Offering Simpler Solutions to a Complex Problem
Improving Management of Seizures and Behavioral Disturbances in Individuals with Intellectual and Developmental Disabilities (IDD)

American Society of Consultant Pharmacists (ASCP)

Caring for persons with intellectual and developmental disabilities (IDD) poses many challenges. Central nervous system complications are common: rates of epilepsy range from 30% to 50% in patients with moderate to severe mental retardation. Behavioral problems co-exist in up to 60% of patients who are both intellectually and developmentally disabled, and have epilepsy as well. Consultant pharmacists often participate in the management of individuals with intellectual and developmental disabilities. Given sufficient knowledge of treatment options, these professionals are in a better position to have positive impacts on patient, family, and caregiver. This symposium, held in conjunction with Senior Care Pharmacy ’05, the ASCP 36th Annual Meeting and Exhibition, was designed to present data on the most current concepts related to the care of patients with IDD.

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People with intellectual and developmental disabilities (IDD) suffer from a combination of long-term sociologic, anatomic and neurochemical disturbances. Along with other complications, there is psychiatric illness, which occurs in IDD patients at three to four times the prevalence of the general population. Psychiatric syndromes are often difficult to identify in persons with severe and profound mental retardation (MR), given their reduced ability to self-report.

Speaker Jessica Hellings, MD, Associate Professor of Psychiatry at the University of Kansas School of Medicine presented a series of problems that clinicians and other caregivers may encounter in the management of patients with IDD.

Diagnostic Difficulties
IDD patients pose a range of diagnostic dilemmas. One common circumstance Dr. Hellings described relates to the verification of seizures. It is not uncommon, she said, to see patients display symptoms of a partial seizure in the office and find that they are not confirmed by EEG monitoring. After proceeding to add an anti-seizure medication, clinicians will often subsequently witness behavior improvement, suggestive of a seizure phenomenon that is simply not picked up on EEG.

Polypharmacy versus Rational Combination Treatments
Polypharmacy is common and sometimes necessary in the treatment of IDD. Still, instead of adopting an approach of one drug for one symptom, Dr. Hellings would argue for a process aimed at arriving at a syndromal diagnosis and devising a rational treatment strategy to target the syndrome.

Multiple Prescribers Who Do Not Communicate
Since patients with IDD commonly see a number of medical professionals, the same symptom can be interpreted and treated differently by different medical professionals. Non-communication among these providers can be a source of medication error and poor outcomes. Tremor is an example. Neurologists will often refuse to assess and treat tremor unless patients are off valproate sodium, and this may not be feasible due to bipolar disorder severity. At the same time, primary care physicians seeing IDD patients with tremor may not be aware of valproate treatment or of its side effects. Convinced that the patient has Parkinson’s disease, they may treat for this condition inappropriately.

Behavioral Toxicity of Older Antiseizure Medications
Phenytoin and phenobarbital, ethosuximide, and carbamazapine are examples of older medications that scientific evidence has shown to be associated with sometimes intolerable effects — mood changes, extreme irritability, aggression and psychosis. And when it occurs, conversion between older and newer medications may be a slow process, paradoxically resulting short-term worsening of the condition — a circumstance that makes it difficult for families to understand (but more easily implemented in a group living situation, where staff are more able to handle it).

Decreased Ability to Advocate for Themselves
IDD patients, because of a lowered ability to communicate, may not verbally refuse medications, but may instead become non-
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compliant when side effects become intolerable. Where patients are unable to speak and advocate for themselves, Dr. Hellings advised, trained observers who are informed about side effects are sorely needed. Unfortunately, in a setting in which the job of being a direct caregiver is neither financially nor personally rewarding, an IDD patient who is not tolerating and therefore not taking medication may fail to be identified.

