that was not captured by the claims processing system. In the context of this apparent limitation, the authors report a significant finding: in each of the 4 years from 1997 through 2000, 10% to 11% of the pool of patients with a diagnosis of acne in their medical claims history received oral isotretinoin. The results of this study would have been more useful to other researchers if days of therapy had been reported in addition to prescription counts.³²

■ JMCP Subject Review—1995 through 2002

The JMCP Article Index by Subject Category that appears in this issue of the *Journal* was created to provide a better perspective on the pioneering work of researchers and authors in areas specific to managed care pharmacy. Sometimes, authors fail to research the work of others that has been published previously. This subject review for all articles in JMCP, from its inaugural issue in July/August 1995 through the May/June 2002 issue, should make some of this preceding work more readily identifiable for future authors. All of these articles are accessible for review and downloading from the AMCP Web site at www.amcp.org. This JMCP Article Index is also intended to provide guidance for students, faculty members, and researchers in the investigation of subjects of interest to managed care pharmacy.

■ The Search for Better Antipsychotics Continues

Marshall et al., in this issue of the *Journal*, found the incidence and relative risk of tardive dyskinesia (TD) to be similar among users of conventional antipsychotics and users of the newer (atypical) antipsychotics.³³ While the authors did not specifically study the relative risk of extrapyramidal syndromes (EPS) among the users of antipsychotics, they suggested that olanzapine may have a lower risk of EPS compared to risperidone. In fact, the matter is quite controversial.

Chlorpromazine was the first prescription antipsychotic agent and has been used since the late 1950s. Middle-aged adult patients with known psychiatric diseases over 10 years or more are most likely not antipsychotic-naïve. One potential risk factor, (which this study and many studies do not address) is the previous exposure to traditional antipsychotic agents and whether this contributes to predisposition to EPS or TD when an atypical antipsychotic trial is attempted subsequently. An antipsychotic-naïve patient with a first exposure to an atypical antipsychotic agent might have a decreased risk for EPS or TD due to less exposure and lower dose.

While little comparative data exist, some authors have ranked the newer antipsychotic drugs according to risk of EPS such as dystonia, pseudoparkinsonism, akathisia, or tardive dyskinesia. The apparent order of EPS risk is clozapine<quetiapine<olanzapine=ziprasidone.³⁴ At higher doses, risperidone is ranked with a higher EPS risk than olanzapine and ziprasidone, but its risk of EPS is apparently lower with lower doses. The search for antipsychotic agents devoid of EPS risk continues. Only clozapine, and perhaps quetiapine, appear to significantly reduce the risk of EPS.

In Veterans Affairs Cooperative Study 394 of 158 patients, the severity of tardive dyskinesia (TD) and EPS was found to be predicted by their respective baseline severity scores. Lower doses of antipsychotic drugs and coincidental use of anticholinergic drugs were also found to be predictors of a relatively favorable course of TD. The authors concluded that the outcomes of TD and EPS in patients with persistent TD can, in fact, be influenced by clinicians.³⁵ Collectively, the work by Marshall et al. and the results from VA Cooperative Study 394 suggest that TD and EPS can be managed but not completely avoided at this time. As antipsychotic agents become more selective and targeted to specific receptors and areas in the brain, the risk of EPS and TD in the future will continue to decrease and hopefully be eliminated.

Frederic R. Curtiss, PhD, RPh, CEBS, Editor-in-Chief

Janice Hoffman, Pharm.D, Clinical Pharmacy Manager, WellPoint Pharmacy Management, contributed to the observations regarding antipsychotic drugs.

Timothy L. Brenner, PharmD, Assistant Professor, University of Arizona, College of Pharmacy, contributed to the subject review on pharmacogenomics.

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