European Urology

European Urology 48 (2005) 5–26

Review—Overactive Bladder

The Effects of Antimuscarinic Treatments in Overactive Bladder: A Systematic Review and Meta-Analysis

Christopher Chapple[a,*], Vik Khullar[b], Zahava Gabriel[c], Julie Ann Dooley[d]

[a]*Sheffield Teaching Hospitals NHS Trust, Royal Hallamshire Hospital, Urology Research, J Floor Office, Glossop Road, Sheffield, S102JF, UK*
[b]*Imperial College, St Mary's Hospital, London, W2 1PG, UK*
[c]*Heron Evidence Development Ltd, UK*
[d]*Pfizer Ltd, UK*

Accepted 24 February 2005

Available online 22 March 2005

Abstract

Objectives: To evaluate the tolerability, safety and efficacy of antimuscarinic drugs used to treat overactive bladder and to identify any differences between individual antimuscarinics.

Methods: Medline, Embase, CCTR and Cinahl databases were searched for published RCTs including an antimuscarinic agent from 1966 to August 2004. Data from included trials were extracted and meta-analysed where possible.

Results: Fifty-six trials were included. The antimuscarinics were found to be safe and efficacious. All antimuscarinics apart from oxybutynin IR were found to be well tolerated. Dry mouth was the most commonly reported adverse event and no drug was associated with an increase in any serious adverse event. There were significant differences between the antimuscarinics in rates of withdrawal and rates and range of adverse events and efficacy outcomes.

Conclusions: The antimuscarinics have different tolerability and safety profiles, which are clinically significant.
© 2005 Elsevier B.V. All rights reserved.

Keywords: Antimuscarinic; Overactive bladder; Detrusor overactivity; Incontinence; Systematic review; Meta-analysis

Abbreviations: (A), trial published in abstract form only; AE, any adverse event; ANMF, the number of patients achieving normal micturition frequency; ASAE, any serious adverse event; BOO, bladder outlet obstruction; CCT, Controlled Clinical Trial; CCTR, Cochrane Controlled Trials Register; CI, confidence interval; CIE, mean change in incontinence episodes per 24 hours; CM, mean change in the number of micturitions per 24 hours; CUE, mean change in the number of urgency episodes per 24 hours; CVV, mean change in volume voided per micturition; dar, darifenacin; DO, detrusor overactivity; ER, extended release; ICI, International Consultation on Incontinence; ICS, International Continence Society; IIQ, Incontinence Impact Questionnaire; IR, immediate release; ITT, intention to treat; IUGA, International Urogynaecological Association; KHQ, King's Health Questionnaire; LUTD, lower urinary tract disease; LUT, lower urinary tract; MI, mixed incontinence; *n*, number of patients included in the analysis; NR, not reported; OAB, overactive bladder; OBJECT, Overactive Bladder: Judging Effective Control and Treatment; OPERA, Overactive Bladder: Performance of Extended Release Agents; oxy, oxybutynin; P, placebo; PP, per protocol; pro, propiverine; PRO, patient reported outcome; QoL, quality of life; RC, the number of patients returned to continence; RCT, randomised controlled trial; RR, relative risk ratio; SF-36, Short-form 36; SF-12, Short-form 12; SIU, Societé Internationale d'Urologie; sol, solifenacin; SUI, stress urinary incontinence; (t), titrated dose; (t 5), titrated from 5 mg/day; (t 7.5), titrated from 7.5 mg/day; (t 15), titrated from 15 mg/day; TDS, transdermal system; tol, tolterodine; tro, trospium; UDI, Urogenital Distress Inventory; UI, urinary incontinence; UTI, urinary tract infection; UUI, urge urinary incontinence; VAS, visual analog scale; WMD, weighted mean difference; WOCN, Wound Ostomy Continence Nurses' Society; (X), trial was of cross-over design.

* Corresponding author. Tel. +44 114 2712559; Fax: +44 114 2798318.
E-mail address: c.r.chapple@sheffield.ac.uk (C. Chapple).

0302-2838/$ – see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.eururo.2005.02.024

ELSEVIER

1. Introduction

Overactive bladder (OAB), otherwise known as the urgency frequency syndrome, is a symptom complex defined by the International Continence Society (ICS) as 'urgency, with or without urge incontinence, usually with frequency and nocturia' [1]. This is distinct from the urodynamic diagnosis of detrusor overactivity (DO), which refers to an involuntary rise in detrusor pressure during filling of the bladder in a laboratory situation in a conscious co-operative patient [1].

