The Use of Baclofen in the Management of Spasticity in Children with Cerebral Palsy

Anne E. Olson

University of North Dakota

Follow this and additional works at: https://commons.und.edu/pt-grad

Part of the Physical Therapy Commons

Recommended Citation
https://commons.und.edu/pt-grad/336

This Scholarly Project is brought to you for free and open access by the Department of Physical Therapy at UND Scholarly Commons. It has been accepted for inclusion in Physical Therapy Scholarly Projects by an authorized administrator of UND Scholarly Commons. For more information, please contact zeinebyousif@library.und.edu.
The Use of Baclofen in the Management of Spasticity in Children with Cerebral Palsy

by

Anne E. Olson
Bachelor of Science in Physical Therapy
University of North Dakota, 1998

An Independent Study
Submitted to the Graduate Faculty of the
Department of Physical Therapy
School of Medicine
University of North Dakota
In partial fulfillment of the requirements
for the degree of
Master of Physical Therapy

Grand Forks, North Dakota
May
1999
This Independent Study, submitted by Anne E. Olson in partial fulfillment of the requirements for the Degree of Master of Physical Therapy from the University of North Dakota, has been read by the Faculty Preceptor, Advisor, and Chairperson of Physical Therapy under whom the work has been done and is hereby approved.

(Faculty Preceptor)

(Graduate School Advisor)

(Chairperson, Physical Therapy)
PERMISSION

Title The Use of Baclofen in the Management of Spasticity in Children with Cerebral Palsy

Department Physical Therapy

Degree Master of Physical Therapy

In presenting this Independent Study Report in partial fulfillment of the requirements for a graduate degree from the University of North Dakota, I agree that the Department of Physical Therapy shall make it freely available for inspection. I further agree that permission for extensive copying for scholarly purposes may be granted by the professor who supervised my work or, in his/her absence, by the Chairperson of the department. It is understood that any copying or publication or other use of this Independent Study Report or part thereof for financial gain shall not be allowed without my written permission. It is also understood that due recognition shall be given to me and the University of North Dakota in any scholarly use which may be made of any material in my Independent Study Report.

Signature

Date 1/8/98
# TABLE OF CONTENTS

List of Figures ........................................................................................................... v
List of Tables ............................................................................................................... vi
Acknowledgements .................................................................................................... vii
Abstract ...................................................................................................................... viii
Chapter I ..................................................................................................................... 1
Chapter II ................................................................................................................... 5
Chapter III .................................................................................................................. 11
Chapter IV ................................................................................................................. 17
Chapter V .................................................................................................................... 27
References .................................................................................................................. 33
# LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Chemical structures of GABA and baclofen</td>
<td>18</td>
</tr>
<tr>
<td>2. Illustration of baclofen pump and catheter</td>
<td>20</td>
</tr>
<tr>
<td>3. Illustration of pump placement within the body</td>
<td>21</td>
</tr>
</tbody>
</table>
# LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ashworth’s Scale for Grading Spasticity</td>
<td>12</td>
</tr>
<tr>
<td>2. Advantages and Disadvantages of Oral Baclofen</td>
<td>26</td>
</tr>
<tr>
<td>3. Advantages and Disadvantages of Intrathecal Baclofen</td>
<td>26</td>
</tr>
</tbody>
</table>
ACKNOWLEDGEMENTS

Many people have been essential in helping me complete my independent study. I would like to begin by thanking the entire staff of the Physical Therapy Department at the University of North Dakota for sharing their knowledge and expertise with me. They have taught me so much and have made my physical therapy school experience rewarding. I would like to extend a special thank you to my advisor and preceptor Dr. Peggy Mohr. I appreciate all of the time and guidance she provided me with, to make this paper and my school career successful.

I would also like to thank my classmates, roommates, and close friends for their support and for putting up with me for these three years of physical therapy school! I probably wasn’t the most fun to be around when I was “stressed out,” but they always stuck by me and helped me see what was really important.

Finally, I would like to thank my family. My parents have given me so much and these few words cannot express how thankful I am! They’ve taught me how to be a good person and a hardworking student! I owe my successful school career and my wonderful life to them!
ABSTRACT

Cerebral palsy is one of the leading developmental disabilities amongst children. The majority of children with cerebral palsy experience some degree of spasticity. This spasticity can be very painful and disabling to the child. It can affect their posture, movements, and their mobility.

Currently, baclofen is one of the most common medications used for the treatment of cerebral spasticity. It can be administered either orally or intrathecally through an implanted pump.

The purpose of this literature review is to discuss the use of oral and intrathecal baclofen in the management of spasticity in children with cerebral palsy. Included is a discussion about cerebral palsy and the spasticity that accompanies it. Also included is a discussion about the physical therapy that is provided to enhance baclofen therapy.
CHAPTER ONE
INTRODUCTION

Cerebral palsy affects one to two newborns per 1000 live births in the United States. The majority of children who are afflicted with this motor disorder experience some degree of spasticity. The spasticity caused by cerebral palsy (cerebral spasticity) results in a life-long increase in muscle tone that interferes with voluntary muscle movements. This can often be very painful and disabling to the child, which in turn affects normal posture, daily activities, and mobility.

Since spasticity is so wide-spread within the cerebral palsy population and because it affects nearly every aspect of the child’s life, an effective treatment program is necessitated. Traditionally, cerebral spasticity was treated by physical therapists in an attempt to maintain range of motion, prevent deformities, and promote proper posture and daily functions. Today, surgical procedures such as selective dorsal rhizotomies; oral medications like dantrolene, diazepam, and baclofen; intramuscular injections of botulinum toxin; and intrathecal baclofen have been used in addition to physical therapy to help aid in the reduction of spasticity. Baclofen, both oral and intrathecal, is one of the most common medications used for the treatment of spasticity in children with cerebral palsy.

