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## Drug therapy

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## Treatment of the urge syndrome with propiverine in the therapeutic practice

### Effectiveness and tolerance in 4390 patients

#### On the subject

*The urge syndrome (urge incontinence and urgency) considerably interferes with the social and professional life of the patients. Such disturbances of the storage function of the urinary bladder are always accompanied by pollakiuria, nycturia and urgency and, in some cases, by urinary incontinence. These dysfunctions are mainly treated with drugs. The main object of the present documentation accompanying the therapy was the proof of the effectiveness of propiverine in patients with incontinence and urge symptoms, incontinence with combined urge and stress symptoms, incontinence in neurological diseases, urge symptoms without incontinence, diurnal and/or nocturnal wetting in patients ≤16 years as well as in patients with post-operative urge symptoms. It was another object to verify the dosage recommendations for propiverine (Mictonorm®/Mictonetten®) for each indication and to acquire under practical conditions in a numerous and representative patient population any adverse reactions which might have been unknown to date. As the pressure of costs in health services is on the increase, the effect of the drug therapy with propiverine on the consumption of auxiliary materials was also considered under economic aspects.*

Etiologically different forms of bladder dysfunctions such as hyperactive and hypersensitive urinary bladder are classed under the terms "urge syndrome" and "unstable bladder". As the causes, neurogenic and myogenic disturbances can be found which may also occur in a combined form. Subjectively, these urinary bladder dysfunctions manifest themselves as pollakiuria, nycturia, urgency with or without urinary incontinence. These dysfunctions are mainly treated with a drug therapy. On the one hand, it can have a pharmacological action through the innervation of the urinary bladder, and, on the other, on the smooth musculature of the urinary bladder. What is required today of a spasmolytic drug therapy is a profile which is low in adverse reactions in addition to a myotropic and anticholinergic effect. Propiverine hydrochloride (propiverine) meets these requirements.

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Propiverine is a tertiary amine having the structural formula shown in Fig. 1

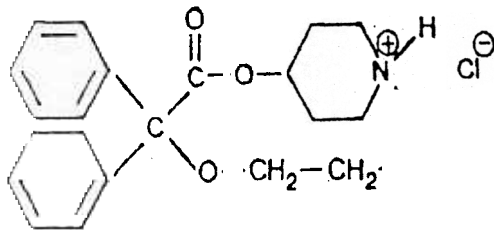


Fig. 1: Structural formula of propiverine

Due to a dual mode of action, propiverine stands out from both anticholinergics and spasmolytics each of which has solitary principles of action. A spasmolysis which directly acts on the smooth musculature is achieved through an inhibition of the inflow of calcium ions into the myocytes of the detrusor and an indirect spasmolysis is achieved via inhibition of acetylcholine through a competitive bonding to muscarinic receptors [1, 11].

The effectiveness of propiverine has been proved by a large number of clinical trials which include a spectrum of indications ranging from detrusor hyperreflexia as well as detrusor hyperactivity and hypersensitivity and infantile urinary incontinence to the postoperative adjuvant spasmolytic therapy [4, 6-8, 10]. Propiverine in its two dosage forms (Mictonorm<sup>®</sup>/Mictonetten<sup>®</sup>) has proved to be a safe and well-tolerated drug even in long-term application [6, 10]. On the basis of the findings of the clinical trials, daily doses of 30 to 45 mg propiverine are recommended as therapeutically optimal doses [6, 7].

The main objects of the present documentation accompanying the therapy were the verification of the effectiveness of propiverine and the exact acquisition of adverse reactions under practical conditions which might have been unknown to date. In addition, it was intended to verify the dosages of propiverine in patients with incontinence and urge symptoms, incontinence with combined urge and stress symptoms, incontinence in neurological diseases, urge symptoms without incontinence, and diurnal and/or nocturnal wetting in patients  $\leq 16$  years as well as in patients with post-operative urge symptoms to modify the dosage recommendations if required. As the pressure of costs in health services is on the increase, it was also intended to study the effect of the drug therapy with propiverine in the treatment of urinary incontinence on the consumption of auxiliary materials.

