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Effects of adding interferential current (IFC) in standard therapy (Lactulose) in cerebral palsy children with constipation: A randomized controlled trial

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***Abstract*---**To determine the addition of interferential current (IFC) in treating constipation in children with cerebral palsy (CP), is more effective than standard therapy (lactulose). An experimental study with a single blind randomized controlled trial. Prior to receiving therapy, the subjects examined the baseline data regarding the Constipation Scoring System (CSS). The total subjects were 18 children with CP who had constipation according to ROME IV criteria, which were divided into two groups, the control group who received standard therapy (lactulose) and the intervention group who received lactulose plus IFC therapy with a frequency of 4000-4100 Hz,

duration 20 minutes, 3 times a week for 1 month. A week after the last IFC, CSS was re-evaluated to assess outcomes. Data were analyzed computerized with SPSS v20.0. There was an improvement of CSS in CP with constipation who received additional IFC (*P*= .002) and lactulose *P*= .014). There was no significant difference of CSS between the two groups after therapy (*P*= .917). The same conclusion was also obtained in delta of CSS between the two groups before and after therapy (*P*= .11), but based on the effect size, the addition of IFC had a large effect (*D*= 1.66) while standard lactulose had a moderate effect (*D*= .6). The addition of IFC to standard therapy (lactulose) is relatively safe and has a larger effect size than lactulose only so that IFC can be an alternative supporting therapy in cerebral palsy with constipation to provide a better clinical response.

***Keywords*---**Interferential Current, Lactulose, Constipation, Cerebral Palsy, Children.

Introduction

The estimated prevalence of children with CP worldwide is between 1.5 to 4 per 1000 live births with an average of 2 per 1000 live births (Stavsky et al., 2017). Gastrointestinal motor dysfunction such as gastroesophageal reflux (GERD), dysphagia, vomiting, and chronic constipation are known to occur frequently in children with varying degrees of central nervous system damage. Impaired neural modulation of gut motility, prolonged colonic transit, and low fiber and fluid intake are thought to play an essential role in constipation in children with neurological disorders. The survival of children with severe neurological disorders such as cerebral palsy is a significant challenge for health workers. Moreover, diagnostic delay is frequently found (Martinelli & Staiano, 2017). Constipation is frequently overlooked in children with cerebral palsy, as it is viewed as a natural consequence of the disability and a result of other factors that are prioritized in therapy, such as seizures and postural deformities. The pain and discomfort that frequently accompany chronic constipation affect behavior and reduce the overall quality of life (Elawad & Sullivan, 2001). Chronic constipation affects between 25% and 75% of children with cerebral palsy (Martinelli & Staiano, 2017).

Lactulose is reported to be effective and safe in children with chronic constipation (Cao & Liu, 2018). However, lactulose is only temporary in relieving symptoms of constipation, and some side effects can occur (Elawad & Sullivan, 2001; Sullivan, 2008). Since IFC has been shown to cause diarrhea when used to treat urinary incontinence (Hosker et al., 2000; Emmerson, 1987), it is assumed that IFC can also be used to treat constipation. Following that, a study was conducted on eight children who suffered from severe constipation. It was discovered that IFC administered for 20-30 minutes per session increased defecation in five of eight children and stopped soiling in seven of eight children, with therapeutic effects lasting more than three months in some children (Chase et al., 2005). IFC is used to treat constipation in children with myelomeningocele and improves bowel control significantly in terms of CSS (Azam, 2017). The effect of IFC on cerebral palsy is unknown. Therefore, this study examined the effect of supplementing

standard lactulose therapy with IFC on constipation in children with cerebral palsy.

Methods

This research was conducted at the Outpatient Polyclinic of the Medical Rehabilitation Installation of the Regional General Hospital (RSUD) Dr. Soetomo Surabaya for 17 months, from February 2020 to July 2021.