Non-surgical treatment is the mainstay of therapy for OAB and available options include bladder training, biofeedback, medication, and a combination of these options. The principal pharmacological treatment utilised to improve the symptoms of OAB is based on muscarinic receptor antagonism (antimuscarinics). To date no proof of concept studies for other oral pharmaco-therapeutic mechanisms have shown any significant efficacy. The mode of action of antimuscarinics, traditionally considered to be on muscarinic receptors lying within the detrusor muscle, has become increasingly controversial. At licensed doses, antimuscarinic treatments do not inhibit the normal voiding phase of the micturition cycle, whilst they do alter bladder sensation during filling as evidenced by an improvement in filling symptoms (urgency, frequency, nocturia and incontinence) and bladder capacity. This has led to a recent hypothesis suggesting that antimuscarinic treatments may act via other mechanisms related to the afferent as opposed to the efferent system.

This systematic review was carried out to assess the safety, tolerability and efficacy of antimuscarinic treatments for OAB and DO. Further objectives of the review were to: (1) consider the effects of antimuscarinics on outcomes such as quality of life (QoL), which are important to patients and (2) assess whether there are differences between individual antimuscarinic drugs that are currently being used to treat OAB. These objectives were included to address criticism of a previous Cochrane review of pharmacological therapies for OAB [2].

The Cochrane review was criticised because the cover statement and conclusions do not appear to reflect the results of the review [3–5]. In particular, the outcome measures reported by Herbison and colleagues were 'not necessarily the most pertinent outcomes to patients with OAB' [6]. Although important factors such as QoL were mentioned in the review, these were not explored further in any detail. To address this criticism, we have analysed all reported QoL data in included trials and carried out meta-analyses of these data where possible. These analyses are described in detail in a separate publication [42].

In addition, the Cochrane review did not attempt to differentiate between individual antimuscarinic drugs. The authors chose to 'lump' the drugs together and evaluate the effects of the class, rather than to 'split' the drugs and assess any variation in effect between drugs. Due to the heterogeneity evident in the meta-analyses of some outcomes such as withdrawals and adverse events it was suggested that the drugs might have different profiles, yet potential differences were not explored further. In addition, a number of active controlled trials that have attempted to differentiate between OAB treatments have been published, but these were not evaluated by Herbison and colleagues [2]. In order to assess whether there are differences between individual antimuscarinic drugs, our methodology was distinctly different from that employed in the Cochrane review. We included active controlled trials in addition to placebo controlled trials and reviewed individual antimuscarinic drugs compared with either placebo or active controls. Our meta-analyses adopted a 'splitting' approach in order to assess any variation in effect between drugs.

2. Methods

2.1. Searching

Databases and conference proceedings were searched. Medline, Embase, CCTR and Cinahl databases were searched from 1966 up to August 31st 2004. The following conference proceedings were hand-searched: American Urological Association (1983–2004), International Continence Society (ICS) (1975–2004), European Association of Urology (1990–2004), International Urogynaecological Association (IUGA) (1999–2004), International Consultation on Incontinence (ICI) (1998–2004), Societé Internationale d'Urologie (SIU) (2002) and Wound Ostomy Continence Nurses' Society (WOCN) (2004). There were no restrictions by language of publication, and bi-lingual medical review professionals translated non-English language publications.

A rigorous process was followed to minimise the risk of overlooking a publication. A team of reviewers independently determined the eligibility of each publication by applying a set of criteria (Table 1). Two different reviewers considered every publication and discrepancies were resolved through discussion. Cited references from included trials and reviews of similar trials were also searched. Many studies were reported in more than one publication and data from all such publications were included.

2.2. Data extraction

Reviewers extracted data from eligible publications in parallel. MS Access® was used to store extracted data and identify possible analyses. A third reviewer checked the resulting extractions and the team resolved any discrepancies.

2.3. Outcome measures

The primary outcome measures of the review were '*total withdrawals*' and '*any adverse event*'. These outcomes, together with secondary outcomes, are shown in Table 2.

Download English Version:

https://daneshyari.com/en/article/9320347

Download Persian Version:

https://daneshyari.com/article/9320347

Daneshyari.com