## Patients and methods

The results of a total of 4390 patients (3473 women, 910 men, 7 patients whose sex was not specified) who had been treated with propiverine for 12 weeks are available. The demographic characteristics of the patient population show an average patient age of 51.2 years, a high percentage of older patients (20 % between 60 and 69 years, 15.7 % between 70 and 79 years, 5.8 % over 80 years) and also a relatively high percentage of younger patients (14.5 %  $\leq 16$  years) (Table 1).

The total population was divided into 6 diagnosis groups (Table 1). It is important to note that the application in the latter patient group was observed before the current terminology of the study group Urological Functional Diagnosis and Urology of the Woman was adopted. Therefore, the differentiation between infantile urinary incontinence and enuresis cannot be

taken into account. Instead, a distinction between Enuresis diurna (0.6 %), Enuresis nocturna (9.6 %) and Enuresis diurna et nocturna (3.5 %) was made in this subgroup. The assignment to the diagnosis groups was based on anamnesis, clinico-urological routine examinations (urinalysis, sonography), and voiding record.

**Table 1:**  
Demographic data and diagnosis groups

	Number of patients		Sex (n <sup>a</sup> )		Age (years)
	(n)	(%)	Female	Male	
Total population	4390	100.0	3473	910	51.2 ± 22.2
I. Incontinence and urge symptoms	1329	30.3	1130	197	60.1 ± 12.5
II. Incontinence and comb. urge/stress symptoms	1413	32.2	1324	87	58.1 ± 13.7
III. Incontinence in neurological diseases	71	1.6	52	19	47.2 ± 16.9
IV. Urge symptoms without incontinence	812	18.5	613	197	54.8 ± 16.4
V. Postoperative urge symptoms	163	3.7	50	113	62.5 ± 12.2
VI. Diurnal and/or noct. incont. in patients ≤16 years	602	13.7	304	297	8.1 ± 2.7

<sup>a</sup>7 patients without specification of sex

The observation period covered 12 weeks of treatment with 3 control examinations at the beginning of documentation (T<sub>0</sub>), at 4 weeks (T<sub>4</sub>) and at 12 weeks (T<sub>12</sub>).

The assessment of effectiveness was done by means of the voiding record through the following parameters:

- diurnal and nocturnal urinary incontinence;
- pollakiuria, nycturia;
- diurnal and nocturnal urgency;
- use of incontinence pads;
- urge score in the incontinence questionnaire according to Gaudenz;
- subjective improvement in symptoms;
- global assessment by the patient.

The assessment of tolerance included the following:

- vital parameters (heart rate, systolic and diastolic blood pressure);
- undesired drug actions questioned actively (incidence and severity);
- residual urine (determined by means of sonography in most cases);
- global assessment of tolerance by questioning of the patient;
- discontinuation of therapy.

In addition, preliminary therapies, concomitant diseases and concomitant medications, changes in the trial medication and dosage which could be freely selected by the physician were documented.

## Results

### 1. Effectiveness

#### Diurnal and nocturnal urinary incontinence

In the total population of patients who reported a urinary incontinence at T<sub>0</sub> (n = 3303), the number of diurnal incontinence episodes markedly reduced in the course of therapy (T<sub>0</sub>: 3.5 ± 3.7, T<sub>12</sub>: 1.0 ± 2.0, p < 0.001). 37 % of all incontinent patients were continent after 12 weeks.

A comparative analysis shows for the subgroup with incontinence and urge symptoms ( $n = 1329$ ) a more favourable tendency of improvement than for the subgroup incontinence with combined urge and stress symptoms ( $n = 1413$ ) (Table 2). In patients with incontinence and urge symptoms, diurnal incontinence decreased under propiverine by 3.3 episodes ( $T_0$ :  $4.6 \pm 3.6$ ,  $T_{12}$ :  $1.3 \pm 2.1$ ). 90.8 % of the patients stated at  $T_4$  an improvement in symptoms, 47.9 % of the patients became continent after 12 weeks. In patients with incontinence with combined urge and stress symptoms, incontinence decreased by 2.9 episodes ( $T_0$ :  $4.3 \pm 3.3$ ,  $T_{12}$ :  $1.4 \pm 2.2$ ) (Fig. 2). 86.8 % of the patients stated at  $T_4$  an improvement in symptoms, 42.7 % of the patients became continent at  $T_{12}$ .

