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Pharmacists' role in clozapine therapy at a Veterans Affairs medical center

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Abstract: A program in which pharmacists have an active role in prescribing and dispensing psychoactive drugs is described.

The Department of Veterans Affairs (VA) has established a National Clozapine Coordinating Center (NCCC) that must approve all clozapine therapy in VA medical centers. Clinical and demographic information is required for all new patients, and weekly status reports are required throughout clozapine therapy. To comply with NCCC requirements, pharmacists with specialized training in psychopharmacology organized a clozapine clinic at one VA medical center, in conjunction with the psychiatry service. The pharmacists screen potential candidates for clozapine therapy and forward the required information to the NCCC for approval. During treatment, they ensure that necessary laboratory tests and clinical evaluations are performed for inpatients and recommend dosage adjustments to the psychiatry residents. The pharmacists see outpatients receiving clozapine weekly to monitor and record vital signs, laboratory results, and response to therapy and make dosage adjustments accordingly. For both inpatients and outpatients, the pharmacists send weekly patient evaluations to the NCCC.

Pharmacists at a VA medical center provide direct care to patients receiving clozapine and help their institution comply with the stringent therapy-monitoring requirements of the NCCC.

Index terms: Administration; Ambulatory care; Clozapine; Department of Veterans Affairs; Dosage; Pharmacists, hospital; Pharmacy, institutional, hospital; Tests, laboratory; Toxicity; Tranquilizers
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Clozapine is considered a breakthrough in the treatment of schizophrenia.[1] It was released in Europe in 1972, but a high frequency of agranulocytosis associated with the drug (2%) delayed approval for marketing in the United States until September 1989.[2] This approval came with prescribing and dispensing restrictions never before imposed by a manufacturer. The manufacturer, Sandoz, requires all prescribers and patients to be registered with the Clozaril National Registry, which requires weekly monitoring of each patient's white blood cell (WBC) count and limits medication dispensing to a one-week supply.[3] The registry permits community and hospital pharmacies to dispense clozapine only upon the pharmacist's verification that the WBC count is within acceptable limits. The Department of Veterans Affairs (VA) requires that patients receiving clozapine through its facilities have weekly monitoring of the WBC count and differential, vital signs, and adverse effects.[4] This complicated process requires the cooperation and coordinated efforts of the patient, physician, laboratory, and pharmacy. Some pharmacists in our institution have specialized training in psychiatry and have acquired clinical privileges that allow them to prescribe psychotropic medications and order laboratory tests.[5] We describe how these pharmacists provide the clinical

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care necessary to meet all the requirements of clozapine therapy.

Practice site

The VA medical center in San Diego is a 450-bed teaching hospital associated with the University of California Medical School at San Diego. The pharmacy department employs 21 inpatient and 11 outpatient and ambulatory-clinic pharmacists.

The psychiatry service comprises 101 total beds: 15 intensive care, 44 acute care, 28 alcohol or drug treatment, and 14 research beds. The mental health ambulatory-care clinic handles approximately 35,000 visits per year. There are two full-time pharmacists and one half-time pharmacist designated as psychiatry clinical pharmacy specialists. The primary function of these specialists is to provide comprehensive care to the psychiatric inpatient and ambulatory-care areas. The specialists also help educate psychiatry residents; medical, pharmacy, and nursing students; and permanent members of the psychiatry staff. All three specialists have the doctor of pharmacy degree and have completed a one-year general hospital pharmacy residency program (two completed an ASHP-accredited program). Although none has completed a specialized psychiatry residency, all three pharmacists have clinical experience in psychiatry (2, 6, and 20 years).

VA program for clozapine monitoring

In 1991 the VA developed its own clozapine monitoring program and received approval from Sandoz to dispense clozapine. The VA Central Office established a National Clozapine Coordinating Center (NCCC). Physicians at the NCCC review each clozapine candidate's file before granting approval for use and review weekly tracking sheets that report patient status. Each VA medical center is required to establish a clozapine treatment team, headed by the chief of the psychiatry service and including representatives from the psychiatry, pharmacy, laboratory, medicine, and nursing services. The clozapine treatment team reviews new applications for clozapine use and provides clinical and demographic information for all new patients to the NCCC.

The NCCC requires that each hospital have a computerized clozapine prescription lockout system. The lockout system ties the hospital's laboratory database to the outpatient pharmacy dispensing software. The program will allow clozapine prescriptions to be processed only when WBC counts are within the defined limits. At our institution, the lockout system prevents the filling of any clozapine prescription if the computer notices three consecutive drops in the WBC count. Only the psychiatry clinical pharmacy specialists and the chief of psychiatry are authorized to override the lockout.

The NCCC guidelines require extensive patient evaluation and documentation. To receive clozapine, a patient must have undergone trials with two different neuroleptics and either failed to derive therapeutic benefit or experienced a significant adverse reaction. A complete physical examination, including laboratory testing and electrocardiographic analysis, is required. According to the NCCC, contraindications to clozapine therapy include a seizure history, cardiac disease, pregnancy, pre-existing leukopenia, a history of hematologic reactions to drugs, or a lymphoproliferative disorder. The NCCC also recommends that clozapine not be used in patients who, because of social situation, substance abuse, or other factors, cannot be relied upon to keep follow-up appointments.