The purpose of this literature review is to discuss in detail cerebral palsy, spasticity, and the use of oral and intrathecal baclofen in the treatment of cerebral...
spasticity. This review draws information from current literature and summarizes the material as it relates to physical therapy. It will answer the question how is baclofen used in the treatment of spasticity in children with cerebral palsy to enhance a physical therapy rehabilitation program. In quest of answering this question, more related inquiries may arise, such as: What exactly is cerebral palsy? Who does it affect? What is spasticity? How does spasticity affect the body? Can spasticity be treated? What kinds of treatments can be used to manage spasticity? Who is a good candidate for baclofen therapy? What kind of research has been done on baclofen? How can physical therapy help manage spasticity? Does the reduction of spasticity improve functional performance?

In an effort to address these questions, this literature review is presented in five chapters. Chapter two defines cerebral palsy as a non-progressive movement disorder caused by an injury to the brain occurring before, during, or shortly after birth. It describes the incidence of cerebral palsy and stresses how common it is amongst children. Several factors are listed as possible causes in an attempt to explain the etiology of cerebral palsy. A system for categorizing the disabilities involved with this disorder is systematically described. It will illustrate how cerebral palsy is classified and the related disorders that may accompany it. Finally, chapter two will briefly present the common treatment approaches that are currently being used to address the plethora of disabilities that stem from cerebral palsy.

Chapter three covers spasticity, specifically cerebral spasticity secondary to cerebral palsy. It defines the anatomy of this disorder as an increase in muscle tone and explains how it is manifested within the body. The Ashworth Grading Scale for Spasticity is described in this chapter to increase that understanding of how the level of
spasticity is determined in the child. A discussion follows of what level and when spasticity treatment is appropriate. Once it is determined that the spasticity within the child is disabling enough to be treated, a type of treatment can be decided upon. Chapter three provides a list of treatment options that are available for the child and which ones are most popular. The importance of enhancing spasticity treatment is also stressed, especially for the physical therapist’s role in supplemental care. A description of how physical therapy optimizes and contributes to the management of cerebral spasticity is included.

Chapter four covers the topic of baclofen. The pharmacology of the drug is explained to clarify how it works within the central nervous system. Specific information about oral and intrathecal baclofen is presented here. The administration of oral baclofen and the involvement of the blood-brain barrier are described. This is contrasted with a description of intrathecal baclofen and how its administration bypasses the blood-brain barrier by being directly delivered to the site of action. An explanation of how the baclofen pump is implanted and how it functions is also provided, along with a complete description of the adverse side effects and possible complications that may accompany the use of baclofen. A list of advantages and disadvantages of each method of delivery is noted to help clarify which type is most appropriate for which patients.

The last chapter of this literature review summarizes the information that has been presented. It reports the results of existing research on baclofen therapy and discusses their findings. It provides answers to the original research questions and links the use of baclofen to physical therapy treatments for spastic cerebral palsy.
This review focuses on educating physical therapists, other health professionals, and interested readers on the use of baclofen in treating spasticity in children with cerebral palsy. It will help the individuals participating in the management of spasticity understand why and how each method of baclofen therapy works. This understanding will help guide the rehabilitation of children with spastic cerebral palsy.
Incidence

Cerebral palsy is not a disease. Rather it is a category of disabilities, with an onset in early childhood, stemming from chronic non-progressive disorders of movement and posture. These disabilities are the result of a static lesion to the developing brain acquired either before birth, during birth, or within the first five years of life. Its occurrence has been reported to range from 1.5 to 5.0 cases per 1000 persons. The differences in the range can be attributed to the new advances in technology and care of premature infants. There has been a decrease in certain types of cerebral palsy due to better prenatal treatments. The incidences of other types of cerebral palsy have increased due to the survival of more premature infants.

Etiology

Ratcliffe explained the etiology of cerebral palsy by describing two separate time periods when different influences on the brain can have a significant impact on its development. Influences that cause damage to the brain either during gestation or the delivery process are termed congenital cerebral palsy. Acquired cerebral palsy is caused by influences that occur after birth and within the first few years of life.
Eighty-five percent of the cases of cerebral palsy are congenital.\(^6\) Prenatal factors such as genetics, viruses and infections, Rh incompatibility between mother and fetus, drugs and alcohol, and fetal positioning can cause brain damage. Any of these incidents can disrupt the delicate environment between mother and child and can result in cerebral palsy. Events during the delivery process and shortly after birth may also contribute to cerebral palsy.\(^6\) The risk factors include premature birth, prolonged labor, breech birth, prolapsed umbilical cord, birth trauma, severe jaundice, and poor nutrition.\(^6\) In many of these cases, a lack of oxygen to the brain is the cause of the damage. Other possible sources of cerebral palsy in infants include ischemia, lung diseases, and heart conditions.\(^4\) Abnormal neonatal signs and low Apgar scores may serve as indicators of cerebral palsy.\(^4\)

The remaining 15% of cerebral palsy cases are acquired.\(^6\) Events occurring after birth or within the first few years of life disrupt the brain while it is still developing rapidly. Post-natal infections, such as meningitis or encephalitis, are the leading cause of acquired cerebral palsy, comprising 60% of the cases.\(^6\) Another 20% of the cases are attributed to head injury or trauma from motor vehicle accidents and child abuse.\(^6\) Other possible causes include, but are not limited to, near drowning accidents, cardiac arrest, cerebral vascular accidents, brain tumors, anemia, and lead exposure.\(^6\)

**Classification**

Once a child is diagnosed with cerebral palsy, a classification of disabilities is made. Classifications are made both anatomically, depending on what extremities are involved; and physiologically, depending on the location of the brain lesion and the type
of motor disorder present. When only one extremity is involved, the cerebral palsy is classified as monoplegia. Paraplegia involves only the lower extremities. If both the upper and lower extremities are involved, it is classified as either quadriplegia (all four limbs are equally involved), diplegia (all four extremities with the legs more involved than the arms), or hemiplegia (just one side of the body is affected). Hemiplegia is the most common form of extremity involvement in cerebral palsy.