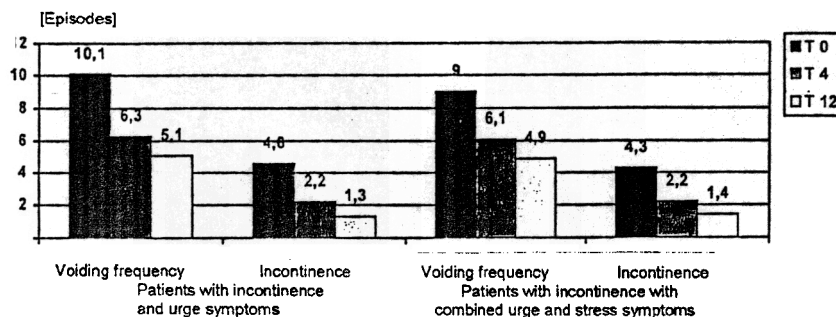
**Table 2:**

Clinical symptoms prior to treatment ( $T_0$ ) and after 12 weeks of treatment ( $T_{12}$ ) with propiverine: total population and selected subpopulations

Clinical symptoms (mean values of the episodes)	Time	Incontinence and urge symptoms	Incontinence with comb. urge/stress symptoms	Incontinence in neurol. diseases	Total population
Diurnal incontinence	$T_0$	4.6	4.3	6.4	3.5
	$T_{12}$	1.3	1.4	2.5	1.0
Nocturnal incontinence	$T_0$	1.6	1.2	3.3	1.3
	$T_{12}$	0.4	0.3	1.2	0.3
Diurnal urgency	$T_0$	10.1	9.0	9.3	9.5
	$T_{12}$	5.1	4.9	5.2	5.0
Nocturnal urgency	$T_0$	3.1	2.5	3.2	2.8
	$T_{12}$	1.0	0.9	1.1	0.9
Pollakiuria	$T_0$	9.6	8.7	8.6	9.1
	$T_{12}$	5.8	5.8	6.1	5.8
Nycturia	$T_0$	2.9	2.4	2.6	2.6
	$T_{12}$	1.0	1.0	1.2	1.0

**Fig. 2:**

Diurnal voiding frequency and incontinence in the 12-week course of the therapy with propiverine (Mictonorm®/Mictonetten®) in patients with incontinence and urge symptoms and in patients with incontinence with combined urge and stress symptoms



Bedwetting (between 10 p.m. and 6 a.m.,  $n = 3253$ ) also significantly decreased from  $1.3 \pm 1.8$  events prior to therapy to  $0.6 \pm 1.2$  after 4 weeks and  $0.3 \pm 1.0$  events after 12 weeks of treatment with propiverine, respectively (Tables 2, 3).

In the subgroup  $\leq 16$  years, 72.2 % ( $n = 434$ ) aged 3 to 9 years and 27.8 % ( $n = 167$ ) aged 10 to 16 years. The evaluation of this subgroup showed a reduction in diurnal incontinence ( $n = 449$ ) from 1.2 ( $T_0$ ) to 0.2 ( $T_{12}$ ) episodes and in nocturnal incontinence ( $n = 535$ ) from 1.5 ( $T_0$ ) to 0.4 ( $T_{12}$ ) episodes. No or dry incontinence pads were documented prior to treatment by 47.3 % ( $T_0$ :  $n = 284$ ) and after 12 weeks by 62.6 %.

### Pollakiuria and nycturia

Diurnal voiding frequency ( $n = 3689$ ) reduced from  $9.1 \pm 3.9$  ( $T_0$ ) to  $5.8 \pm 2.1$  ( $T_{12}$ ). Nocturnal voiding frequency ( $n = 3601$ ) reduced from  $2.6 \pm 1.9$  ( $T_0$ ) to  $1.0 \pm 1.1$  ( $T_{12}$ ) (Table 2). Altogether, the voiding frequency returned to normal in 80.1 % of the patients.

