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RESPONSE TO DAVID NACE AND PAUL DRINKA

To the Editor: We appreciate the thoughtful comments of Drs. Nace and Drinka concerning our article.[1,2] They highlighted our definitions of clinical and strict urinary tract infection (UTI) and concluded that, by using the clinical definition, it is not possible to infer any benefit from cranberry capsules in the prevention of UTI.

We agree that, for many studies, the appropriate criterion standard for diagnosing UTI is detection of the pathogen in the presence of clinical symptoms. A less-rigorous definition can easily lead to overdiagnosis and false conclusions, but residents in long-term care facilities (LTCF) are a vulnerable population, mostly with severe cognitive impairment, multiple chronic comorbidities, functional disabilities, and urinary incontinence. Signs and symptoms of UTI are frequently absent,[3] and differentiating asymptomatic from symptomatic UTI in older persons with dementia is difficult and challenging.[4,5] The use of the criterion standard for diagnosing UTI is not suitable for LTCF residents and would lead to substantial underdiagnosis. As a result, there is no criterion standard in diagnosing UTI in LTCF populations, and most clinical criteria to ascertain UTI in LTCF residents are based on consensus.[6–8]

To make research in real-world LTCF populations possible, we have chosen a clinical UTI definition. Our clinical definition is a broad and practical definition, following clinical practice guidelines for LTCF residents[9,10] and based on the experience of the elderly care physician and nursing staff, which is consistent with a previous study.[5] Experienced staff can achieve even better diagnostic precision than urine culture.[11] There is also recent evidence that micturition-related signs and symptoms are predictive of UTI.[4] Although our clinical definition is different from the strict definition, it closely reflects clinical care in LTCF and adds knowledge to practice guidelines to assist physicians in making decisions. Moreover, our cost-effectiveness analysis showed the relevance of our clinical definition, because clinical UTIs were followed by a significant deterioration in quality of life, survival, care dependency, and costs.[12]

Our study concludes that, for elderly LTCF residents with high UTI risk, taking cranberry capsules twice daily results in a lower incidence of clinical UTI. In daily practice, prevention with cranberry will also reduce antibiotic prescription, including inappropriate prescriptions.

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REVIEWING THE SAFETY OF LORATADINE FOR ELDERLY ADULTS: A POTENTIAL SHORTCOMING OF THE 2012 BEERS CRITERIA

To the Editor: Anticholinergic drugs produce a variety of adverse effects, including dry mouth and eyes, constipation, blurred vision, rapid heart rate, dizziness, sedation, confusion, delirium, hallucinations, and cognitive impairment.[1,2] Furthermore, anticholinergic toxicity has been reported as a common problem in elderly adults, and anticholinergic drug use is closely associated with serious negative outcomes in this population, such as risk of falls, behavioral symptoms (including agitation), and high mortality.[1,2] Anticholinergic drugs are often mentioned in explicit criteria for inappropriate medication use in older adults, such as the Beers criteria.[1,3] In 2012, the American Geriatrics Society revised these criteria and included loratadine on the list of potentially inappropriate medication for elderly adults owing to its strong anticholinergic properties; these drugs were to be avoided in cases of lower urinary tract symptoms, benign prostatic hyperplasia, chronic constipation, and cognitive impairment and delirium.[3]

Loratadine is a second-generation H1 antihistamine, as are levocabastine, azelastine, bilastine, desloratadine, ebastine, cetirizine, fexofenadine, levocetirizine, and rupatadine; the characteristics of second-generation H1 antihistamines make them more effective and safer than first-generation H1 antihistamines (e.g., diphenhydramine, hydroxyzine, promethazine, clemastine, triprolidine). Moreover, first-generation H1 antihistamines are associated with undesirable sedation and anticholinergic side effects.[4–6] Under the umbrella term "sedation" is a range of conditions including somnolence, impaired concentration, and poor learning ability.[5] Central nervous system (CNS) and cardiac toxicity have been the most serious adverse effects associated with H1 antihistamines. Cardiac toxicity is rare but is of considerable concern because of the associated risk of death. CNS toxicity produced by first-generation H1 antihistamines is widespread, but even during the years when first-generation H1 antihistamines were widely used, case reports of cardiac toxicity were uncommon, and epidemiological studies involving large sample sizes identified only a few cases of H1 antihistamine–associated ventricular arrhythmias.[7] Thereafter, several second-generation H1 antihistamines, the use of which was devoid of any associated cardiac toxicity and significant CNS toxicity,[5,7] became the H1 antihistamines of choice.[7]

Loratadine is considered a nonsedating antihistamine. At recommended doses (10 mg/d), no significant differences between loratadine and placebo for any measure of cognitive or psychomotor performance, mood, or sedation were observed.[5,6] In contrast, other performance studies that used higher doses of loratadine (20 and 40 mg) showed significant performance impairment and sedation in some tests (e.g., choice reaction time, adaptive tracking, digit-symbol substitution) in comparison with placebo.[5] In light of the evidence demonstrating its safety, the inclusion of loratadine in the list of potentially inappropriate medications solely on the basis of the studies that the 2012 revised Beers criteria reference is not justified. Those three studies, which the American Geriatrics Society cited,[8–10] do not provide any evidence of loratadine being an antihistamine with strong anticholinergic properties. One of these studies[9] gave loratadine 2 points on the Anticholinergic Risk Scale, indicating that it entails intermediate risk; another study[8] gave loratadine 0 points, which means that it has no known anticholinergic properties. Moreover, a recent systematic review of anticholinergic risk scales in older adults[1] did not mention that loratadine has strong anticholinergic properties or the potential for serious adverse effects in elderly adults. That review[1] cited two of the three studies that the 2012 Beers criteria referenced;[8,9] the third study,[10] also used as a reference by the American Geriatrics Society, was not included in the systematic review, probably because it was a narrative review that did not provide any evidence of loratadine possessing strong anticholinergic properties.

That review[1] has great clinical implications because the summarized studies describe different drugs with anticholinergic properties. Although this study was not a systematic review of randomized clinical trials, the data can be applied to clinical practice. The findings of this review provide insights into a broad issue that could have not been addressed through clinical trials. The finding that loratadine is safe for elderly adults is of great consequence to health professionals concerned with providing treatment for people of this age group. In addition, it highlights a probable shortcoming of the Beers criteria, which are currently used as a basis for supporting prescription for elderly adults.[3]

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