European Association of Urology – press release

Concern over high US prescribing levels of common drug linked to dementia

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A new analysis raises concern over high prescription rates in the USA of a common drug used to treat overactive bladder. The drug, oxybutynin, when taken orally, is consistently linked with cognitive impairment and dementia in the elderly. The analysis shows that oxybutynin, is prescribed in more than a quarter of cases of overactive bladder (27.3%), even though other more suitable drugs are available. This work is presented at the European Association of Urology conference in London, where concerns are also being expressed about the lack of funded alternatives to oxybutynin in Europe.

Overactive bladder (OAB) is extremely common in persons over 65. Initial treatment is normally via behavioural modifications, which can then be followed by first-line medical treatment such as antimuscarinic medications, including oxybutynin. Antimuscarinic drugs are synthetic compounds, originally derived from mushrooms, which block the activity of the muscarinic acetylcholine receptor. They have several uses, including control of OAB. Oxybutynin is the least expensive antimuscarinic used for OAB, and so tends to be the drug of choice for health care plans such as Medicare. However, a body of evidence has shown that oxybutynin is linked to greater cognitive decline in the elderly [ref1].

An international group of clinicians, led by Dr Daniel Pucheril (Vattikuti Urology Insitute, Henry Ford Hospital, Detroit), looked at evidence from the National Ambulatory Medical Care Survey, where 1,968 patients had received antimuscarinic medications. They found that oxybutynin was prescribed to 27.3% of patients aged over 65 receiving a new antimuscarinic prescription for OAB. Additionally, despite the United States Food and Drug Administration recommendation that patients starting oxybutynin be closely monitored for adverse central nervous system side effects, the authors found that only 9% of elderly persons received a neurologic exam at the time of drug prescription. (Ref 2 – see PDF FDA Label)

Around 16% of US adults suffer from overactive bladder [ref2], which translates into tens of millions of sufferers in the US.

According to Dr Pucheril, "*We looked at a representative sample, but when you extrapolate to the US population the figures are huge. We estimate that over the six years of our analysis, 47 million individuals in the USA were taking various types of antimuscarinic drugs for OAB, with around 55% of new prescriptions going to the over 65's.*

After lifestyle modifications, antimuscarinic medications constitute the most common first line therapies. In the United States, the majority of elderly persons are insured by Medicare. Medicare insurance plans have often have tiered medication formularies to minimize drug expenses. Oxybutynin is the least expensive antimuscarinic drug available, but its pharmacologic properties may cause significant cognitive side effects in elderly persons. Despite evidence of these side effects, physicians are not commonly checking for cognitive effects in those using these medications".

Dr Pucheril continued "*We're not saying that everyone should change from oxybutynin to another drug – it still has its uses, and coming off the drug without medical supervision is not recommended. Nevertheless, doctors need to look closely at the levels of prescribing. More than anything else, the funding bodies have to make it easier for doctors to prescribe newer antimuscarinics which are much less likely to cause cognitive dysfunction".*

Commenting, on the European situation, Professor Helmut Madsbacher (Innsbruck) said:

"This new work from the US highlights a more general problem which also exists here in Europe. In Europe, oxybutynin use varies from country to country. What we find is that where a range of antimuscarinic drugs is funded, as for example happens in Germany, Austria and Switzerland, then oxybutynin use is low, at around 5% to 7%, for obvious reasons. However, in some countries only oxybutynin is funded, and this creates a problem. For example, the only antimuscarinic funded by Italian health Authorities is oxybutynin, and this leads to some areas with around 70% of antimuscarinic prescriptions being oxybutynin".

Professor Andrea Tubaro (Sapienza Università, Roma) added:

"If an alternative drug is not funded by the health system then it becomes too expensive for a patient to buy themselves. In Italy generic oxybutynin costs around €5/month, but someone wishing to pay for a different antimuscarin or an up-to-date alternative such as a beta3 agonist will end up paying around €50/month. Even in strictly economic terms, there's no sense in saving a few Euros on a drug which risks worsening dementia, one of the most costly conditions which medicine can treat. This is a problem in Italy, but funders in all countries really need to support the use of a range of drugs".