Table 3:

Dosage of propiverine and severity of the clinical symptoms prior to treatment ( $T_0$ ) and after 12 weeks of treatment ( $T_{12}$ ) with propiverine

Clinical symptoms (mean values of episodes)	Time	Daily dose [mg]			
		≤15 (n = 727)	≤30 (n = 1897)	≤45 (n = 1700)	>45 (n = 47)
Diurnal incontinence	$T_0$	1.8	3.4	4.3	5.5
	$T_{12}$	0.4	0.9	1.3	1.9
Nocturnal incontinence	$T_0$	1.4	1.1	1.5	2.4
	$T_{12}$	0.4	0.2	0.4	1.1
Diurnal urgency	$T_0$	6.7	9.7	10.1	9.3
	$T_{12}$	4.6	5.1	5.1	4.4
Nocturnal urgency	$T_0$	1.7	2.7	3.1	3.2
	$T_{12}$	0.6	0.9	1.0	0.6
Pollakiuria	$T_0$	7.2	9.1	9.6	9.5
	$T_{12}$	5.5	5.8	5.8	5.9
Nycturia	$T_0$	1.8	2.5	2.9	2.8
	$T_{12}$	0.7	1.0	1.1	0.9

### Diurnal and nocturnal urgency

Urge symptoms improved in the total population under treatment with propiverine by 4.5 diurnal episodes ( $T_0$ :  $9.5 \pm 4.8$ ,  $T_{12}$ :  $5.0 \pm 2.9$ ; 47 %) and by 1.9 nocturnal episodes ( $T_0$ :  $2.8 \pm 2.3$ ,  $T_{12}$ :  $0.9 \pm 1.1$ ; 67.9 %).

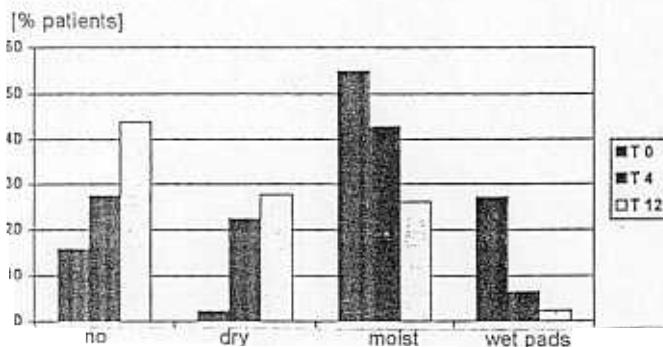
### Use of incontinence pads

A total of 2117 patients used incontinence pads prior to the start of the therapy. The consumption of incontinence pads correlates with the improvement in incontinence: 35.8 % of the patients had no or dry pads at the beginning, whereas this percentage rose to 78.4 % of the patients at the end of the observation period. The number of patients with moist pads reduced to half ( $T_0$ : 40.7 %,  $T_{12}$ : 20.5 %).

When the subpopulations are analyzed, this change becomes particularly clear. For example, 18.0 % of the patients with incontinence and urge symptoms used no pads or had dry pads at  $T_0$ , whereas this percentage increased to 71.3 % at  $T_{12}$  (Fig. 3). Results in a comparable order were achieved in patients with incontinence in neurological diseases ( $T_0$ : 5.3 %,  $T_{12}$ : 36.9 %).

Fig. 3:

Use of auxiliary materials in the 12-week course of therapy with propiverine (Mictonorm®/Mictonetten®) in incontinence and urge symptoms



## Urge score in the incontinence questionnaire according to Gaudenz

The therapeutic results of propiverine are reflected in the urge score according to Gaudenz which fell from 15.0 (T<sub>0</sub>) to 8.4 (T<sub>12</sub>) in the total population. This parameter was also clearly improved in patients with more distinct urge symptoms and thus a higher basis value, e. g. in the subpopulation incontinence and urge symptoms (T<sub>0</sub>: 17.1, T<sub>12</sub>: 9.4) as compared with the patients with incontinence with combined urge and stress symptoms (T<sub>0</sub>: 14.1, T<sub>12</sub>: 8.1).

## Subjective improvement in symptoms

After the first control date (T<sub>4</sub>), 88.2 % of patients treated with propiverine stated an improvement in clinical symptoms.

## Global assessment of effectiveness by physicians and patients

At the conclusion of the treatment (T<sub>12</sub>), the physicians classified the effectiveness as very good in 46.1 %, as good in 37.0 %, as satisfactory in 10.4 % and as inadequate in 6.5 % of the patients.

Almost in agreement with the above result, 46.7 % of the patients regarded propiverine as "very good", 36.0 % as "good" and 10.1 % as "sufficiently effective". 7.3 % of the patients classified the effectiveness as "inadequate".

## 2. Tolerance

### Vital parameters

The vital parameters systolic and diastolic blood pressure and heart rate remained clinically stable.

