A Report by
The Office of the Ombudsman
for Mental Health and Mental Retardation

Report on the Behavioral Side Effects of Barbiturate Antiepileptic Drugs

Issued under the Authority of
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and Mental Retardation

In cooperation with

Maria R. Gomez
Commissioner of Department of Human Services

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Dear Reader:

This Educational Bulletin on the Behavioral Side Effects of Barbiturate Antiepileptic Drugs was developed and is being published as a collaborative effort by: (1) the Department of Human Services, (2) Arc Minnesota, (3) Minnesota Disability Law Center, (4) Dr. John Gates, Director of Adult Services with the Minnesota Epilepsy Group, P.A., and (5) the Office of the Ombudsman for Mental Health and Mental Retardation. Its objective is to educate case managers and providers about the potential behavioral side effects of barbiturate antiepileptic drugs (AEDs) when used with persons with developmental disabilities.

The impetus for this publication came about due to studies undertaken at Faribault Regional Center with developmentally disabled clients prescribed barbiturate AEDs. These studies demonstrated that decreasing and, ultimately, terminating the use of barbiturate AEDs led to reduction in both the frequency of problematic behaviors and to reduction in the use of psychotropic medications. Several of these studies have been published in professional journals.

It is hoped if a person with developmental disabilities is receiving a barbiturate AED, the interdisciplinary team can undertake a careful review of possible behavioral side effects. This publication outlines red flag profiles to assist the team in deciding whether a review is indicated. Extreme caution must be exercised to insure that before the barbiturate AED is reduced or removed that the team agrees and that a comprehensive evaluation of the client is done by a neurologist.

Please note that under no circumstances should a client's barbiturate AED be reduced or removed without first a team decision and a thorough evaluation by, and under the guidance of, a neurologist and the client's primary care physician.

Special thanks is extended to Tom Hanzel, Psychologist, Faribault Regional Center, and John Kalachnik, Planner, Department of Human Services, for the drafting, writing and researching of this Educational Bulletin.

Sincerely,

Roberta C. Opheim
Ombudsman for Mental Health and Mental Retardation

Maria R. Gomez
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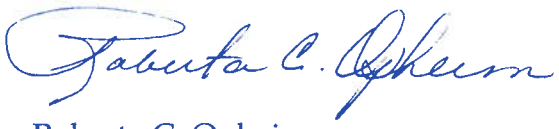
Preface

The Office of the Ombudsman for Mental Health and Mental Retardation is charged under Minn. Stat. § 245.94 with promoting the "highest attainable standards of treatment, competence, efficiency, and justice for persons receiving services for mental health, developmental disabilities, chemical dependency, or emotional disturbance." This review of the behavioral side effects of barbiturate antiepileptic drugs (AED) is consistent with that charge.

It is our hope that this bulletin will help to provide a layperson's understanding of what symptoms to be aware of and what questions to be raised and answered. Again, any final decision about a particular client's care and treatment should rest with the treatment team acting together in the best interest of their individual client.



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Introduction

Behavioral side effects of antiepileptic drugs (AED) are an often overlooked and underrecognized problem for individuals with developmental disabilities. These side effects are easily confused with other behavioral, mental, or physical problems. Recognition of AED behavioral side effects is imperative because quality of life activities and active treatment programs are potentially compromised. Inadvertent use of psychotropic medications or aversive and deprivation procedures may also occur.

The behavioral side effects associated with barbiturate AEDs are of particular concern. The purpose of this information is to: (1) review barbiturate AED behavioral side effects, and (2) provide "red flag" profiles suggesting possible presence and prompting further clinical inquiry.

Findings

DRUGS INVOLVED

Phenobarbital (Luminal) and primidone (Mysoline) are the primary barbiturate AEDs prescribed. Occasionally, mephobarbital (Mebaral) is prescribed.

SPECIFIC BEHAVIORAL SIDE EFFECTS

Behavioral side effects associated with barbiturate AEDs are:

- Aggression
- Depressive symptoms
- Disruptive vocalizations
- Hyperactivity
- Irritability
- Noncompliance
- Property destruction
- Self-injurious behavior
- Sleep disturbance
- Temper tantrums

These behavioral classes require more specific definition for an individual. For example, property destruction may involve tipping over furniture or tearing items such as clothing. Self-injurious behavior may involve biting one's arms or hands. Depressive symptoms may involve suicide ideation, frequent and unprovoked crying, and loss of interest in normally rewarding activities.

POSSIBLE RISK FACTORS

Phenobarbital and primidone generally exacerbate existing behavior problems. Individuals with preexisting behavior problems are thought to be at higher risk for barbiturate AED behavioral side effects. Organic brain damage, psychomotor epilepsy, and multiple anticonvulsants may also place an individual at higher risk.

PREVALENCE

Despite the advent of newer AEDs, approximately 33% of individuals with coincident developmental disabilities and epilepsy are prescribed phenobarbital or primidone. Overall, approximately 7% of all individuals with developmental disabilities are prescribed barbiturate AEDs.

The prevalence of behavioral side effects in children is 20-40%. This figure may be as high as 60% for individuals with developmental disabilities. Some authorities consider individuals with developmental disabilities more susceptible to barbiturate AED behavioral side effects, especially those with behavior problems before barbiturate AEDs are started.

There are approximately 20,000 individuals with developmental disabilities living in Minnesota receiving case management services. Given barbiturate AEDs are prescribed for 6-7%, 1200 to 1400 individuals are at risk. If 40% actually develop these side effects, 480 to 560 individuals may be experiencing barbiturate AED behavioral side effects to varying degrees.