Somnolence, Withdrawn Behavior or Mental Confusion

Newer medications do not render IDD patients as totally inactive as do earlier medications such as haloperidol, mellaril, and thorazine. Nevertheless, there is still a need for vigilance with newer medications when instituting medication regimens. Accordingly, the preferred approach is to keep the doses low and to go slow, Dr. Hellings said. Newer medications are not without serious, negative effects. Patients receiving valproate sodium, for example, should be monitored for elevated ammonia. In a five-year, double-blind placebo-controlled study of valproate in adolescents with aggression recently completed by Dr. Hellings and colleagues, two patients had elevated ammonia levels. Rather than withdrawing the patients from the valproate, the investigators added carnitine then successfully monitored their ammonia level.

Ongoing psychiatry and neurology input is needed to discern the sources of symptoms of mental confusion and withdrawn behavior. In patients older than age 40, Dr. Hellings stated, an assessment of Alzheimer’s disease and major depression may be called for.

Increased Sensitivity to Medication Side Effects

Especially in physically frail patients or those with cerebral palsy, greater attention must be paid to medication side effects because of an increased sensitivity to medication. For these patients, the standard rule of “start low and go very slow” applies, along with attention to the emergence of clumsiness, falling and/or sedation. Also, Dr. Hellings said, it may be necessary to wait longer for a drug response before increasing doses. “I have had patient families that tell me the patient can’t tolerate this medication. When we [investigate], we often find that the medication was started too high,” Dr. Hellings said.

Guardian Consent

Guardian consent, while necessary and appropriate, is “another level of red tape” in treating IDD patients, and may be negatively affected by lack of information on the part of guardians, or by wrong information. In some instances, consent may be overlooked or missing.

Defining Effective Methods to Improve the Management of Seizures and Behavioral Disturbances in People with IDD

Seizures are a highly treatable condition in patients with IDD, and may be both over-diagnosed and under-diagnosed in this patient population, according to speaker Michael Smith, MD, Director of the Rush Epilepsy Center in Chicago.

No single seizure type is characteristic in this population of patients. However, most patients have symptomatic epilepsy with partial and/or secondarily generalized tonic-clonic (GTC) seizures. Generalized epilepsies are also common, according to Dr. Smith. Secondary symptomatic types such as Lennox-Gastaut syndrome, which include tonic, atonic, and myoclonic (mixed) seizures, occur as well as “weird seizures” arising from a frontal lobe source.

The goals of anti-seizure therapy in patients with IDD should be neither too optimistic nor too “nihilistic,” Dr. Smith emphasized, with efforts aimed at reducing the amount and severity of damage from the more serious types of seizures, such as drop seizures, and planning medication regimens that optimize outcomes and reduce side effects without the use of polypharmacy. He added that “Study after study has shown that we can successfully reduce polypharmacy even in this hard-to-control patient population.” The patient’s general health status, his/her self-medication skills, and costs of medications are also considerations. Temporal lobe resection may be an option with a single seizure type arising from one area, leading to sometimes dramatic improvements of quality of life. Vagal nerve stimulation (VNS) is also a good additive measure in the mental retardation (MR) developmental disabilities (DD) patient population.

Seizure Control

Seizure classification is important when choosing an anti-epileptic drug (AED) and to determine prognosis, especially since some medications make certain seizure types worse. The principles of anti-epilepsy treatment, including surgery, are the same for individuals with and without MR. As such, it is related to the number of seizure types being treated. In special populations, general principles of efficacy, safety and simplification govern the treatment of epilepsy. Several guidelines are encompassed within each general category. For example, monotherapy should be a goal whenever possible, Dr. Smith said, with an agent that is appropriate for the seizure type. If the seizure type is mixed or unknown, a broad spectrum agent that will not exacerbate the seizures and minimize trough levels should be selected.

Monotherapy should be a goal whenever possible... with an agent that is appropriate for the seizure type.