Ref 1 See *JAMA Intern Med*. 2015;175(3):401-407. doi:10.1001/jamainternmed.2014.7663

Ref 2 http://emedicine.medscape.com/article/459502-overview#a2

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Notes for Editors

PLEASE MENTION THE EUROPEAN ASSOCIATION OF UROLOGY CONGRESS IN ANY STORY RESULTING FROM THIS PRESS RELEASE

The 32nd European Association of Urology conference takes place in London from 24th to 28th March. This is the largest and most important urology congress in Europe, with up to 13,000 expected to attend. Conference website http://eau17.uroweb.org/

Contact details

Dr Daniel Pucheril dpucheril@gmail.com

Prof. Helmut Madersbacher helmut.madersbacher@tirol-kliniken.at

Prof. Andrea Tubaro andrea.tubaro@mac.com

EAU Press Officer, Tom Parkhill: tom@parkhill.it telephone +39 349 238 8191

How has this work been reviewed? This work has not gone through a journal peer-review process. This work is amongst the top-rated 150 abstracts (out of 1171 accepted from around 5000 submissions) from the EAU congress. It was reviewed for suitability and accuracy by members of the EAU communications group at more than one stage in development, and subsequently reviewed by a specialist in the field on behalf of the EAU.

ABSTRACT No. 533 Antimuscarinic use in the elderly: A poisoned apple

Meyer, C.[1], Pucheril, D.[2], Karabon, P.[2], Gild, P.[1], Von Landenberg, N.[1], Atiemo, H.[2], Menon, M.[2], Chughtai, B.[3], Fisch, M.[4], Chun, F.[4], Trinh, Q-D.[1]. [1]Brigham and Women's Hospital, Harvard Medical School, Division of Urological Surgery and Center For, Division of Urologic Surgery and Center For Surgery and Public Health, Boston, United States of America, [2]Henry Ford Health System, VUI Center for Outcomes Research, Analytics and Evaluation, Vattikuti Urology Institute, Detroit, United States of America, [3]Weil Cornell Medical College/New York Presbyterian Hospital, Dept. of Urology, New York, United States of America, [4]University Medical Center Hamburg-Eppendorf, Dept. of Urology, Hamburg, Germany

Introduction & Objectives

Overactive bladder (OAB) is characterized by urinary urgency, frequency, nocturia, and urinary incontinence (UI). The prevalence of OAB increases significantly with age. The first-line therapy for OAB is antimuscarinic medication, some of which have deleterious side-effects, including cognitive decline. We sought to examine the incidence and prevalence of antimuscarinic prescriptions among elderly persons ≥ age 65.

Material & Methods

The 2006-12 National Ambulatory Medical Care Survey (NAMCS) were queried for patients with newly given or renewed prescriptions for any of 6 antimuscarinics: oxybutynin, tolterodine, fesoterodine, darifenacin, solifenacin, and trospium. Within these cohorts, frequencies of patient/physician attributes and annual trends in drug prescription were determined utilizing drug-mention weighting methodology.

Results

A weighted estimate of 47.68 million individuals (unweighted n=1,968) had their antimuscarinics renewed, and 12.77 million patients (unweighted n=641) received a new prescription (Table 1). The majority of new antimuscarinics were prescribed in elderly (≥ age 65) (55.2%), female (69.2%), white (61.7%), and Medicare insured (84.1%) individuals. Oxybutynin was a frequently prescribed (incidence 27.3%) and continued (prevalence 33.2 %) antimuscarinic among elderly patients. In 2010, there was a sharp decrease in the number of all continued antimuscarinic prescriptions, followed by annual increases in oxybutynin continuation versus continued decline in other antimuscarinic continuation (Figure 1). Figure 1: Continued Antimuscarinic Prescriptions in Patients > 65 Years of Age, NAMCS 2006-2012.

Conclusions

We found alarmingly high prescription rates of oxybutynin (27.3%), pharmacologically the least suitable antimuscarinic, for which studies have consistently demonstrated higher rates of cognitive impairment in the elderly. Frequent oxybutynin prescription is likely driven by tiered Medicare formularies which require patients to trial oxybutynin, a cheaper, generic antimuscarinic, before allowing access to newer, more costly yet safer, antimuscarinics. This work is the first population-based study demonstrating both the alarming rate of oxybutynin prescription and the lack of a proper safety net for a growing and vulnerable elderly population. Our work demands an increased consideration of the possible deleterious effects of unmonitored antimuscarinic use in elderly patients.

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