### Undesired drug actions

When the patients were questioned about symptoms such as dryness of the mouth or disturbance of accommodation prior to the beginning of the therapy with propiverine (T<sub>0</sub>), 18.1 % stated dryness of the mouth and 6.6 % stated disturbance of accommodation. 33.8 % of the patients stated dryness of the mouth at time T<sub>4</sub>. This percentage reduced to 26.0 % at time T<sub>12</sub>.

Disturbance of accommodation was stated by 11.4 % of the patients at time T<sub>4</sub>. Obstipation was given by 9.8 %. These phenomena reduced to 6.3 and 7.6 %, respectively, at the end of therapy.

At time T<sub>4</sub>, 9.1 % of the patients stated tiredness and 4.8 % vertigo. These symptoms reduced to 6.0 % and 2.8 %, respectively, at the end of therapy. As a rule, the severity of adverse reactions was mild and it further reduced with the duration of the therapy (Table 4).

In the subgroup  $\leq 16$  years (n = 602), 5.3 % stated a dryness of the mouth prior to the beginning of therapy (T<sub>0</sub>), 14.1 % and 11.2 % stated it under the therapy (T<sub>4</sub> and T<sub>12</sub>). 1.3 % stated disturbance of accommodation prior to the therapy (T<sub>0</sub>, n = 8) and 1.5 % at the end of documentation (T<sub>12</sub>, n = 9).

**Table 4:**  
Incidence and severity of anticholinergic adverse reactions after 4 (T<sub>4</sub>) and 12 weeks of treatment (T<sub>12</sub>) with propiverine

Adverse reaction [%]	Time	Severity		
		Mild	Moderate	Strong
Dryness of the mouth	T <sub>4</sub>	25.8	6.0	2.0
	T <sub>12</sub>	22.2	3.1	0.7
Disturbance of accommodation	T <sub>4</sub>	8.7	1.9	0.8
	T <sub>12</sub>	5.4	0.6	0.3
Obstipation	T <sub>4</sub>	8.6	0.9	0.2
	T <sub>12</sub>	7.0	0.5	0.1
Tiredness	T <sub>4</sub>	8.1	0.8	0.2
	T <sub>12</sub>	5.6	0.3	0.1
Vertigo	T <sub>4</sub>	3.7	0.8	0.3
	T <sub>12</sub>	2.4	0.3	0.1

### Residual urine

Residual urine was documented in 1863 patients (in most cases sonographically). In more than half of these patients (58.2 %), the volume of residual urine was ≤20 ml and was therefore clinically not significant. In the final measurement after the 12-week treatment period, in comparison with T<sub>0</sub> no change was documented in 72 % of the cases and a decrease in 22.8 %. An increase was seen in 5.1 % of the cases, levels between 100 and 200 ml were determined in 2 cases.

### Pretreatment of incontinence

A pretreatment with oxybutynin was stated by 142 patients (3.2 %), with trospium chloride by 156 patients (3.6 %) and with flavoxate, emepronium or desmopressin by 43, 14 and 28 patients, respectively. 10 patients had been treated with propiverine.

### Concomitant medication

During the 12-week treatment period, up to 4 concomitant medications were documented for 1410 patients. Preparations acting urologically and cardiovascularly came first (23.1 and 21.4 %, respectively).

## Dosage

In the total population, a daily dose of 30 mg propiverine was prescribed in 40.1 % of the patients and 45 mg in 38.4 % at the beginning of treatment. 21.5 % of the patients were treated with daily doses of <30 mg. The average daily dose was therefore  $33.9 \pm 12$  mg at  $T_0$  and  $29.4 \pm 11.9$  mg after 12 weeks.

The highest dosages were prescribed for the subgroup of the patients with incontinence in neurological diseases ( $T_0$ :  $39.4 \pm 12.3$  mg,  $T_{12}$ :  $38.8 \pm 12.4$  mg) and for patients with postoperative urge symptoms ( $T_0$ :  $41.2 \pm 7.9$  mg,  $T_{12}$ :  $33.7 \pm 11.1$  mg). In patients with urge symptoms without incontinence ( $T_0$ :  $34.3 \pm 9.9$  mg,  $T_{12}$ :  $28.8 \pm 10.6$  mg), lower dosages were used on average than in patients with incontinence and urge symptoms ( $T_0$ :  $37.2 \pm 9.9$  mg,  $T_{12}$ :  $32.0 \pm 10.2$  mg).