Efforts should be directed at minimizing drug/drug interactions and side effects. Preferred is an agent with a known, manageable side effect and risk profile that will not exacerbate other conditions,” Dr. Smith advised. “...p450 inducers reduce by half many of the other medications the patient may be taking. In an older patient, this caveat may pertain to statins or calcium channel blockers. If phenytoin is added to a regimen with these drugs, their potency will be reduced by one-half.” Simplification is key. “Minimize the number of agents, the daily doses, and the medication administration process and try to reduce the cost.” Keep in mind the overall objective is improving the quality of life of the patient.

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Maximizing the Role of the Consultant Pharmacist

A Case Study

Speaker Joseph Gruber, RPh, CGP, FASCP, Regional Clinical Director of Omnicare, Inc. in St. Louis highlighted the role of the consultant pharmacist, especially its multidisciplinary character, with an IDD case study.

Patient Background and History
JS is a 57-year-old white male living in a large MRDD county group home. His mother died some years prior and his brother has served as guardian since that time. Along with other family members, the brother maintains close contact with JS through frequent visits, cards, and packages.

Diagnosis
- Schizophrenia, dementia, myoclonic seizures, profound MR.
- Physical ailments include hearing and vision impairment; dental decay with long-standing gingival hyperplasia and poor dental hygiene; BPH and a recently resolved UTI; and a 20-lb weight gain over the past 6 months.
- The patient has experienced 3 myoclonic seizures in the last 6 months.

Psychosocial
JS is friendly, enjoys walking, watching TV, and sports. His compliance with medical staff at day training is poor (often returns with medications not administered). He exhibits explosive behaviors when staff approaches with medication and staff reports forms of agitated/aggressive behavior (striking, pinching, kicking, pulling hair, biting, door slamming, stomping feet, hitting/pushing inanimate objects and so forth).

Behavioral Objectives
- Maximize and reinforce activities, likes, and day training.
- Minimize physically and verbally aggressive behaviors to 2 or fewer per month for 6 consecutive months.

Care Plan Objectives
- Stabilize and reduce rate of dementia decline; improve dental health; eliminate seizure activity.

Medications
- Dilantin 100 mg tid (9 yrs)
- Folic acid 1 mg daily (9 yrs)
- Zyprexa 20 mg daily (18 mo)
- Aricept 10 mg daily (11 mo)
- Namenda 10 mg bid (9 mo)
- Depakote DR 500 mg bid (8 mo)
- Lactulose 10 gm/115 cc, 30 cc daily (6 mo)
- Senna S daily (9 mo)

Recent Laboratory Findings
- Lipid profile: TC 210; TG 296; HDL 36; LDL 135
- Valproate 59.4 (50–100)
- Dilantin 15.0 (10–20)
- Albumin 2.7 (3.4–4.7)
- Glucose (fasting) 145 (60–110)
- Lytes normal
- BUN 24 (8–20)
- Cr 1.2 (0.6–1.2)
- HgA1c 7.5 (<6.5–7.0)
- MRI — central and cortical atrophy
- Lytes normal
- PSA 1.2 (<4.0)

Staff Report
JS seems sluggish and depressed at times. Behaviors have been charted at between 7 and 35 per day for the last six months. Oral hygiene is deteriorating, and interventions are met with aggressive behaviors. Patient has poor medication compliance. Seizures persist. JS is not progressing to behavioral goals, despite current antipsychotic therapy. The team contemplates interventions for continued agitated/aggressive behaviors, seizure activity, and comorbid medical concerns.

Case Question 1

Based on this individual’s persistent agitated and aggressive behaviors, are we using the most appropriate and effective psychotropic agents?

Joseph Gruber

Case Question 2

Based on this individual’s persistent agitated and aggressive behaviors, do we have the right medications on board, and if not, what changes might we explore?

Michael Smith

As we have discussed, phenytoin can exacerbate myoclonic epilepsies, and therefore we should consider whether this is the wrong medication, and whether we should slowly bring the patient down to one medication from two. The levels of the valproate are not high because the phenytoin is in effect cutting the valproate dose in half. The free levels of both valproate and phenytoin are probably significantly higher, and I wouldn’t be surprised if the patient were not intermittently ataxic after dosing. I would suggest slowly weaning the phenytoin and perhaps increasing the valproate dose. I would also change the 500 bid valproate DR to valproate ER 1500 milligrams to ease medication administrations problems.

