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FLEXIBLY ADDING OXYBUTYNIN ON THE FIRST ANTIMUSCARINICS IN PATIENTS WITH REFRACTORY OVERACTIVE BLADDER – THERAPEUTIC EFFECTS AND COMPLICATIONS

Hypothesis / aims of study

To evaluate the effect of add-on oxybutynin ER in patients with overactive bladder (OAB) who were refractory to monotherapy with the first muscarinic antagonist.

Study design, materials and methods

A total of 143 patients with refractory OAB were included in a prospective, open label protocol. Inclusion criteria were persistent symptoms after behaviour therapy and an optimized dose of one antimuscarinic agent (Solifenacin 5 mg or Tolterodine 4 mg) for at least 3 months. Patients with neurogenic diseases were excluded from this study. Oxybutynin ER 5 mg to 15 mg once daily was added-on flexibly and escalated every month depending on patient's report of therapeutic effectiveness and tolerability to the adverse events. At the baseline, 4 and 12 weeks after oxybutynin ER adding-on, we assessed International Prostate Symptom Score (IPSS), Overactive Bladder Symptom Score (OABSS), Patient Perception of Bladder Condition (PPBC), the Urgency Severity Scale (USS) questionnaires, uroflowmetry and postvoid residual (PVR). The therapeutic effect was considered as successful if there was a reduction of PPBC of 2 from baseline and a reduction of USS of 1 from baseline, or the USS value was 0 at 12 weeks. The adverse events and tolerability of this combined therapy were also assessed.

Results

The mean age of patients was 75.5 ± 9.6 years (range 48-93). Of them, 102 patients were male and 41 were female. Compared with baseline, total IPSS, IPSS storage subscore, quality of life, OABSS, USS and PPBC were significantly decreased at 4 and 12 weeks. The changes of IPSS voiding subscore, peak urinary flow rate and voided volume were comparable during the follow-up. PVR was significantly increased at 4 weeks (62 ± 59 v 91 ± 77 mL, $p<0.05$) and 12 weeks (62 ± 59 v 104 ± 84 mL, $p< 0.001$) (Table 1). Twenty-one (35.6%) patients reported successful therapeutic effect at 12 weeks. Thirty-two (22.4%) and 35 (24.5%) patients withdrew from the study at 4 weeks and 12 weeks respectively. Dry mouth (45.8%) was the most common adverse event. Acute urinary retention was only noted in one patient (Table 2).

Interpretation of results

Monotherapy with antimuscarinic medication may not be sufficient to achieve satisfactory therapeutic results for OAB patients. Our results demonstrated that flexible adding-on a second antimuscarinic agent could effectively improve OAB symptoms without jeopardizing the voiding symptoms. The reasons for the enhanced efficacy may be due to synergistic activation of different muscarinic receptors or interaction of receptors on different parts of the bladder wall. Although increase of PVR and dry mouth are two major concerns, a combination of two different antimuscarinic agents may be worth considering for these specific patients before seeking more invasive intervention.

Concluding message

Flexibly adding-on a second antimuscarinic agent is an effective treatment in one third of patients with OAB refractory to the first antimuscarinic treatment.

Table 1. The changes of symptom scores and urofow parameters at baseline and after adding on the second animuscarinic agent

	Baseline (N=143)	1 M (N=109)	2M (N=54)	3M (N=59)
IPSS-E	7.51±5.50	6.38±5.29*	6.54±5.02	5.90±4.82
IPSS-S	8.54±3.30	8.51±3.19**	5.63±3.54**	5.25±3.57**
IPSS-T	16.04±7.23	12.55±6.78**	12.17±6.78*	11.15±7.45*
QoL	4.20±1.12	2.87±1.18**	2.61±1.04**	2.71±1.37**
OABSS	8.39±3.39	6.67±3.40**	5.89±3.56**	5.97±3.90*
USS	3.46±0.86	2.96±1.15**	3.02±1.12*	2.97±1.05*
PPBC	4.63±1.37	3.01±1.52**	2.61±1.51**	2.78±1.76**
Qmax	12.30±7.41	11.67±7.10	13.00±8.23	11.41±6.49
Volded vol.	159.70±102.05	176.53±123.74*	189.53±117.18	176.31±124.92
PVR	62.39±59.38	91.44±76.95*	106.76±80.46*	103.95±84.46**
CBC	220.75±122.03	266.22±150.76*	288.82±141.69*	267.41±158.35*

Table 2. Adverse events

	1M (N=109)	2M (N=54)	3M (N=59)
None	40 (36.7%)	18 (33.3%)	16 (27.1%)
UTI	2 (1.8%)	-	-
AUR	1 (0.9%)	-	-
Dry mouth	37 (33.9%)	21 (38.9%)	27 (45.8%)
Constipation	6 (5.5%)	3 (5.6%)	2 (3.4%)
Dizziness	1 (0.9%)	1 (1.9%)	-
Dysuria	5 (4.6%)	1 (1.9%)	-
Dry mouth + Dizziness	1 (0.9%)	-	1 (1.7%)
Dry mouth + Constipation	12 (11%)	7 (13%)	11 (18.6%)
Dry mouth + Dysuria	1 (0.9%)	-	-
Dry mouth + UTI	1 (0.9%)	1 (1.9%)	1 (1.7%)
Dry mouth + Blurred vision	2 (1.8%)	2 (3.7%)	1 (1.7%)

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