Apart from the indication, the dosage was analyzed by the severity of the clinical symptoms. Independent of the indication, pronounced symptoms were treated with higher dosages and lower degrees of severity were treated with lower daily doses (see Table 3).

## Discussion

The present data of the documentation of 4390 patients which accompanies the therapy substantiate the good effectiveness and tolerance of propiverine in urinary incontinence and urge symptoms in a patient population whose age distribution, demographic characteristics and spectrum of symptoms are to be regarded as representative of the clinical picture.

In most cases, even the careful anamnesis, clinico-uological routine examination and the voiding diary may lead to the diagnosis. In about 80 % of these patients, they may lead to an efficient conservative treatment. Subjectively, the success of therapy becomes obvious to the patients by way of the reduction in incontinence and voiding frequency as well as in urgency, particularly as these are the most essential problems from the patients' point of view. The documentation of application is in agreement with the clinical trials of propiverine in which the improvement in subjective symptoms correlates with the improvement in objective urodynamic parameters (increase in bladder capacity at the first and maximum desire to void, decrease in the detrusor pressure, increase in compliance) [4, 6, 7, 10]. The studies of the dose optimization for propiverine in particular show an improvement in symptoms in 70 % of the patients treated with a daily dose of 15 mg and in 80 % of the patients treated with a daily dose of 30 to 60 mg [6, 7]. Quantitatively, the results under propiverine are in agreement with those for oxybutynin and trospium chloride: When the effectiveness of these preparations was assessed, 46 % of the propiverine patients who regarded the drug as "very good" and 36 % who regarded it as "good" contrast with 34 and 36 % of the oxybutynin patients who regarded the drug as "very good" or "good", respectively, and 87 % of the trospium chloride patients who regarded the drug as "very good" or "good" [3, 5].

The results also show that the effect of propiverine is the stronger the more distinct the symptoms were prior to the beginning of therapy. As expected, this becomes apparent in the reduction in the urge score and is also in agreement with the results of clinical trials with propiverine in a comparable patient population [4].

The gradual differences in the response to the pharmacotherapy are of practical significance when subpopulations are comparatively analyzed: As expected, the improvement in urinary incontinence is, according to the pathomechanisms which can be influenced, more



pronounced in patients with incontinence and urge symptoms than in patients with incontinence with combined urge and stress symptoms which require an additional approach to treatment. These differences between the subpopulations are also reflected in the consumption of pads. The good effectiveness of propiverine and the low incidence rate of adverse reactions in the patient group  $\leq 16$  years are noticeable. A special analysis of these patients is under preparation for publication in another paper.

The total consumption of auxiliary materials which is reduced by half is remarkable: The number of patients without or with dry pads increased, whereas the percentage of wet or moist pads decreased. According to published computations of costs [12], a patient without pharmacotherapy needs to pay about DEM 35,- per week for pads and other auxiliary materials. If the patient achieves continence under the average prescribed dose of 1 coated tablet of Mictonorm<sup>®</sup> twice a day, he/she may save up to DEM 14,- per week or DEM 738,-. This economic aspect of a therapy with propiverine is remarkable and should be quantified in more detail in future studies.

It was an object of the present documentation to acquire adverse reactions under a therapy with propiverine which might have been unknown to date. It is therefore to be taken into account that for the assessment of tolerance the patients were directly questioned about anticholinergic symptoms (dryness of the mouth, disturbance of accommodation, obstipation, tiredness, vertigo) and other adverse reactions. Such a procedure always produces markedly higher incidence rates than an acquisition of symptoms about which patients complain merely spontaneously as trials of propiverine (rate of adverse reactions: 8.2 and 64.4 %) and oxybutynin (rate of adverse reactions: 31.2 and 63 %) show [3, 4, 7, 6, 10]. This is also confirmed by the present documentation of application in which even prior to the beginning of the documentation ( $T_0$ ) anticholinergic adverse reactions were reported for every fifth patient. In this context, account is also to be taken of the anticholinergic premedication in 365 patients (8.3 %), which may explain the incidence of dryness of the mouth and disturbance of accommodation even before the prescription of propiverine, as a wash-out phase is not obligatory for a documentation of application.