Jessica Hellings

Gary Sachs at Harvard has done a risperidone versus placebo, add-on to Depakote for bipolar disorder with agitation study, and showed good results. However, the problem with an antipsychotic like olanzapine or risperidone is the huge weight gain, and elevated lipid profile. This patient already has problems with his glucose control, and so what we would be doing essentially [in this patient] is substituting one public health problem (aggression) with another public health problem (obesity and medical illness). We have done a 5-year study with risperidone for aggression in this population, with good results, but the weight gain was really prohibitive and ongoing. One of my favorites is loxapine. We may consider adding 5 mg per day of loxapine and then gradually taper down the olanzapine. Often, [with this treatment] the patient’s well-being is remarkable and the weight gain is much less. With weight loss, sugar control can get better, and lipids could improve.
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The availability of a number of FDA-approved medications allow for efforts to customize therapy based on comorbidities. Some examples Dr. Smith mentioned are valproate or topiramate for a person with migraine and epilepsy, and valproate or lamotrigine for a patient with bipolar disorder and epilepsy.

Certain AEDs not only do not treat all seizures well, but actually may make some seizures worse. Sodium channel blockers, carbamazepine, phenytoin and lamotrigine, are examples of drugs that tend to make myoclonus, and sometimes absence, worse. “In Lennox-Gastaut syndrome, a number of medications make certain seizure types worse, but felbamate, lamotrigine, levetiracetam, zonisamide and topiramate are all helpful in this patient population, as is VNS.” Dr. Smith added that in the hard-to-control Lennox-Gastaut patient, valproate and lamotrigine have synergistic activity. Overall AED options are shown in Figure 1.

U.S. and U.K evidence-based guidelines and expert opinions have been published for the use of AEDs. From the U.K. is the National Institute of Clinical Excellence (NICE) evidence-based recommendations (Available at: http://www.nice.org.uk/cat.asp?c=20119). For absence, NICE first-line drugs of choice are valproate and ethosuximide; second-line choices are lamotrigine and topiramate. For myoclonus, valproate first-line is recommended, with levetiracetam and topiramate and lamotrigine second-line. From the U.S. expert opinions on AEDs, valproate is the preferred agent for absence (Karczeski S et al. Epilepsy Behav. 2001;2:A1-A50).

New AEDs offer improved efficacy, but not without special problems. For example, topiramate, zonisamide and felbamate all cause weight loss. Kidney stones with topiramate and zonisamide are an important hidden problem.

“Behavior problems occur with every AED we have,” Dr. Smith stated, and because of this, treatment for psychological problems is a standard aspect of patient management. A multidisciplinary approach to psychological problems is ideal. This should include simplification of the AED regimen, moving to monotherapy; optimizing seizure control; and implementing environmental management strategies, including behavioral management. Conversion to monotherapy, even in individuals who have traditionally been treated with 3 or more AEDs, including barbiturates, is possible in most patients, and has been shown in a number of AED reduction studies (Schmidt D. Epilepsia. 1983;24:368-376. Clancy RR. Curr Prob Pediatr. 1987;17:133-209. Mirza WU, Credeur LJ, Penny JK. Drug Invest. 1993;5:320-326. Pellock JM, Hunt PA).

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<th>Partial</th>
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- ACTH
- Topiramate?
- Tiagabine?
- Vigabatrin?

Ethosuximide

Valproate, Lamotrigine, Topiramate (Felbamate), Zonisamide, Levetiracetam?


“Reducing AED should be the mantra that we all leave here today with,” Dr. Smith concluded, adding that it is possible to reduce the AED drug load and thereby improve quality of life for IDD patients throughout their lives.

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