Pharmacists' duties

Psychiatry residents at our facility rotate to other hospitals monthly; this creates concerns about continuity of patient care and follow-up. The psychiatry clinical pharmacy specialists coordinate the education of residents on the screening and physical-examination requirements for clozapine evaluation. As a member of the clozapine treatment team, the pharmacist screens potential candidates before they undergo extensive evaluation. The screening involves reviewing the patient's case with the requesting practitioner, reviewing the patient's file, and interviewing the patient to ensure that the patient and family members are committed to weekly blood tests and follow-up. This screening ensures that the physician does not waste time evaluating patients who are ineligible for clozapine therapy. After the physician completes the evaluation, the pharmacist reviews the documentation with the rest of the clozapine treatment team. After a patient has been determined eligible for clozapine therapy, the pharmacist forwards all pertinent information to the NCCC. After NCCC approval, the pharmacist enrolls the patient into the hospital's clozapine tracking system, and clozapine therapy is begun.

Role in inpatient care. Because of the severity of their illness, most patients are hospitalized when their current neuroleptic is withdrawn and clozapine is added. During the patient's hospitalization, the pharmacist ensures that the psychiatry resident orders the necessary laboratory tests, performs the required clinical evaluation, and documents the results in a weekly tracking sheet, which the pharmacist forwards to the NCCC. The pharmacist meets with the patient many times during the hospitalization to assess adverse effects and monitor target symptoms to gauge response. In addition, the pharmacist acts as a consultant to the psychiatry resident by suggesting dosage adjustments and treatment of any adverse effects.

Role in outpatient clinic. At our facility, the care of outpatients receiving clozapine therapy is provided directly by pharmacists, under the supervision of a physician. All outpatients in the clozapine prescription program are seen by a psychiatry clinical pharmacy specialist weekly, as required by the NCCC. Patients are monitored for agranulocytosis, sedation, hypotension, tachycardia,

sialorrhea, seizures, constipation, hyperthermia, weight gain, and other adverse effects. In addition, the pharmacist monitors and records vital signs, psychiatric target symptoms, laboratory results, and response to therapy. The pharmacist adjusts the clozapine dosage as necessary and treats serious adverse effects after consulting with a psychiatrist. Once the pharmacist and psychiatrist have selected a drug regimen for treating the adverse effects, the pharmacist makes routine dosage adjustments. After each weekly follow-up appointment, the pharmacist faxes a tracking sheet containing an evaluation of the patient to the NCCC and places the original document in the patient's medical record.

Conclusion

Pharmacists working with patients receiving clozapine at a VA medical center provide direct patient care and help the institution comply with the stringent therapy-monitoring requirements of the NCCC.

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Stability of aztreonam and ampicillin sodium–sulbactam sodium in 0.9% sodium chloride injection

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Abstract: The stability of aztreonam, ampicillin sodium, and sulbactam sodium admixed in 0.9% sodium chloride injection and stored at room temperature and under refrigeration was studied.

Each of the following admixtures was prepared in 0.9% sodium chloride injection: (1) aztreonam 10 mg/mL; (2) ampicillin 20 mg/mL (as the sodium salt) and sulbactam 10 mg/mL (as the sodium salt); and (3) aztreonam 10 mg/mL, ampicillin 20 mg/mL, and sulbactam 10 mg/mL. Three minibags of each admixture were stored at room temperature and three were refrigerated. Every 12 hours, up to 96 hours, the admixtures were visually inspected and 5-mL samples were withdrawn for high-performance liquid chromatography and pH testing.

No color change or precipitation was observed in any sample. In admixtures containing ampicillin, ampicillin was the first or only drug to lose more than 10% of initial concentration. In the ampicillin–sulbactam admixture, ampicillin was stable for 32 hours at room temperature and 68 hours refrigerated. In the aztreonam–ampicillin–sulbactam admixture, ampicillin was stable for 30 hours at room temperature and 94 hours refrigerated.

Aztreonam 10 mg/mL, ampicillin 20 mg/mL (as the sodium salt), and sulbactam 10 mg/mL (as the sodium salt) in 0.9% sodium chloride injection were stable in combination for up to 30 hours at room temperature and 94 hours under refrigeration.

Index terms: Additives; Ampicillin sodium; Antibiotics; Aztreonam; Dosage forms; Incompatibilities; Penicillins; Sodium chloride; Stability; Storage; Sulbactam sodium; Temperature; Vehicles

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Aztreonam, a monocyclic β-lactam antibiotic, is active against aerobic gram-negative organisms but inactive against anaerobic and gram-positive organisms.[1] It is not appropriate monotherapy for intra-abdominal infections, because both aztreonam-sensitive (enteric gram-negative rods) and aztreonam-resistant (*Bacteroides fragilis*) organisms are encountered.[2] In such situations, an antimicrobial (such as ampicillin–sulbactam) must be added to provide coverage against anaerobic organisms.[3]

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