The type of motor disorder that is present with cerebral palsy is dependent upon the area of the brain that is affected. When the motor cortex is injured, the resulting abnormality is spastic cerebral palsy. If other areas of the brain, such as the basal ganglia or the cerebellum, are involved, the result is dyskinetic cerebral palsy.

Spastic cerebral palsy, the most common type, affects 50 - 75% of the children with cerebral palsy. Spasticity is characterized by a velocity dependent increase muscle tone. Children with spasticity often find voluntary movement difficult or impossible. If voluntary movement is possible, it is usually demonstrated with stiff, jerky motions of the body. Specific aspects of spasticity will be discussed in greater detail in chapter three.

Abnormal synergy patterns, mass patterns of movement in which muscles are abnormally linked together in predictable directions, are often seen in patients with spastic cerebral palsy. These patients most often exhibit a flexion synergy pattern, where linked muscles are held in a flexed pattern. But extension synergies, where the muscles are all held in extension, are not uncommon. Spasticity can also lead to poor and abnormal postures. This can result in muscle contractures, scoliosis, and orthopedic impairments. Pain may also accompany the
increase in muscle tone and can contribute to the interference with motor development.\textsuperscript{6,7} These characteristic factors usually lead to a decrease in the initiation, speed, and strength of movement; poor balance and coordination; increased energy requirements; and an overall decrease in stability.\textsuperscript{6}

Dyskinetic cerebral palsy involves intermittent tension of trunk or extremities and a variety of uninhibited movement patterns.\textsuperscript{8} Types of dyskinetic cerebral palsy include athetosis, dystonia, choreiform movements, ballismus, and tremors.\textsuperscript{4} \textit{Athetosis} is characterized by fluctuating muscle tone throughout the body and face.\textsuperscript{4,6} This is present in about 1/4 of all children with cerebral palsy and is characterized by slow writhing movements observed as the person involuntarily moves between the extreme ranges of motion.\textsuperscript{4,16} Athetosis often develops following a hypotonic infancy.\textsuperscript{6} \textit{Dystonia} affects 15 - 25\% of persons with cerebral palsy and involves sustained muscle contractions, causing twisting and repetitive movements or abnormal postures of the extremities.\textsuperscript{4,11} This condition is associated with pain and causes fixed postures and tone changes in the trunk.\textsuperscript{11} \textit{Choreiform movements} are also present in the face and extremities; however these movements are characterized by rapid, irregular, and jerky motions of the body.\textsuperscript{4} \textit{Ballismus} includes wild flailing or flinging motions of the extremities within a wide range of motion. \textit{Tremors} are seen as fine, shaking movements of the head and extremities.\textsuperscript{4}

Two more rare types of movement disorders associated with cerebral palsy are \textit{ataxia} and \textit{rigidity}. Ataxic cerebral palsy results from a cerebellar lesion and affects only affects 5 - 10\% of people with cerebral palsy.\textsuperscript{8,18} Ataxia is characterized by a lack of proprioception in the joints and hypotonicity in the muscles, affecting the balance and
coordination of voluntary movements. Rigidity indicates a severe brain lesion at the level of the brain stem. It can be demonstrated in several different forms including extension of all extremities, flexion of the arms and extension of the legs, or with a "cog-wheeled" affect (involves the muscles on both sides of the joint which release and catch intermittently with passive movement). Unlike the tone present with spasticity, rigidity is not velocity-dependent and it remains the same throughout the range.

Mixed cerebral palsy is a condition that can include several different combinations of movement disorders either present at the same time or at different stages throughout development. Nearly 25% of persons with cerebral palsy have mixed disorders. Hypotonicity (low muscle tone) is often a precursor of spasticity or athetosis and is generally present in conjunction with ataxia.

**Related Disorders**

In addition to the movement abnormalities, children with cerebral palsy often exhibit related disorders. Mental retardation has been reported in 50 - 75% of children with cerebral palsy. Further examination found that some types of cerebral palsy have a greater distribution of cognitive impairments. Children with quadriplegia were found to have mental retardation 60 - 65% of the time. Seizure disorders are also common among the cerebral palsy population. It was found that nearly 30% of children with quadriplegia have seizures and those with acquired cerebral palsy were at an increased risk.

**Hearing and vision impairments** often affect children with cerebral palsy. Vision problems are seen in approximately 50% of the cases because proper vision relies on the
motor ability of the eye muscles.\textsuperscript{6} \textit{Speech deficits} are present in 50\% of the children with cerebral palsy.\textsuperscript{6} This is also due to motor abnormalities in the musculature needed to perform speech patterns properly. \textit{Sensory and behavioral disorders} are often present due to damage in their respective areas in the brain.\textsuperscript{6}

