11A

Joachim Misselwitz[1], Ulrike John[1], Tytti Tamminen-Möbius[2], Hildegard Lax-Gross[2], Herbert Hirche[2], Jan D. van Gool[3], Tom P.V.M. de Jong[3], Pauline Winkler-Seinstra[3], Rien M. Nijman[4], Marijke Vlasblom[4], Piet Hoebeke[5], Johan Vande Walle[5]—on behalf of the European Bladder Dysfunction Study. Grant: EEC Biomed I CT94-1006.

[3]*Pediatric Renal Center, University Children's Hospital, PO Box 85090, NL-3508 AB Utrecht, The Netherlands <jd.vangool@ibm.net>*

OXYBUTYNINE-HCl VERSUS PLACEBO IN CHILDREN WITH URODYNAMICALLY PROVEN URGE SYNDROME—A PLACEBO-CONTROLLED STUDY

Background. Based upon a few open studies on efficacy and safety, and on experience from treatment of children with neuropathic bladder-sphincter dysfunction, oxybutynine-HCl, is widely used to combat detrusor overactivity in neurologically normal children with urge syndrome. However, prospective and placebo-controlled studies on oxybutynine-HCl are lacking for the pediatric age group, and there are no solid data on pharmacokinetics or safety of oxybutynine-HCl in pediatric patients.
In Branch I of the European Bladder Dysfunction Study (EBDS), children with urodynamically proven urge syndrome (detrusor overactivity during filling of the bladder) are randomly allocated to either bladder rehabilitation with biofeedback or pharmacotherapy. In planning the EBDS, this pharmacotherapy module was designed as a double blinded placebo-controlled part of Branch I. In the EBDS, the randomly allocated treatment modules are interventions, added to a uniform package of standard therapy assigned to every recruited child at enrollment.

Methods. Pharmacotherapy is double blinded, either oxybutynine-HCl or placebo, 0.3 mg/kg bodyweight per day, prescribed as syrup. Stratified randomization for pharmacotherapy automatically generates the code numbers for the medication, which correspond to 2 as yet undisclosed categories: 'Pharmacotherapy I' and 'Pharmacotherapy II'.
Standardized bladder rehabilitation with biofeedback has urine flowrate/EMG recordings displayed on-line on a personal computer as biofeedback, and consists of at least 12 sessions of 3 hours each.
Outcome is assessed with a clinical as well as a urodynamic score, and investigations for both scores are performed before and after the 6-month treatment period; follow up thereafter covers 1 year.
Clinical scores are obtained with a questionnaire on voiding and wetting, voiding diaries, follow-up notes, post-void residuals, and the incidence of urinary tract infections. The urodynamic score is derived from detrusor activity, pelvic floor activity, and cystometric bladder capacity.

Results. Since mid-1995, 97 children have been enrolled in Branch I of the EBDS. Clinical results for the 64 children who passed the 6-month follow-up mark are tabulated below, in the categories 'cured', 'same' and 'worse'; 33 children still are being followed, about 10 for each of the 3 groups in Branch I.

Clinical outcome EBDS Branch I, urge syndrome

	cured	same	worse	
Biofeedback	**9** (39%)	**11** (48%)	**3** (13%)	23
Pharmacotherapy I	**14** (70%)	**5** (25%)	**1** (5%)	20
Pharmacotherapy II	**9** (43%)	**11** (52%)	**1** (5%)	21
Total at T12	**32** (50%)	**27** (42%)	**5** (8%)	64

With the χ^2-test (Mantel-Haenszel), there is no statistically significant difference in outcome between pharmacotherapy I and pharmacotherapy II. Even the difference in outcome between pharmacotherapy I and biofeedback is statististically not significant. However, at this stage numbers are critical, and we have to wait for the results of the 20 patients on pharmacotherapy still being followed, before we can conclude that oxybutynine-HCl has no significant effect on urge syndrome in neurologically normal children. The final urodynamic outcome is not yet available for comparison with the clinical outcome: all urodynamic studies currently are being reviewed, blindly, by a panel.

[1]Dept of Pediatric Nephrology, University Children's Hospital Jussuf Ibrahim, D-07740 Jena, Germany
[2]Institute for Medical Informatics, Biometry and Epidemiology, D-45122 Essen, Germany
[4]Dept of Pediatric Urology, Erasmus University, NL-3000 LL Rotterdam, The Netherlands
[5]Pediatric Renal Centre, Ghent University Hospital, B-9000 Ghent, Belgium

11B

Jan D. van Gool[1], Tom P.V.M. de Jong[1], Pauline Winkler-Seinstra[1], Tytti Tamminen-Möbius[2], Hildegard Lax-Gross[2], Herbert Hirche[2], Rien M. Nijman[3], Marijke Vlasblom[3], Piet Hoebeke[4], Johan Vande Walle[4], Kelm Hjälmås[5], Anna-Lena Hellström[5], Hansjörg Bachmann[6], Kathrin Heilenkötter[6], Joachim Misselwitz[7], Ulrike John[7]—on behalf of the European Bladder Dysfunction Study. Grant: EEC Biomed I CT94-1006.

