

TREATING OAB WITH ANTIBIOTICS

Hypothesis / aims of study

The aim of this study was to measure the outcomes of a treatment model for OAB that incorporated the use of antibiotics with antimuscarinics for protracted periods.

A growing body of evidence identifies a group of patients who, despite presenting with negative routine urinalyses, appear to have an infection, or an inflammatory process, lying at the heart of the aetiology of their overactive bladder (OAB) symptoms. This seems to apply to about 50% of patients presenting with OAB.

The microscopic, non-dipstick, detection of pyuria ≥ 10 wbc ul^{-1} has proved to be the best surrogate marker of urinary infection available, superior to dipsticks and to routine MSU culture (1). This raised the implication that patients, with OAB symptoms, but manifesting microscopic pyuria, despite negative urine culture, should be treated with antibiotics as an adjunct to antimuscarinics and bladder retraining.

Cognisant of this, a new treatment model for OAB has been evolved over ten years (1993 to 2003). By trial and error, using pyuria, symptom responses, and patient views, a process akin to evolutionary cultural Darwinism produced a protocol incorporating antibiotic prescription, over periods of between six and nine months, achieving successful resolution of symptoms. Any new treatment should be tested definitively by randomised control trial (RCT). Given the protracted treatment courses necessary, such a study whilst feasible, would be expensive. It is usual in such circumstances to conduct a proof of concept study prior to seeking the substantial investment necessary for the RCT.

This abstract presents the data obtained from such an early phase study.

Study design, materials and methods

The treatment model was evaluated in an observational cohort study of 440 patients conducted from 2003 to 2010. Group 1 (n=147) had OAB & pyuria and were treated with antibiotics (primarily Nitrofurantoin or Cephalexin), in addition to antimuscarinics and bladder retraining. Group 2 (n=212) had OAB, no pyuria and received only antimuscarinics and bladder retraining. Group 3 (n=81) had OAB but manifested pyuria late at subsequent follow-up at which point antibiotics were commenced. Treatment response was monitored by urge scores, 24-hour frequency and incontinence, and time taken to symptom resolution and pyuria clearance, where appropriate. This study had greater than 80% power to detect a clinically significant difference ($\alpha = 0.05$).

Results

There were 380 females and 60 males (mean age=54, sd=18) equally distributed between groups. At presentation 75% of group 1, 88% of group 2 and 85% of group 3 were MSU culture negative. There was a significant improvement in all symptoms and in all groups over the treatment period ($F=59$, $p<.0001$).

Group 3, prescribed antibiotics late, took significantly longer to recover (95%CI 198-321 days) compared to group 1 (95%CI 165-229 days). ($F=8$, $p<.001$). The late introduction of antibiotics was followed by significant symptom improvement (95% CI diff daily frequency= 0.75 to 3.5 $p=.002$). Group 2, always without pyuria, recovered the fastest (95%CI 138-180 days).

Figure 1 illustrates these data: There are three disparate groups; each group was treated differently based on presentation; **given** the different treatments, the groups improved similarly.

Interpretation of results

These data come from open observational work and must be viewed as provisional. Patients treated with antibiotics clearly improved. Antibiotic efficacy, if present, would be expected to achieve a recovery narrative with similar characteristics to non infected OAB patients, treated only with antimuscarinics. This is true for the overwhelming majority of open, observational studies of effective, novel treatment methods. The key question is would group 1 have followed the same path without antibiotics? Differential efficacy can only be measured by a RCT, which is now justified and no extravagance.

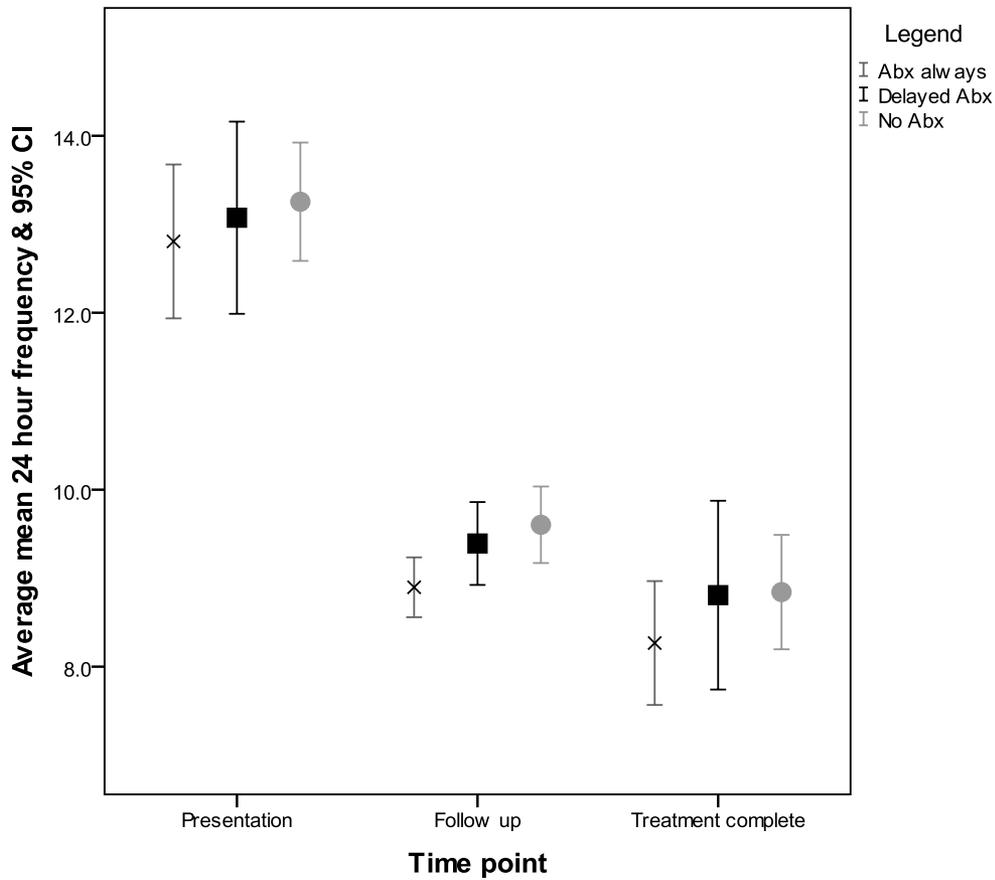
Important circumstantial evidence of antibiotic efficacy was demonstrated by clearance of pyuria in group 1. The effects of introducing antibiotics late into group 3, followed by strong evidence of a response, favours efficacy. Infection as a significant disease complication is implied by the shorter time-course of treatment in group 2

Concluding message

The data are strong justification for a large-scale randomised, placebo controlled trial of antibiotic use in patients with OAB, pyuria, but negative urine culture.

Figure 1

Response to treatment - 24 hour frequency



References

1. J.Urol., 17-3-2010, 183; 1843, 1847.

Specify source of funding or grant	None
Is this a clinical trial?	No
What were the subjects in the study?	HUMAN
Was this study approved by an ethics committee?	Yes
Specify Name of Ethics Committee	This work was conducted with approval from the Whittington and Moorefield's Research Ethical Committee, London.
Was the Declaration of Helsinki followed?	Yes
Was informed consent obtained from the patients?	Yes