo. J Urol 1991;145:813–6.

[3] Gajewski JB, Awad SA. Oxybutynin versus propantheline in patients with multiple sclerosis and detrusor hyperreflexia. J Urol 1986;135:966–8.

[4] Andersson KE, Appell R, Cardozo L, Chapple C, Drutz H, Fourcroy J, et al. Pharmacological treatment of urinary incontinence. In: Abrams P, Cardozo L, Khoury S, Wein A, editors. Incontinence. Edition 2005. Paris: Health Publication Ltd; 2005. p. 809–54, Chapter 14.

[5] Chapple C, Khullar V, Gabriel Z, Dooley JA. The effects of antimuscarinic treatments in overactive bladder: a systematic review and meta-analysis. Eur Urol 2005;48:5–26. Corrigendum. Eur Urol 2005;48:875.

[6] Bennett N, O'Leary M, Patel AS, Xavier M, Erickson JR, Chancellor MB. Can higher doses of oxybutynin improve efficacy in neurogenic bladder? J Urol 2004;171:749–51.

[7] Madersbacher H, Mürtz G. Efficacy, tolerability and safety profile of propiverine in the treatment of the overactive bladder (non-neurogenic and neurogenic). World J Urol 2001;19:324–35.

[8] Madersbacher H, Halaška M, Voigt R, Alloussi S, Höfner K. A placebo-controlled, multicentre study comparing the tolerability and efficacy of propiverine and oxybutynin in patients with urgency and urge incontinence. BJU Int 1999;84:646–51.
[9] Dorschner W, Stolzenburg JU, Griebenow R, Halaska M, Schubert G, Mürtz G, et al. Efficacy and cardiac safety of propiverine in elderly patients – A double-blind, placebo-controlled clinical study. Eur Urol 2000;37:702–8.
[10] Jünemann KP, Halaska M, Rittstein T, Mürtz G, Schnabel F, Brünjes R, Nurkiewicz W. Propiverine versus tolterodine – efficacy and tolerability in patients with overactive bladder. Eur Urol 2005;48:478–82.
[11] Mazur D, Göcking K, Wehnert J, Dorschner W, Schubert G, Herfurth G, et al. Klinische und urodynamische Effekte einer oralen Propiverintherapie bei neurogener Harninkontinenz. Urologe [A] 1994;33:447–52.
[12] Stöhrer M, Madersbacher H, Richter R, Wehnert J, Dreikorn K. Efficacy and safety of propiverine in SCI-patients suffering from detrusor hyperreflexia – a double-blind, placebo-controlled clinical trial. Spinal Cord 1999;37:196–200.
[13] Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology of lower urinary tract function: Report from the Standardisation Sub-committee of the International Continence Society. Neurourol Urodynamics 2002;21:167–78.
[14] Madersbacher H. The various types of neurogenic bladder dysfunction: an update of current therapeutic concepts. Paraplegia 1990;28:217–29.
[15] Stöhrer M, Castro-Diaz D, Chartier-Kastler E, Kramer G, Mattiasson A, Wyndaele J-J. EAU Guidelines on neurogenic lower urinary tract dysfunction. European Association of Urology 2003 http://www.uroweb.org/files/uploaded_files/guidelines/neurogenic.pdf.
[16] Ockrim J, Laniado ME, Khoubehi B, Renzetti R, Agro EF, Carter SS, et al. Variability of detrusor overactivity on repeated filling cystometry in men with urge symptoms: comparison with spinal cord injury patients. BJU Int 2005;95:587–90.
[17] Madersbacher H, Stöhrer M, Richter R, Burgdörfer H, Hachen HJ, Mürtz G. Trospium chloride versus oxybutynin: A randomized, double-blind, multicentre trial in the treatment of detrusor hyperreflexia. Br J Urol 1995;75:452–6.
[18] Stöhrer M, Bauer P, Giannetti BM, Richter R, Burgdorfer H, Mürtz G. Effect of trospium chloride on urodynamic parameters in patients with detrusor hyperreflexia due to spinal cord injuries. A multicentre placebo-controlled double-blind trial. Urol Int 1991;47:138–43.
[19] Schurch B, Stöhrer M, Kramer G, Schmid DM, Gaul G, Hauri D. Botulinum-A toxin for treating detrusor hyperreflexia in spinal cord injured patients: a new alternative to anticholinergic drugs ? Preliminary results. J Urol 2000;164:692–7.
[20] Ethans KD, Nance PW, Bard RJ, Casey AR, Schryvers OI. Efficacy and safety of tolterodine in people with neurogenic detrusor overactivity. J Spinal Cord Med 2004;27:214–8.
[21] Madersbacher H, Menarini M, Dörsam J, Sember ME, Chiang H. Anticholinergic therapy of neurogenic detrusor overactivity: Evaluation of an oral trospium chloride (TC) dose adjustment. German Society of Urology. Poster presented at the Annual Meeting 2004.