

IS THE PLACEBO EFFECT OF ANTICHOLINERGICS RELATED TO THE PELVIC FLOOR?

Hypothesis / aims of study

The treatment of overactive bladder has a placebo effect. It is unknown what causes this. It has been suggested that this may be caused by a bladder retraining effect from using urinary diaries. However this still does not inform us about the mechanism of action of this effect. The two mechanisms which have been suggested are central inhibition of involuntary detrusor contractions or the detrusor contractions occurring and the symptoms being controlled by the patient by contracting the levator ani and closing the bladder and terminating symptoms of urgency and leakage. This prospective study assesses the placebo response and how it is related to the opening detrusor pressure which is an indirect measure of urethral outlet resistance and levator ani function. If the placebo effect is caused by the pelvic floor and local control of symptoms then a higher opening pressure should be related to the patients who get the strongest placebo effect.

Study design, materials and methods

This study was prospective, multi-centred and double-blinded trial of placebo against an active comparator. Women with overactive bladder symptoms were recruited and underwent conventional urodynamic studies. Opening and closing detrusor pressures as well as detrusor pressure at maximum flow were measured. The women recorded the number of incontinence episodes, number of micturition episodes and volume of micturition prior to commencement of treatment, at four weeks and following 12 weeks of treatment with placebo using urinary diaries. Women also completed the Kings Health Questionnaire prior to and on completion of treatment. The difference in micturition volume was recorded and the women were stratified into responders, if they showed an increase in micturition volume after treatment, or non-responders if they showed no change or a decrease in micturition volume. The women were also assessed on the change in domain scores on the basis of completion of the Kings Health Questionnaire.

Results

197 women with overactive bladder symptoms were recruited. Of these 97 (49.2%) were found to have detrusor overactivity (DO) and 100 (50.8%) had normal urodynamic studies (NUDS). Women with DO had a mean opening detrusor pressure of 30.7 (sd: 22.0), women with NUDS has a mean opening detrusor pressure of 39.2 (sd: 28.1).

Eighty four women were treated with placebo. Seventy nine women recorded micturition volumes pre- and post-treatment. There were 24 responders (30.4%) who reported decreased micturition volume with a mean of -15.8ml (sd: 12.6) per void and 55 women (69.6%) reported an increased or unchanged micturition volume with a mean of 30.0ml (sd: 25.9). The women with decreased mean micturition volume had a mean opening detrusor pressure of 28.6 cmH₂O (sd: 23.8) and those with increased mean micturition volume had a mean opening detrusor pressure of 44.1 cmH₂O (sd: 32.0). This difference was statistically significant ($p < 0.05$ Mann Whitney U).

Regarding the Kings Health Questionnaire results, patients with increased micturition volumes (responders) had statistically significantly lower scores in severity scale, incontinence impact and physical limitations, after treatment with placebo. ($p < 0.05$ Mann Whitney U). The patients with increased micturition volumes also had statistically significant scores for severity scale when compared to those with decreased micturition volumes.

Interpretation of results

Symptoms of overactive bladder do not reliably determine whether detrusor overactivity is demonstrated on conventional urodynamic studies. Women with DO tend to have higher opening detrusor pressures than women who have a stable detrusor on urodynamics. This may indicate increased urethral outlet resistance relating to increased levator ani activity and thus the woman may be able to contract the levator ani to control symptoms of urgency. This would be particularly important during urodynamics leading to a negative (stable) test. Approximately 70% of women when treated with a placebo will report improvement in their symptoms and micturition volumes. Those that responded to the placebo treatment had statistically significantly higher opening detrusor pressures compared to those that did not. This suggests that the placebo effect is moderated by urethral outlet sphincter activity such as from the levator ani and urethral sphincter.

Concluding message

A symptomatic response to placebo occurs in the majority of women with overactive bladder symptoms. Those who respond to placebo treatment, have increased opening detrusor pressures compared with those who do not have a

placebo response. The placebo response appears to be a locally derived mechanism related to the outlet resistance rather than a centrally driven suppression of involuntary detrusor activity.

References

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HUMAN SUBJECTS: This study was approved by the St. Marys LREC and followed the Declaration of Helsinki Informed consent was obtained from the patients.