140

Authors: K J Kreder
Institution: University of Iowa

Title: CLINICAL EFFECTIVENESS OF ANTIMUSCARINIC THERAPY: THE RELATIONSHIP BETWEEN EFFICACY AND TOLERABILITY

Aims of Study:

The aim of this study was to examine the relationship of efficacy and tolerability of tolterodine immediate release (IR) and tolterodine extended release (ER) and to calculate the clinical effectiveness of these two formulations.

Methods:

Data from a double blind randomized, placebo controlled, multinational, multi-center trial was used for this analysis [1]. 1529 patients with overactive bladder (all with incontinence, 80% female, 47% naïve to drug therapy) were randomized into 3 groups (placebo: 508; tolterodine IR: 514; Tolterodine ER: 507) and treated for 12 weeks. Efficacy was measured as percentage reduction in incontinence episodes from baseline to study end and tolerability was assessed as degree of dry mouth at 12 weeks (none, mild, moderate or severe). Different levels of optimal efficacy were defined as 33%, 50%, 67% or 75% reduction in incontinence episodes and different levels of tolerability were defined as any dry mouth or moderate/severe dry mouth. The data was then subdivided into 4 groups of increasing utility based on efficacy and dry mouth: sub-optimal efficacy with dry mouth; sub-optimal efficacy with no dry mouth; optimal efficacy with dry mouth; optimal efficacy with no dry mouth. Clinical effectiveness was defined as efficacy multiplied by tolerability and computed as follows:

Median % reduction in incontinence episodes x % patients without dry mouth.

Results:

The reduction in incontinence episodes was 71% for tolterodine ER, 60% for tolterodine IR and 33% for placebo (tolterodine ER versus placebo: $p<0.001$, versus IR: $p<0.05$). The dry mouth rate (any severity) for these groups was 23%, 30% and 8% respectively (tolterodine ER versus IR: $p<0.02$). Moderate to severe dry mouth rates were being 8.9%, 12.1% and 1.6% respectively.

The table shows the statistical significance related to any combination of efficacy/tolerability cut-off and for each pair the pattern of distribution for the different utility groups is similar to that shown in the figure. As can be seen from the figure, the distributional shift from IR to ER results in a reduction in the worst utility category and an increase in the best utility category.

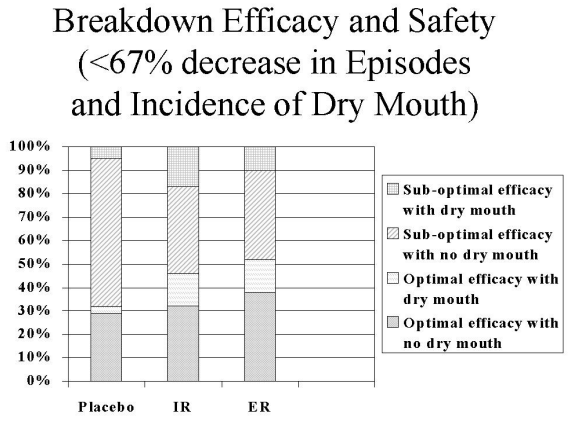
The clinical effectiveness for tolterodine IR was 42% and for ER was 55% indicating that the extended release formulation has 31% more clinical effectiveness.

Conclusions:

These analyses allow response to therapy to be examined for efficacy and tolerability in combination. The superior therapeutic benefit of the extended release formulation is observed not only in enhanced efficacy but also in increased tolerability. Clinical effectiveness, as it is a single measure, can be used to easily compare different formulations and may have a role in comparing antimuscarinic drugs for clinical utility.

References :

1.Van Kerrebroeck et al, Urology 2001;57:414-21



Efficacy cut-off	Any dry mouth		Moderate/severe dry mouth	
Reductions	*Chi-square*	*Probability*	*Chi-square*	*Probability*
33%	121.261	0.001	81.511	0.001
50%	126.791	0.001	89.968	0.001
67%	129.392	0.001	91.212	0.001
75%	130.246	0.001	94.061	0.001

Source of Funding : Pharmacia Corporation