**Treatment**

Cerebral palsy is a motor disorder that is characterized by several different forms and combinations of disabilities. Some treatment is necessary, whether the child is severely disabled or just has mild impairments. Management of cerebral palsy can take on several different approaches, although the main focus is usually on the management of the central motor disorder.\textsuperscript{6} Related disorders that accompany central motor disorder may be treated with additional specialized treatments.
Spasticity is present in approximately 2/3 of the children with cerebral palsy.\textsuperscript{1,2,3,7,9,10,11,12} Spasticity is characterized by a velocity-dependent increase in tonic stretch reflexes or muscle tone in response to quick stretching.\textsuperscript{13} It is often associated with hyperreflexia, hypersensitivity to sensory stimuli, clonus, weakness, persistent primitive reflexes, and abnormal posturing and movement of the extremities.\textsuperscript{6,7,14} This increase in muscle tone can occur in any voluntary muscle of the body causing awkward, difficult, and often painful movements.\textsuperscript{3} In turn, this condition interferes with motor development, habilitation, and activities of daily living.\textsuperscript{7}

**Anatomy of Spasticity**

Spasticity is the result of an injury or disease; in cerebral palsy it is the result of a brain injury and is classified as cerebral spasticity. Spinal spasticity is caused by an insult to the spinal cord as in a spinal cord injury or multiple sclerosis.\textsuperscript{1} Cerebral spasticity results in involuntary muscle tightness and stiffness due to the inability of the damaged brain to send messages to the spinal cord instructing it to release the relaxing chemical called $\gamma$-aminobutyric acid (GABA).\textsuperscript{3} Without GABA, the excitatory interneurons within the spinal cord are not suppressed, allowing them to fire
continuously. Muscles receive excitatory information and contract repeatedly producing stiff or spastic muscles.\textsuperscript{15}

**Grading Spasticity**

The level of spasticity in a child with cerebral palsy can range from very mild to extremely severe.\textsuperscript{15} Physicians, physical therapists, and other health professionals often use the Ashworth Muscle Tone Scale to determine the level of spasticity and make decisions regarding the type and level of treatment that would be most appropriate for the child.\textsuperscript{17,19} Ashworth's scale grades the muscle's resistance to passive stretch (spasticity) on a five-point ordinal scale.\textsuperscript{13} MacKenzie and Charlson found this scale to have high validity because it measures spasticity when the muscle is moved passively.\textsuperscript{13,19,20} The Ashworth Scale for grading spasticity is shown in table 1.

**Table 1. Ashworth's Scale for Grading Spasticity\textsuperscript{13,17,19}**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal muscle tone</td>
</tr>
<tr>
<td>1</td>
<td>Slight increase in muscle tone, giving a 'catch' when the limb is moved in flexion or extension</td>
</tr>
<tr>
<td>2</td>
<td>More marked increase in muscle tone through the range of motion, but the limb is easily flexed</td>
</tr>
<tr>
<td>3</td>
<td>Considerable increase in muscle tone, passive movement is difficult</td>
</tr>
<tr>
<td>4</td>
<td>Limb rigid in flexion or extension</td>
</tr>
</tbody>
</table>

Bohannon and Smith\textsuperscript{13} introduced a modification to the Ashworth Scale in a study in 1985. An intermediate grade of 1+ was added to describe a slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder
(less than one half) of the range of motion.\textsuperscript{13} This was created to reduce the clustering
effect around the middle grades.\textsuperscript{17} Testing of the modified Ashworth Scale by Bohannon
and Smith\textsuperscript{13} indicated a high interrater reliability score.

\textbf{When is Treatment Appropriate?}

Treatment for cerebral spasticity is recommended when it is disabling to the
child.\textsuperscript{7} Disabilities occur when the spasticity interferes with normal daily activities or
caregiving; is painful for the patient; produces abnormal posture; or when it results in
contractures and/or a loss of joint range of motion.\textsuperscript{3,15} However, not all spasticity needs
to be treated, because not all spasticity is detrimental.\textsuperscript{21} In some cases, patients use their
spastic muscles to compensate for motor deficits. Spasticity in the lower extremities can
help maintain leg extension during standing, transferring, and walking.\textsuperscript{22} Increased tone
in the trunk musculature can aid a child in sitting in an upright posture.\textsuperscript{23} There has also
been documentation of spasticity improving vascular flow to the muscles and maintaining
muscle bulk.\textsuperscript{24}

\textbf{Treatments of Spasticity}

Spasticity cannot be cured; rather, it is managed.\textsuperscript{15,25} Management is attempted
with various types and combinations of treatment methods. A single plan of treatment
for spasticity will not be effective for all children with cerebral palsy. Spasticity is
manifested differently in each individual; thus therapy must be tailored for the child to
address his/her unique functions and disabilities.\textsuperscript{26}
The ultimate goal of spasticity treatment is to either increase the patient’s independence with ADLs and/or to ease caregiving responsibilities. Current treatments that are available for the management of cerebral spasticity are oral medications such as baclofen, diazepam, and dantrolene; intramuscular injections of botox; infusion of intrathecal baclofen; and an orthopedic surgery called selective dorsal rhizotomy. With each treatment comes a diverse set of indications, contraindications, side effects, and success rates. To determine which treatment would be most appropriate, a multidisciplinary team—usually consisting of physicians, physical therapists, occupational therapists, nursing staff, social workers, and the family—will collectively evaluate the child. Together they will define the tone abnormality, the severity of the disability, and recommend the treatment.

Currently, baclofen (the focus of this review) is a widely used medication for the treatment of spasticity. Baclofen can be administered both orally and intrathecally. Each method of delivery produces varying degrees of effectiveness and may be accompanied by different adverse effects.

Enhancing Spasticity Treatment

The treatment of spasticity will not be completely successful unless it is followed by supplemental care. Supplemental care is usually provided by a variety of professionals from a multidisciplinary team. The team usually consists of the physician, a physical therapist, an occupational therapist, a speech/language pathologist, a psychologist, a nurse, a social worker, and the family. Together they work to assist the
child in achieving his/her highest functional status. Individuals from each discipline will focus on their areas of expertise to optimize the impact of spasticity treatment.

