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NEUROGENIC DETRUSOR OVERACTIVITY: A METAANALYSIS OF THE EFFICACY AND TOLERABILITY OF ORAL PHARMACOTHERAPY

Aims of Study

To evaluate the efficacy and tolerability of those four compounds with anticholinergic or mixed mode of actions, which are considered to be effective in detrusor overactivity, especially in neurogenic detrusor overactivity by the International Consultation on Incontinence[(1)]. A comparative metaanalysis of oxybutynin (oxy.), propiverine (prop.), tolterodine (tolt.) and trospium chloride (trosp.) will be presented.

Methods

The references were scrutinized for randomized clinical trials in patients with neurogenic detrusor overactivity. In the 6 studies[(2–7)] identified to meet the criteria oxy. was involved with 3, prop. with 2, tolt. with 1, trosp. with 3 treatment groups. This metaanalysis is focused on the change in max. cystometric bladder capacity and max.detrusor pressure as primary, residual urine and compliance as secondary outcome measures, despite the varying outcomes addressed in the studies presented. In terms of tolerability the incidence of adverse events and the incidence of dry mouth were evaluated.

Results

Altogether 393 patients (age 14 – 77 ys) were included, the treatment periods were either 2 or 3 weeks. The overall results are presented in table 1.

Table 1:

Compound (dosage in mg)		**Oxy. 3 x 5**	**Oxy. 3 x 5**	**Oxy. 3 x 5**	**Prop. 3 x 15**	**Prop. 3 x 15**	**Tolt. 2 x 2**	**Trosp. 2 x 20**	**Trosp. 2 x 20**	**Trosp. 2 x 20**
References		**Stöhrer** 2002[(7)]	**Maders-Bacher** 1995[(3)]	Osca-Garcia 1997[(4)]	**Stöhrer** 2002[(7)]	**Stöhrer** 1999[(6)]	**Kerre-broeck** 1998[(2)]	**Maders-Bacher 1995**[(3)]	Osca-Garcia 1997[(4)]	**Stöhrer** 1991[(5)]
n		61	43	31	70	53	18	52	36	29
Max. cystometric bladder capacitay (ml)	pre post **diff**.	164 298 **+134.7**	188 351 **+166**	239 335 **+107**	198 309 **+110**	262 366 **+104**	159 221 **+62**	215 312 **+96.6**	243 326 **+79**	missing data **+138**
Detrusor pressure (cm H_2O)	pre post **diff.**	69 43 **-25.6**	82 44 **-38**	69 34 **-35**	57 38 **-19**	81 54 **-27**	missing data	82 53 **-38**	86 41 **-35.8**	missing data **-38**
Compliance (ml / cm H_2O)	pre post **diff.**	13 38 **+25**	60 78 **+18**	Missing data	11 23 **+12**	17 22 **+5**	29 37 **+8**	75 93 **+18**	Missing data	missing data **+12**
Residal urine (ml)	pre post **diff.**	65 149 **+84**	48 154 **+106**	Un-changed	73 141 **+68**	50 87 **+37**	25 41 **+16**	49 128 **+79**	Un-change d	missing data **+15**

Subjective outcomes were only scarcely reported: Stöhrer[(5)] mentioned increased micturition intervals, detailed results on micturition frequency and leakage episodes are only reported in the prop. study by Stöhrer[(7)] and in the tolt. study by van Keerebroeck[(2)]. Incidence rates of adverse events, even with the same compound, show a wide range (50 – 94%). This is also true for the incidence rates for dryness of mouth (17 – 67%), see table 2.

Table 2:

Compound (dosage in mg)	**Oxy. 3 x 5**	**Oxy. 3 x 5**	**Oxy. 3 x 5**	**Prop. 3 x 15**	**Prop. 3 x 15**	**Tolt. 2 x 2**	**Trosp. 2 x 20**	**Trosp. 2 x 20**	**Trosp. 2 x 20**
References	Stöhrer 2002[7]	**Maders-bacher** 1995[3]	**Osca-Garcia** 1997[4]	Stöhrer 2002[7]	Stöhrer 1999[6]	Kerre-broeck 1998[2]	**Maders-bacher** 1995[3]	**Osca-Garcia** 1997[4]	Stöhrer 1991[5]
Incidence total (%)	77.8	m.d.*	94.3	63	m.d.*	50	m. d.*	64.5	Extremly low
Dry mouth (%)	67	56	58.3	47	37	17	54	29	
Methodology	prompted	prompted	prompted	prompted	prompted	spont. rep. ** ?	prompted	prompted	spont. rep.**

* m.d. = missing data
** spont. rep. = spontaneous reporting

Conclusions

The max. cystometric bladder capacity was increased through all four drugs. However, the effect was not only dependent on the drug applied, but also influenced by the baseline values, respectively: the effect was more pronounced with an initially small bladder capacity. The mean decrease in detrusor pressure amplitude varied from 19 to 38 cm H_20 corresponding to an decrease between 33% and 46%. Only the tolt. study[2] did not report contractility outcomes. In the other five studies[3,4,5,6,7] detrusor contractility, a risk factor for upper urinary tract damages, decreased, and the pathologic compliance was shifted to normal values. No study reports on the percentage of patients achieving continence. In further studies, crucial clinical parameters should be included (e.g. continence) to emphasize the benefit of pharmacotherapy with regard to the quality of life. Incidence rates of adverse events, dryness of the mouth especially, seemed to depend on the drug and dosage applied as well as on the method of evaluation: reports of adverse events, prompted by questioning, were more frequent than spontaneous reports of adverse events.

References

[1] Andersson et al., 2001
[2] van Kerrebroeck et al., 1998
[3] Madersbacher et al., 1995
[4] Osca-Garcia et al., 1997
[5] Stöhrer et al., 1991
[6] Stöhrer et al., 1999
[7] Stöhrer et al., 2002