The Use of Botulinum Toxin as an Adjuvant in Managing Children with Chronic Constipation and Obstructed Defecation

A Thesis

Submitted for Partial Fulfillment of Master Degree in General Surgery

By

Mohammad Reda El-Shahawy
M.B.B.Ch, 2012

Under supervision of

Prof. Dr. Ayman Ahmed Talaat
Professor of General Surgery
Faculty of Medicine – Ain Shams University

Prof. Dr. Ayman Ahmed Albaghdady
Professor of Pediatric Surgery
Faculty of Medicine – Ain Shams University

Dr. Ahmed Bassiouny Arafa
Assistant Professor of Pediatric Surgery
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
2020

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to **ALLAH**, *the Most Kind and Most Merciful.*

I'd like to express my respectful thanks and profound gratitude to ***Prof. Dr. Ayman Ahmed Talaat,*** *Professor of General Surgery Faculty of Medicine – Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to ***Prof. Dr. Ayman Ahmed Albaghdady,*** *Professor of Pediatric Surgery Faculty of Medicine – Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

I am deeply thankful to ***Dr. Ahmed Bassiouny Arafa****, Assistant Professor of Pediatric Surgery Faculty of Medicine – Ain Shams University, for his great help, active participation and guidance.*

Mohammad El-Shahawy

Dedication

Words can never express my sincere thanks to ***My Family*** *for their generous emotional support and continuous encouragement, which brought the best out of me. I owe them all every achievement throughout my life.*

I would like also to thank the ***Patients*** *who agreed willingly to be part of my study and without them; I would not have been able to accomplish this work.*

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List of Abbreviations

Abb.	Full term
Ach	Acetylcholine
ARA	Anorectal angel
ARJ	Anorectal junction
ARM	Anorectal Manometry
BMP	Best Management Practices
BTX A	Botulinum neurotoxin type A
BTX	Botulinum neurotoxin
CFC	Chronic functuonal constipation
CLC	Chloride channel
CTT	Colonic transit time (CTT)
DRE	Digital rectal exam
ESPGHAN	The European Society for pediatric Gastroenterology Hepatology and Nutrition
FC	Functional constipation
GI	Gastrointestinal
IAS	Internal anal sphincter
LES	Lower esophageal sphincter
NASPGHAN	North American Society for Pediatric Gastroenterology, Hepatology and Nutrition
NICE	National Institute for health and Clinical Excellence
NMJ	Neuromuscular junction
ODS	Obstructed defecation syndrome
PACCT	The Paris Consensus on Childhood Constipation Terminology
PCL	Pubococcygeal line
PEG	Polyethylene glycol

List of Abbreviations Cont...

Abb.	Full term
RAIR	Rectoanal inhibitory reflex (RAIR)
SBL	Senna laxative
SNAP-25	Synaptosomal-associated protein of 25 kd
SNM	Sacral neuromodulation

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INTRODUCTION

Functional constipation (FC) is a common pediatric healthcare problem worldwide, with reported prevalences ranging between 0.7 and 29.6 % and a mean female-to-male ratio of 2.1:1. FC is characterized by infrequent bowel movements, hard and/or large stools, painful defecation, and fecal incontinence, and is often accompanied by abdominal pain. These symptoms can have a significant impact on a child's well-being and health-related quality of life ***(Koppen et al., 2015).***

Functional constipation is one of the commonest digestive complaints in children, which has become quite a proportion in public health problem. Like many other functional disorders, its etiology, pathophysiology and prognosis are ill-understood. This made its management a current work in progress field to reach a better satisfying outcome for the children and their families ***(Rajindrajith and Devanarayana, 2011).***

As regards the clinical diagnosis of FC; the evaluation primarily consists of a thorough medical history and a complete physical examination. Additional investigations are not necessary in most cases. The physician should seek to understand the patient's perception of their current bowel habit, compared to the past and should include stool frequency, form and the ease of passage of stool. The use of the Bristol Stool

Chart may aid the patient in their description of the stool form ***(Thayalasekeran et al., 2013).***

However, family physicians must be alert for red flags that may indicate the presence of an uncommon but serious organic cause of constipation, such as Hirschsprung's disease (congenital aganglionic megacolon), pseudo-obstruction, spinal cord abnormality, hypothyroidism, diabetes insipidus, cystic fibrosis, gluten enteropathy, or congenital anorectal malformation ***(Biggs and Dery, 2006).***

Treatment of functional constipation involves disimpaction using oral or rectal medication. Polyethylene glycol is effective and well tolerated, but a number of alternatives are available. After disimpaction, a maintenance program may be required for months to years because relapse of functional constipation is common. Maintenance medications include mineral oil, lactulose, milk of magnesia, polyethylene glycol powder, and sorbitol ***(Koppen et al., 2015).***

Despite treatment, only 50 to 70 percent of children with functional constipation demonstrate long-term improvement, hence the search for novel methods of treatment ***(Biggs and Dery, 2006).***

AIM OF THE STUDY

This study aimed to evaluate the effectiveness of adding anal Botox injection to those already followed management plan for pediatric age group suffering from chronic functional constipation.

Chapter 1

DEFINITION AND PATHOPHYSIOLOGY OF CHRONIC FUNCTIONAL CONSTIPATION IN PEDIATRICS

Chronic functional constipation prevalence:

Functional constipation (FC) is a common disorder in children worldwide. Available data show that its prevalence is higher in the South Asian region and in South America, than in any other part of the world ***(Rajindrajith et al., 2016).*** While constipation occurs in all continents, currently there is a lack of prevalence data in children from Africa and Oceania ***(Levy et al., 2017).***

The prevalence varies according to age groups. The peak incidence of constipation occurs between 2 and 4 years of age, when the potty training starts. A recent systematic review found that the median prevalence of constipation in children was 12%. The incidence of constipation reported in infants varies between 0.05% and 39.3% but based on expert consensus the prevalence is estimated at 15%. At this age, feeding is a major contributing factor ***(Levy et al., 2017).***

Gender specific prevalence of constipation also varies between studies. Some studies have reported no difference in prevalence of constipation between girls and boys, while others

found significantly higher prevalence in girls ***(Rajindrajith and Devanarayana, 2011; Levy et al., 2017).***

Defecation physiology:

In order to understand the physiology of defecation, deep knowledge of the anatomy of the rectum and anal canal is very important. The rectum is the last part of the large intestine, located in the lower pelvis. Rectal function is crucial for retention of stool (continence) and for evacuation (defecation). The rectum in adult measures about 15–17 cm in length, descending along the sacrococcygeal concavity and passing through the pelvic floor to the anal canal. The major part is called the rectal ampulla, which is a wide segment, with a perimeter that can extend to more than 15 cm. The lowest and narrowest part is the anal canal. The anorectal junction is formatted by the constant traction of the puborectal sling. The levator ani muscle, formed by the iliococcygeus, the pubococcygeal, and the puborectal muscles, serves as the pelvic floor. The relaxation of levator ani, and mainly the puborectalis muscle, the perineum and contraction of the lower abdomen, and the relaxation of the anal sphincter, all work in tandem in order to provide a normal defecation. Distention of rectal wall stimulates contractions of colon and rectal wall, mediated by the parasympathetic defecation reflex. Thus, phasic rectal contractions start and tone increases, formatting a conduit shape of rectum rather than a reservoir **(Figure 1)** ***(Palit et al., 2012).***