An important aspect of spasticity treatment is to begin when the children are young. Childhood is the time when most motor development takes place. In fact, most children reach their expected functional capacity by the time they reach school age. If spasticity can be reduced early, this will minimize the adaptations the children learn to compensate for their motor deficits. Early intervention can also minimize muscle contractures and bone deformities, thus reducing the need for orthopedic surgeries.

**Physical Therapy’s Role**

Physical therapy plays a major role in enhancing spasticity treatments. Both before and after the patient has received medication or has undergone a spasticity reduction procedure, physical therapists often aid in the management process. Physical therapy is aimed at making normal movements easier, inhibiting abnormal motor functions, minimizing posture deficits, and preventing deformities. The ultimate goal of physical therapy is to decrease the degree of disability in the child.

Before the initial spasticity treatment, a physical therapist will evaluate the child’s gross motor functions, often using the Gross Motor Function Measure (GMFM) scores. This evaluation includes assessment of tone, active and passive range of motion, strength, coordination, and functional abilities, such as sitting, standing, rolling, and ambulation. These findings assist the therapist in recommending the type of treatment that would be most appropriate in reducing the child’s spasticity.
Once the treatment has begun, physical therapy will work with the children to teach them how to function with the reduction of spasticity.\textsuperscript{15} Depending on the extent of the child’s disability, the therapist may provide adaptive equipment such as wheel chairs, walkers, braces, and positioning aids to help the child achieve independent mobility.\textsuperscript{25}

Besides mobility, some other concerns of physical therapy include helping the children strengthen their weak muscles and improving their overall function.\textsuperscript{7,15,25} This is accomplished by incorporating a variety of activities into a physical therapy regime that often includes range of motion exercises, strengthening exercises, functional activities, and balance training.\textsuperscript{15}
Baclofen (trade name: Lioresal®) was introduced in the United States in 1967 and then approved in the early 1970's as a medication for the management of muscle spasticity. Originally, baclofen was intended for use as an anticonvulsant; however, during the evaluation of the drug's effectiveness, baclofen was discovered to be more effective at reducing spasticity. Baclofen acts on the central nervous system (CNS) to produce muscle-relaxing effects as well as to relieve muscle spasms and cramping caused by medical conditions such as multiple sclerosis, traumatic brain injury, and cerebral palsy. Antispasmodic action is now the main indication for the drug. Albright summarized from a study completed by Van Hemert that spasticity was reduced in 16 of the 18 patients treated with baclofen, while only 1 of the 17 patients treated with a placebo had a reduction.

Pharmacology

The precise action of baclofen is not yet fully understood. Baclofen is thought to act as an agonist, or replacement, of the inhibitory neurotransmitters γ-aminobutyric acid (GABA). A comparison of the chemical structure of GABA and baclofen is shown in figure 1. GABA is a muscle-relaxing chemical found throughout the central nervous system (CNS). Children with cerebral palsy and other brain injuries are GABA...
deficient.\textsuperscript{1,34} As an agonist, baclofen is allowed to combine with membrane receptors that are normally influenced by GABA.\textsuperscript{22,35} There are two types of GABA receptors found in the CNS: GABA-A and GABA-B receptors. Baclofen has a direct effect on GABA-B at spinal cord level by impeding the release of the excitatory neurotransmitters used to stimulate a muscle contraction.\textsuperscript{1,9,22,24,35}

It is important for physical therapists and other health care professionals who work with patients on baclofen treatment to understand the mechanism of action. Awareness of how baclofen affects the patient will aid therapists in making educated decisions about rehabilitation programming.

![Chemical structure of GABA and baclofen.](image)

Figure 1. Chemical structure of GABA and baclofen.\textsuperscript{1}

**Oral Baclofen**

Oral baclofen is taken in tablet form. Once ingested into the body, it is quickly absorbed from the gastrointestinal system into the blood stream.\textsuperscript{1,30} From the blood stream the medication must reach GABA receptor sites within the spinal cord.\textsuperscript{2,30} To do this, the drug must first cross the blood-brain barrier. This is often difficult because this barrier is intended to keep drugs and other harmful substances from entering the cerebral
spinal fluid (CSF). High concentrations of baclofen must be present in the blood so that it can push the drug down the concentration gradient, through the blood-brain barrier, and into the CNS.\textsuperscript{30}

The antispasmodic effects of oral baclofen vary considerably among children with cerebral palsy.\textsuperscript{1,9,30} Most children begin baclofen therapy at doses of 5 – 10 mg/day, increasing the dose until a total of 20 - 60 mg is taken per day. Some children have required up to 160 mg/day for an observable effect.

Peak serum levels occur within the body approximately 2 - 3 hours after ingestion and the drug has half-life of 3 - 4 hours.\textsuperscript{1} The daily amount must be divided into several different doses in order to keep peak serum levels within the body constant.

**Intrathecal Baclofen**

The Food and Drug Administration approved intrathecal baclofen for the treatment of cerebral spasticity in June, 1996.\textsuperscript{30} Intrathecal baclofen is usually prescribed when oral baclofen is unsuccessful in controlling spasticity or when the patient experiences disabling side effects, such as extreme drowsiness or fatigue, from the oral drug.\textsuperscript{22,33} However, it is not necessary that oral baclofen be given unsuccessfully before choosing intrathecal baclofen.\textsuperscript{10}

Intrathecal baclofen takes the same action as oral baclofen except that it is administered directly into the CSF.\textsuperscript{1,2,3,9,10,11,12,21,23,27,29} This is an advantage over oral baclofen because it allows the drug to bypass the blood-brain barrier and to have immediate access to the GABA receptors at the spinal cord level.\textsuperscript{1,22,23} This reduces the
systemic effects the drug has on the body. The adverse effects of baclofen will be discussed later.