DETECTION PROBLEMS

It is easy to overlook barbiturate AED behavioral side effects for a number of reasons: (1) unlike the general population, many individuals with developmental disabilities cannot effectively communicate the presence of behavioral side effects; (2) behavioral side effects often resemble and are assumed to be underlying behavior problems commonly associated with developmental disabilities or mental illness; and (3) behavioral side effects occur within normal therapeutic ranges and are not necessarily detected through monitoring blood levels. An individual may tolerate barbiturate AEDs initially and subtly develop behavioral side effects over time. Combined with an existing behavior problem which may vary over time, an association with the barbiturate AED may not be made. Seizure control concerns and a lack of detection instruments may also contribute.

POTENTIAL CONSEQUENCES OF NONDETECTION

A number of potentially adverse consequences can occur if barbiturate AED behavioral side effects are not recognized. These consequences generally fall under three categories: (1) psychotropic medication, (2) behavior programs, and (3) quality of life outcomes.

- Psychotropic medication may be inadvertently prescribed in an effort to control barbiturate AED behavioral side effects. As a result, other side effects may occur. For example, antipsychotic medication may cause tardive dyskinesia which is a potentially persistent movement disorder. Similiarly, higher antipsychotic doses may cause increased restlessness as well as other movement disorders. Efforts to

minimize psychotropic medication may fail because barbiturate AED behavioral side effects may increase when psychotropic medication is decreased.

- Positive behavioral procedures may be repeatedly attempted in an effort to manage barbiturate AED behavioral side effects. Valuable time and resources may be allocated. Aversive or deprivation procedures may be used in more severe cases. As a result, unintended consequences or a high level of restrictiveness may occur. For example, social interactions between the individual and others may be avoided or strained. Efforts to discontinue the aversive procedure may prove unsuccessful because barbiturate AED behavioral side effects may increase when the aversive procedure is removed.

- Quality of life indices may be affected. Severe barbiturate AED behavioral side effects can be associated with injuries to self or others which require medical treatment. Removal from a less restrictive living environment may occur with diminished opportunity to engage in activities of normal daily living. Unsuccessful efforts to manage the barbiturate AED behavioral side effect can eventually lead to "living with the problem" and a resignation that the problem is an unchangeable characteristic of the individual.

PROFILES SUGGESTING CASE REVIEW

The interdisciplinary team should remain alert to the following "red flag" profiles which suggest possible barbiturate AED behavioral side effects. These profiles indicate review by appropriate medical and neurological personnel.

"The individual is prescribed a barbiturate AED and displays a behavior problem as listed under the Specific Behavioral Side Effects section **and**..."

- Profile 1: positive intervention procedures: (a) are repeatedly attempted for the behavior, **or** (b) are minimal because the behavior is accepted as an unchangeable characteristic of the individual.

- Profile 2: psychotropic medication: (a) is currently prescribed for the behavior and has not eliminated the behavior despite long-term use, **or** (b) historically failed in the presence of the barbiturate AED.

- Profile 3: psychotropic medication, especially an antipsychotic medication: (a) is currently prescribed for the behavior, **and** (b) dosage reduction attempts have failed in the presence of the barbiturate AED.

- Profile 4: aversive or deprivation procedures: (a) are currently in place for the behavior, **or** (b) have not eliminated the behavior despite long-term use.

COMPLICATING CLINICAL ISSUES

Once a potential case is identified, several complicating clinical issues may be involved. These can make the assessment and evaluation of barbiturate AED behavioral side effects difficult.

First and foremost, there is no absolute test for confirming barbiturate AED behavior side effects. In most cases, the only confirmation may be the removal of the barbiturate AED. Specific measurement of the behavior using techniques such as frequency count, time sample, or interval recording is helpful. Since phenobarbital takes approximately 21 days to reach steady blood levels after a dose change, it is likely behavior does not represent the new dose until a steady blood level is reached.

Second, barbiturate AEDs are associated with withdrawal effects. These may include seizures, irritability, sleep problems, and even the temporary increase of the very behaviors suspected of being behavioral side effects. Unless the individual is being treated in a specialized inpatient program, barbiturate AED reductions should proceed slowly. This may take a number of months. Even with gradual reductions, withdrawal effects may still occur in some cases. It is important not to overreact to temporary behavioral increases.

And third, some individuals may be seizure free for 2 to 4 years or more. Barbiturate AED prescription may no longer be necessary. However, other individuals may have ongoing seizure activity which complicates the barbiturate AED withdrawal process. Other AEDs may need to be adjusted or initiated. Since most AEDs affect blood levels of other AEDs, seizure control during a barbiturate AED withdrawal is a complex process. At times this can lead to staff, professional, or family resistance to change.

Conclusion

Use of the "red flag" profiles to identify potential cases combined with medical and neurological reviews of these cases can minimize barbiturate AED behavior side effects. If it is concluded these side effects are present, gradual barbiturate AED reductions increase the likelihood of long-term success and minimize withdrawal effects. Graphically organizing behavioral and seizure data by drug and dose conditions during this process greatly contribute to structured physician reviews.

Overall, this information is not suggesting that barbiturate AEDs never be used. Not everyone develops behavioral side effects. Problem behaviors displayed by an individual may not be explained by these side effects. Rather, the purpose is to alert care providers and professionals about the possibility of these often overlooked and underrecognized side effects, especially for those cases where other factors do not explain a behavior problem, or the behavior problem continues despite great efforts to correct it. Lack of recognition of barbiturate AED behavioral side effects can potentially compromise the quality of an individual's life.

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