Despite the large number of the patient population, no adverse reactions which have so far been unknown were found. The incidence rates of dryness of the mouth and disturbance of accommodation are in practice lower than stated in clinical trials. In the documentation accompanying the therapy, tiredness, obstipation, vertigo, tachycardia, unrest, hyperthermia, and hypersensitivity were stated and were given as causes of the discontinuation of the therapy only rarely to very rarely, although they had been questioned directly.

It is shown both in clinically controlled trials [4] and long-term studies of propiverine [10] that the incidence rate and severity of adverse reactions decrease with increasing duration of therapy. The results of these studies are in agreement with the data of the documentation of the 12-week application. This may be attributed to a habituation effect. The alternative way of explanation, a selection effect, is not supported by the analysis of the patient data available for the entire period of documentation.

In the present documentation accompanying the therapy, no increase in residual urine was seen in most cases, being contrary to expectations: An increase in residual urine in a total of 5.1 % of the patients contrasts with a decrease in 22.8 %. This finding from the documentation of application is confirmed by clinical trials of propiverine [4] and of other anticholinergics [2] on patients with urodynamically established detrusor hyperactivity or hypersensitivity. By contrast, a clinical trial of propiverine on patients with reflex incontinence shows an increase in residual urine [8]. Consequently, the residual urine should be consistently checked throughout the course of therapy in patients with reflex incontinence or organogenic intravesical obstruction.

Globally, tolerance was regarded as "very good" by 41.8 % of the patients and as "good" by 45.0 %. This is comparable to the results of the clinically controlled trial of propiverine [6] and documentations of trospium chloride application over 28 days and of oxybutynin application over 3 months. However, the number of patients who discontinued the therapy for adverse reactions was in comparison with propiverine higher under oxybutynin for the same period of documentation and was higher under trospium chloride for a substantially shorter observation period [3, 5].

The dosage of propiverine in practice generally complied with the recommendations. But it clearly reflects a prescription according to the clinical severity of the symptoms, with a clear tendency towards the prescription of higher dosages for pronounced symptoms at the beginning of therapy. In addition, a tendency towards a dose reduction in the course of therapy can be seen, which is accompanied by the improvement in clinical symptoms.

The therapeutic application of propiverine shows four tendencies:

- When the drug is used for a prolonged time, an increasing improvement becomes apparent, although physicians tend to reduce the dose when they continue the therapy.
- The incidence and severity of adverse reactions decrease with increasing duration of therapy.
- Contrary to expectations, the residual urine does generally not increase.
- The dosages are adapted to the diagnosis and the severity of symptoms.

Altogether, the results of a treatment with propiverine (Mictonorm<sup>®</sup>/Mictonetten<sup>®</sup>) under practical conditions prove its good effectiveness and tolerance. The reduced consumption of incontinence pads underlines that the pharmacotherapy in the treatment of urinary incontinence is an indispensable part of a comprehensive therapy concept and also plays an important role under economic aspects.

## **Upshot for the practice**

The effectiveness of propiverine (Mictonorm<sup>®</sup>/Mictonetten<sup>®</sup>) was documented under practical conditions in 4390 patients with incontinence and urge symptoms, incontinence with combined urge and stress symptoms, incontinence in neurological diseases, urge symptoms without urinary incontinence, diurnal and/or nocturnal incontinence in patients  $\leq 16$  years as well as in patients with postoperative urge symptoms. The present results of a 12-week treatment period cover about 1100 patient years and broaden the therapeutic experiences with propiverine to more than 260,000 patient years since the launch on the market in 1981. They prove that physicians determine the dosage of propiverine in dependence on the indication and severity of the symptoms.

Of importance are the phamaco-economically significant results in terms of the reduction of auxiliary materials which are documented for a very large patient population for the first time.

In the multi-stage therapy of urinary incontinence accompanied by urge symptoms, drug therapy in addition to a behaviour therapy with bladder and toilet training and electrostimulation is recommended for the first treatment phase. Due to its dual mode of action, propiverine conforms to the pharmacological principle of action demanded of a modern bladder spasmolytic.

The potential of propiverine as both an effective and a well-tolerated drug for the treatment of urge symptoms with or without urinary incontinence could be confirmed without limitation in the present practice-related documentation accompanying the therapy and underlines the good benefit-risk ratio known from clinical trials.

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