Intrathecal baclofen is delivered to the patient from a battery operated pump that is implanted within the abdominal wall. The pump resembles a hockey puck and weighs about 6 ounces. A small, subcutaneous catheter runs from this device to the lumbar intrathecal space, where the medication is consistently delivered into the CSF. An illustration of the baclofen pump and catheter is shown in figure 2. The catheter is usually inserted around the L4-5 interspace. The placement of the pump within the body is shown in figure 3.

![Illustration of baclofen pump and catheter](image)

Figure 2. Illustration of baclofen pump and catheter.1,3,23,33

The pump communicates with an external computer via radiotelemetry. Currently, SynchroMed pump, by Medtronic, Inc., is the only commercially available implantable pump that is externally programmable. The external computer can read information stored within the pump concerning the amount of drug remaining in the
pump, the concentration of the drug, and the rate at which the medication is being
delivered to the patient.\textsuperscript{30}

Figure 3. Illustration of pump placement within the body.\textsuperscript{1,3,23,33}

Once the baclofen is introduced into the CSF, it travels up through the spinal cord,
decreasing progressively in concentration.\textsuperscript{1,3} Once the medication has reached T2 it is
about 43\% the concentration it was at T12.\textsuperscript{22} Spasticity in the lower extremities is more
affected by the drug than the upper extremities and the brain.\textsuperscript{22}

Intrathecal administration of the drug requires a smaller dosage to achieve larger
CSF concentrations.\textsuperscript{22} The drug is available in two concentrations 500 or 2000 $\mu$g/ml and
the physician will determine which is appropriate. Dosages range from 150 - 350 μg/day.\textsuperscript{3} The half-life of intrathecally administered baclofen is 5 hours.\textsuperscript{1}

The pump needs to be refilled every 1 - 3 months depending on the rate of infusion.\textsuperscript{7} This is done via a percutaneous injection into the pump.\textsuperscript{7} An audible beep will be heard if the volume of the baclofen drops below a certain point.\textsuperscript{30} Once the battery gets low, usually after 4 - 5 years, the pump will need to be replaced with a fresh one.\textsuperscript{1}

The patient must be thoroughly screened prior to implantation to determine if he/she would be a good candidate for intrathecal baclofen.\textsuperscript{7} This is determined by injecting a test bolus of baclofen into the lumbar CSF. A physical therapist, or another trained professional, will then grade the patient's muscle tone at 2, 4, 6, and 8 hours following the procedure.\textsuperscript{1,7} If a significant reduction in spasticity (at least a 1-point drop on the Ashworth muscle tone scale) is observed, and the patient is free of adverse neurological effects, the patient is recommended to start the therapy.\textsuperscript{7} The trial dose can be effective for determining success of intrathecal baclofen, but it will not necessarily predict the outcome.\textsuperscript{3} If the patient does not respond to the treatment or if complications arise, the implantation is completely reversible and the hardware can be removed without permanent damage to the child.\textsuperscript{7}

**Side Effects and Complications of Baclofen**

This research of current literature has found that the side effects of oral baclofen and intrathecal baclofen are very similar.\textsuperscript{1,3,9,10,12,22,23,33} The side effects of baclofen often include drowsiness and lethargy, fatigue, muscle weakness, nausea, dizziness, diplopia, diarrhea, urinary retention or incontinence, and dry mouth.\textsuperscript{31,32,33} Oral baclofen tends to
have an increased incidence of side effects due to the higher doses at which it is administered.\textsuperscript{22}

Generally only minor complications arise when the drug is given within the therapeutic range.\textsuperscript{30} Most of these can usually be minimized when the dosage is reduced.\textsuperscript{3}

According to Abbott\textsuperscript{30}, more serious complications occur when the medication levels exceed what is appropriate for the patient. With this type of overdose situation extreme sleepiness can lead to respiratory depression and even coma. If the drug is discontinued in time and the patient is put on a ventilator, most long-term effects can be avoided.\textsuperscript{30}

Abrupt withdrawal from baclofen should be avoided if at all possible. Sudden absence of the drug can cause serious hazards such as hallucinations and seizures, and thus can subsequently be a threat to the child’s life.\textsuperscript{31,32,33} Except for when overdose situations occur, baclofen should be reduced slowly.\textsuperscript{30} The physician who prescribed the drug would be the best at recommending how to gradually decrease the dosage.\textsuperscript{32}

According to Campbell et al,\textsuperscript{22} intrathecal baclofen therapy carries a few additional risks to oral baclofen. Since intrathecal baclofen requires an invasive surgical procedure, it involves the risk of anesthetic exposure.\textsuperscript{22} The surgery also increases the risk of infection at the site of incision. Mechanical hardware complications can include catheter kinks, blockage or dislodging of the catheter, and/or pump failure.\textsuperscript{23}

Manufacturers of the earliest pumps admitted to having a 3 - 7\% failure rate; however manufacturers claim the newer models are more reliable and equipped with safety features. If the hardware fails, it needs to be replaced surgically. Kinks in the catheter and other disruptions are common, but they can be easily fixed under local anesthesia.\textsuperscript{22}
Tolerance to both oral and intrathecal baclofen has been noted in some patients on long term therapy.\textsuperscript{1,23} However, this has not been a significant clinical concern because of its infrequency.\textsuperscript{1}