Pediatric Renal Center, University Children's Hospital, PO Box 85090, NL-3508 AB Utrecht, The Netherlands <jd.vangool@ibm.net>

A COMPARISON OF STANDARD THERAPY, BLADDER REHABILITATION WITH BIOFEEDBACK, AND PHARMACOTHERAPY IN CHILDREN WITH NON-NEUROPATHIC BLADDER-SPHINCTER DYSFUNCTION

Background. The European Bladder Dysfunction Study (EBDS) is a multi-center prospective study, comparing treatment plans for neurologically normal children with bladder-sphincter dysfunction. In Branch I of the EBDS, children with urodynamically proven urge syndrome (detrusor overactivity during filling of the bladder) are randomly allocated to either bladder rehabilitation with biofeedback or pharmacotherapy. In Branch II, children with urodynamically proven dysfunctional voiding (pelvic floor overactivity during voiding) are randomly allocated to either standard therapy or bladder rehabilitation with biofeedback. In both Branches, all children receive standard textbook therapy, with the randomly allocated EBDS treatment plans added as interventions, on an out-patient basis.
Outcome is assessed with a clinical as well as a urodynamic score, and investigations for both scores are performed before and after the 6-month treatment period; follow up thereafter covers 1 year.
Methods. Clinical scores are obtained with a questionnaire on voiding and wetting, voiding diaries, follow-up notes, post-void residuals and the incidence of urinary tract infections.
Urodynamic studies consist of continuous registration of bladder pressure, abdominal pressure, pelvic floor electromyogram (EMG), and urine flowrate, during at least 2 cycles of filling and emptying of the bladder. The urodynamic score is derived from detrusor activity, pelvic floor activity, and cystometric bladder capacity.
Standard therapy consists of low-dose chemoprophylaxis and treatment of constipation whenever indicated, complemented with elaborately standardized sets for explanation of the bladder-sphincter dysfunction problem and for instructions how to cope with it. There are separate sets for Branch I and Branch II.
Pharmacotherapy is double blinded, either oxybutynine-HCl or placebo, 0.3 mg/kg bodyweight per day.
Standardized bladder rehabilitation with biofeedback has urine flowrate/EMG recordings displayed on-line on a personal computer as biofeedback, and consists of at least 12 sessions of 3 hours each.

Results. Since mid-1995, 216 children have been enrolled in the EBDS, 97 in Branch I, 104 in Branch II, and 15 with non-groupable bladder-sphincter dysfunction. Clinical results for the children who passed the the 6-month follow-up mark are tabulated below, for Branch I and Branch II, in the categories 'cured', 'same' and 'worse'.

Clinical outcome Branch I (64 patients, 33 still in follow up)

	cured	same	worse	
Biofeedback	**9** (39%)	**11** (48%)	**3** (13%)	23
Pharmacotherapy	**23** (56%)	**16** (39%)	**2** (5%)	41
Total at T12	**32** (50%)	**27** (42%)	**5** (8%)	64

Clinical outcome Branch II (59 patients, 45 still in follow up)

	cured	same	worse	
Biofeedback	**20** (59%)	**12** (35%)	**2** (6%)	34
Standard therapy	**18** (72%)	**6** (24%)	**1** (4%)	25
Total at T12	**38** (64%)	**18** (31)	**3** (5%)	59

With the χ^2-test (Mantel-Haenszel), no statistically significant differences in outcome emerge between bladder rehabilitation and pharmacotherapy in Branch I, neither between the outcome of standard therapy and bladder rehabilitation in Branch II. This overall conclusion will not change when the patients still being followed pass their 12-months follow-up marks.
This conclusion strongly supports the hypothesis that the EBDS module for standard therapy contains the key for success. Adding pharmacotherapy or bladder rehabilitation with biofeedback does not significantly improve the outcome. With standard therapy alone, approximately 65% of neurologically normal children with bladder-sphincter dysfunction can be cured.

[2]Institute for Medical Informatics, Biometry and Epidemiology, D-45122 Essen, Germany
[3]Dept of Pediatric Urology, Erasmus University, NL-3000 LL Rotterdam, The Netherlands
[4]Pediatric Renal Centre, Ghent University Hospital, B-9000 Ghent, Belgium
[5]Dept of Pediatric Urology, Östra Barnsjukhuset, SE-41695, Sweden
[6]Dept of Pediatrics, Zentralkrankenhaus Links der Weser, D-28277 Bremen, Germany
[7]Dept of Pediatric Nephrology, University Children's Hospital Jussuf Ibrahim, D-07740 Jena, Germany

12

P.F. Austin, Y.L. Homsy, A.J. Casale, M.P. Cain, R.C. Rink

Riley Children's Hospital, Indiana University, Indianapolis, IN, and University of South Florida, Tampa, FL, USA

ALPHA-ADRENERGIC BLOCKADE IN CHILDREN WITH VOIDING DYSFUNCTION

Aims of Study: Inadequate bladder emptying is a common urinary dysfunction encountered in children and the therapeutic benefits of alpha blockers on lower urinary tract symptoms in adults with bladder outlet obstruction are well established. Because of the promising impact of alpha blocker therapy, the aim of this study was to investigate the potential benefits of selective alpha blocker therapy to improve bladder emptying in the pediatric population.
Methods: Twenty children with documented poor bladder emptying ranging from 3 to 15 years of age (mean 8 y.o.) were treated with the alpha-1 adrenergic receptor antagonist doxazosin. Poor bladder emptying was documented by post void residual (PVR) measurements, symptomatology, as well as by demonstration of new hydronephrosis on ultrasound. All patients were initially placed on 0.5-1.0 mg of doxazosin nightly and followed weekly or monthly with PVR measurements and ultrasonography. Maximum urinary flow rates were