**Advantages and Disadvantages**

One advantage that oral baclofen has over intrathecal baclofen is that it is a non-invasive treatment.\textsuperscript{22} Oral baclofen is taken by mouth and therefore does not require surgical intervention. As explained above, intrathecal baclofen carries the additional risks that accompany the surgical procedure used to implant the pump.\textsuperscript{23} When patients are not in good enough health to endure this type of procedure, oral baclofen may be the better route of treatment. Although intrathecal baclofen carries these additional risks, it is totally reversible and the pump and hardware can be removed without permanent damage to the child.\textsuperscript{7}

Another advantage oral baclofen has over intrathecal, is that the intrathecal baclofen pump needs maintenance.\textsuperscript{7} As stated previously, the pump needs to be refilled with the medication every 1 - 3 months and it needs to be replaced every 4 - 5 years as the battery wears out.\textsuperscript{1,7} There is also the slight chance that the mechanical hardware within the pump or catheter could become displaced or fail.\textsuperscript{23}

The benefits of intrathecal baclofen come with the method of delivery and the amount of drug concentrations administered.\textsuperscript{1} First of all, intrathecal baclofen is delivered directly to the site of action within the CSF; therefore it does not need to cross the blood-brain barrier to be available to the GABA receptors.\textsuperscript{7} This allows the drug to be administered in smaller doses while still achieving relatively larger CSF
concentrations. It is suggested that intrathecal baclofen has a greater efficacy due to its tenfold higher CSF concentrations as compared to oral baclofen. Oral baclofen doses would need to be 100 times higher to produce a tenth of the concentration achieved intrathecally. All of these factors reduce the systemic effects the drug has upon the body.

Another advantage of intrathecal baclofen is that it provides a steady flow of medication, thus avoiding the fluctuation of serum levels within the body. The pump has precise programming capabilities to produce the optimum in spasticity reduction effects. It can be programmed to change dosage levels throughout the day to address the needs of alternating muscle tone. For instance, a higher dose can be administered during the day when spasticity is more prevalent and a lower dose at night when the patients are sleeping and their spasticity is naturally decreased. A lower dose can be given during the day when the patients uses their spasticity for maintaining leg extension during ambulation, with higher doses at night to reduce spasms that may occur at night and disturb sleep.

One important consideration that must be made before deciding on the appropriate method of baclofen treatment is that of the family's geographical location. Intrathecal baclofen pumps are only implanted and refilled in certain locations. If the family is not located near one of these sites a significant amount of travel may be necessitated to keep proper maintenance of the pump. This can be a disadvantage of using intrathecal baclofen. A chart of the specific advantages and disadvantages of oral baclofen are listed in table 2. The advantages and disadvantages of intrathecal baclofen are listed in table 3.
Table 2. Advantages and Disadvantages of Oral Baclofen

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does not require surgical intervention</td>
<td>Must be taken in large doses to be effective</td>
</tr>
<tr>
<td>Maintenance is not required (no hardware)</td>
<td>Drug must cross blood-brain barrier</td>
</tr>
<tr>
<td>Prescription can be refilled anywhere</td>
<td>Increased side effects</td>
</tr>
</tbody>
</table>

Table 3. Advantages and Disadvantages of Intrathecal Baclofen

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication is delivered directly to site of action; bypasses blood-brain barrier</td>
<td>Requires surgical intervention to implant pump</td>
</tr>
<tr>
<td>Can be administered in smaller doses</td>
<td>Requires maintenance; e.g. refilling pump, replacing after battery dies</td>
</tr>
<tr>
<td>Provides steady flow of medication</td>
<td>Need to be located close to or travel to appropriate intrathecal baclofen site for implantation and refilling site</td>
</tr>
<tr>
<td>Decrease in side effects due to lower dosage</td>
<td></td>
</tr>
</tbody>
</table>

Decisions about which type of baclofen therapy would be most appropriate for the patient are ultimately up to the physician and the family. However, physical therapists are often involved in the evaluation and assessment of the patients and often recommend the treatment they believe would be most beneficial for the patient. This is why it is important to understand the reasoning behind each type of spasticity treatment. It is also important because the type of treatment given will help guide the therapists in properly planning the rehabilitation of their patient.
CHAPTER FIVE
REVIEW OF RESEARCH

The purpose of this review is to present information from current literature on the use of baclofen in the treatment of spasticity in children with cerebral palsy. To better understand the function of baclofen and how it is used in reducing cerebral spasticity, a review of cerebral palsy and spasticity is included. The benefits of physical therapy that provide supplemental care to enhance spasticity treatment are also reported. Even though there are some differences in how baclofen is administered, both oral and intrathecal baclofen are effective in treating spasticity in children with cerebral palsy. Several studies supporting this conclusion are summarized below.

Influence of Baclofen in Treating Spasticity in Cerebral Palsy

Oral Baclofen

Van Hemert assessed the effectiveness of oral baclofen in a double-blind study of oral baclofen and a placebo. Van Hemert found that spasticity was reduced in 16 of 18 patients participating in the test group of oral baclofen, while only one of the 17 patients in the control group who were treated with a placebo experienced a reduction in spasticity. In a similar study, Hattab summarized that oral baclofen reduced spasticity in 80% of the 315 patients examined. The same study also concluded that baclofen was equal to or better at reducing spasticity than diazepam.
Intrathecal Baclofen

Subsequent reports by Albright and colleagues\textsuperscript{1,2,3,9,10,11,12,36} have indicated that intrathecal baclofen is effective in reducing spasticity in children. A study with 37 patients with cerebral spasticity, whose mean age was 14 years, found that the muscle tone in the upper and lower extremities decreased significantly. This reduction in spasticity was independent of whether the cerebral spasticity was due to cerebral palsy, anoxia, trauma, or encephalitis.\textsuperscript{1} Another study by Albright et al.\textsuperscript{2} detected a significant increase in the range of motion of the knee following continuous intrathecal baclofen. In the same study, subjects were tested on their performance on four daily skills: communication, hygiene, eating, and dressing. They were graded on a scale of 0 to 5 on each skill and then the grades were averaged. The scores of the subjects on the personal independence scale increased significantly, rising from 2.06 prior to treatment to 2.75 following two years of treatment.\textsuperscript{2}

Campbell, et. al.,\textsuperscript{22} reviewed the effects of intrathecal baclofen on patients with both spinal and cerebral spasticity. In an informal analysis, this study graded the patients’ ADLs on a functional scale. It was found that there was a 60 - 70% improvement in patients’ transfers, self-care, and mobility, and a 10 - 30% improvement in quality of life.

A study by Latash and Penn\textsuperscript{37} studied the effects of intrathecal baclofen upon voluntary movements. It measured the kinematic/dynamic and electromyographic (EMG) patterns of voluntary muscle contractions. Latash and Penn\textsuperscript{37} concluded intrathecal baclofen improved the selectivity of muscle activation in two patients with
cerebral palsy and that single joint movements became smoother with a visible increase in the peak speed of muscle activity.

Penn, Gianino, and York\textsuperscript{40} reported that two cerebral palsy patients with athetosis treated with intrathecal baclofen therapy were found to have a decrease in Ashworth scores by 2 and 2.85 respectively. Similarly, a study examining intrathecal administration of baclofen in patients with spasticity of cerebral origin found a clinically significant reduction in muscle tone (measured on the Ashworth Muscle Tone Scale) in 9 of the 10 children.\textsuperscript{36}

Almedia et al.\textsuperscript{28} described a case of an 11-year-old boy with spastic diplegia who was able to discard his orthoses shortly after starting intrathecal baclofen therapy. Hip and ankle range of motion increased, independence in dressing and transfers improved, and Gross Motor Functional Measure (GMFM) scores were 7.8% above baseline after one year on baclofen therapy.\textsuperscript{28} In a variety of studies, it was found that intrathecal baclofen effectively reduced spasticity, improved voluntary motions, and improved the quality of life in children with cerebral palsy.\textsuperscript{1,2,3,9,10,11,12,36,37,38,39,40}

Conclusion

The reduction of abnormal muscle tone with the aim of improving functional performance has long been a goal of physical therapy.\textsuperscript{22} With the aid of spasticity reduction from baclofen therapy, physical therapists are now able to help children with cerebral palsy achieve a higher functional status. Physical therapists teach children how to function with their reduced spasticity.\textsuperscript{15} This is accomplished by focusing on the child’s abilities and maximizing them so that they are functional for the child.
Baclofen helps the physical therapist treat patients with cerebral palsy by reducing spasticity within the body. This decrease in muscle tone enables the child to produce voluntary muscle movements with less pain and difficulty. Therefore, this allows for the therapist to work with the child on increasing normal posture, increasing strength in the muscles, and developing mobility skills. Before the use of baclofen (or other spasticity reducing treatments) was approved for use in treating spasticity in cerebral palsy, physical therapists focused on the prevention of deformities and contractures. This was accomplished with range of motion and stretching exercises. The use of orthotics and assistive devices were also used to promote proper posture. Although these techniques are still a large part of physical therapy provided today, therapists can now use additional techniques in the rehabilitation programs due to the increase in the potential of patients. Thanks to spasticity treatments such as baclofen, instead of just prevention, therapists can now work with their pediatric cerebral palsy patients to improve functional activities. Range of motion exercises can be modified from passive to active to increase independent range. Once spasticity is reduced, strengthening exercises are used to increase the strength of the muscles that were weakened due to the spasticity. Depending on the level of involvement of disability in the patient, therapists may work with patients on increasing their independence in daily functions and mobility, or they may work with patient and caregiver on decreasing the difficulty of caregiving tasks. Assistive devices such as orthotics or wheel chairs and walkers may either be added, upgraded, or removed completely, depending on the needs of the particular patient. Some patients who once needed a walker for mobility may be able to discard it due to an
increase in independent ambulation. Patients who were not able to move independently previously may be able to add an assistive device to do so.

Answer to the Research Question

How is baclofen used in the treatment of spasticity in children with cerebral palsy to enhance a physical therapy rehabilitation program?

Baclofen, whether it is delivered orally or intrathecally, is used in children with spastic cerebral palsy to decrease the high muscle tone or spasticity within the children’s muscles. The reduction of spasticity allows more opportunity for controlled voluntary movements by patients. This in turn, can lead to an overall increase in children’s functional abilities and quality of life. Physical therapy acts as a supplement to baclofen therapy or vise versa. Baclofen reduces spasticity and physical therapy increases activity and independence. Together baclofen therapy and physical therapy work to help children with cerebral palsy to reach their highest functional status.

Recommendations

Although the studies reviewed have clinically conclusive data measuring several factors supporting baclofen therapy as an effective treatment in reducing spasticity in children with cerebral palsy, research needs to continue.\textsuperscript{1,2,9,11,21,22,26,28,36,37} Since the FDA just recently approved the intrathecal pump for use in cerebral palsy children in 1996, it would be beneficial to determine if intrathecal baclofen therapy is effective over time. Research of long-term oral and intrathecal baclofen therapy in children with
cerebral palsy needs to be followed closely to determine if these treatments are safe and effective.

Another component that would be useful in evaluating the effectiveness of baclofen and physical therapy in the management of cerebral spasticity would be a standardized measurement for grading spasticity reduction. This type of measurement tool would increase the reliability and validity of long-term baclofen studies that used muscle tone grades to reflect effectiveness of spasticity treatments.
REFERENCES