Study Design and Treatment

The study employed an experimental design with a control and treatment group (controlled trial). The data were collected before and after treatment (pre/post-test) randomly (pre-test and post-test with open trial single-blind Randomized Controlled Trial (RCT)). While participants were aware of the treatment they received, research staff were unaware of the treatment received by each group when completing study measurements with participants. Randomization was used to assign subjects who agreed to participate in the study to the control or treatment group. Prior to initiating therapy, the research staff collected baseline data on the subject's basic characteristics and CSS. In general, subjects received lactulose therapy as standard therapy, while the treatment group received IFC therapy. The lactulose preparations were carried out by the Pharmacy Installation of RSUD Dr. Soetomo with the trademark LACONS in bottles, @ 60 mL. Lactulose was administered by parents at a dose of 1-3 mL/kgBW/day orally, given 2x/day for six days. The IFC equipment is located at the Medical Rehabilitation Polyclinic, RSUD Dr. Soetomo Surabaya. IFC therapy (brand ENDOMED 982) with a dose of carrier frequency 4000-4100 Hz, beat frequency 100 Hz, amplitude 1-50 mA, sweep mode was carried out by the researchers three times a week with a duration of 20 minutes, with a total of one child undergoing 12 treatments (Ayuningrum et al., 2022). One week after the last therapy, CSF was re-evaluated. The side effects of giving lactulose and IFC therapy were managed according to the procedures in force at RSUD Dr. Soetomo

Table 1. Inclusion/Exclusion Criteria

Inclusion criteria	Exclusion criteria
1. Children aged 4 years 0 days to 17 years 364 days at the time of the study. 2. Diagnosed with cerebral palsy by a consultant pediatric neurologist or a specialist in physical medicine and rehabilitation at RSUD Dr. Soetomo. 3. Experiencing symptoms of constipation according to ROME IV criteria. 4. For at least 72 hours prior to treatment, refrain from taking drugs that can cause constipation (muscle relaxants, antiemetics, antacids, antidiarrheals, antidepressants, antipsychotics, antispasmodics, analgesics, decongestants, iron supplements), except those used to treat epilepsy, hypertension, and bronchodilation.	Patient with: 1. Congenital anatomic abnormalities of the urogenital area, including Hisprung's disease, spina bifida, anorectal malformations, urethral strictures. 2. Down syndrome or hypothyroidism. 3. Gastrointestinal bleeding, intestinal perforation, ileus obstruction, inflammatory bowel disease, and toxic megacolon. 4. Metal implants or pacemakers in the abdominal area. 5. Open wounds in the abdominal and thoracic region. 6. History of surgery on the stomach 7. Malignancy. 8. Patients with a history of allergy to lactulose and the electrodes used in this study.

Patient Population

Children who are eligible to participate in this study are those aged 4-18 years, diagnosed with cerebral palsy with symptoms of constipation according to ROME IV criteria (Muhardi et al., 2022; Hyams et al., 2016), not taking drugs that can cause constipation and without any congenital anatomic abnormalities, and all conditions that contraindicate the therapy used in this study. The full inclusion/exclusion criteria are presented in Table 1.

Outcomes

The primary assessment is to determine the improvement of constipation complaints using an assessment system designed to simplify and objectively quantify the severity of complaints, namely the CSS, which consists of eight items, including frequency of defecation, difficulty or pain during defecation, feelings of incomplete defecation, abdominal pain, and time required to defecate. The amount of time spent on the toilet, the number of laxatives or digital aids/enema used, the number of failed evacuation attempts per 24 hours, and the duration of constipation symptoms. The Wexner score (minimum: 0; maximum: 30) had a high correlation with the objective physiologic findings and thus served as the basis for evaluating the constipated patient (Alame & Bahna, 2012). The CSF was assessed before and one week after the last therapy was administered, along with the child's basic characteristics (age, gender, weight, height, and body mass index (BMI)). Any adverse events associated with the

administration of lactulose and IFC therapy were documented on the data collection sheet.

Statistical Analyses

The data were analyzed and computerized using SPSS v20.0 and various tests. Shapiro-Wilk was used to determine the normality of the data. A parametric analysis test is used if the data are normally distributed; otherwise, a nonparametric statistical analysis test is used. To compare CSS before and after treatment in each group (control and treatment), the paired t-test was used if the data were normally distributed; otherwise, the Wilcoxon Signed-Rank test was used. The independent t-2 test (independent t-test) was used to compare the post value and the difference between the pre and post-values between the treatment and control groups if the data were normally distributed, or the Mann Whitney test if the data were not normally distributed. If $p < 0.05$, the p-value is considered significant. To compare the efficacy of increasing CSS between the treatment and control groups, the effect size (Cohen's d) was calculated.

Results

A total of 18 research subjects were divided into two groups: those who received standard lactulose therapy alone and those who received standard lactulose therapy plus IFC therapy. All research subjects in both the control and treatment groups can complete the study to the conclusion. At the conclusion of the study, data on nine individuals from the control group and nine individuals from the treatment group were analyzed (Figure 1).

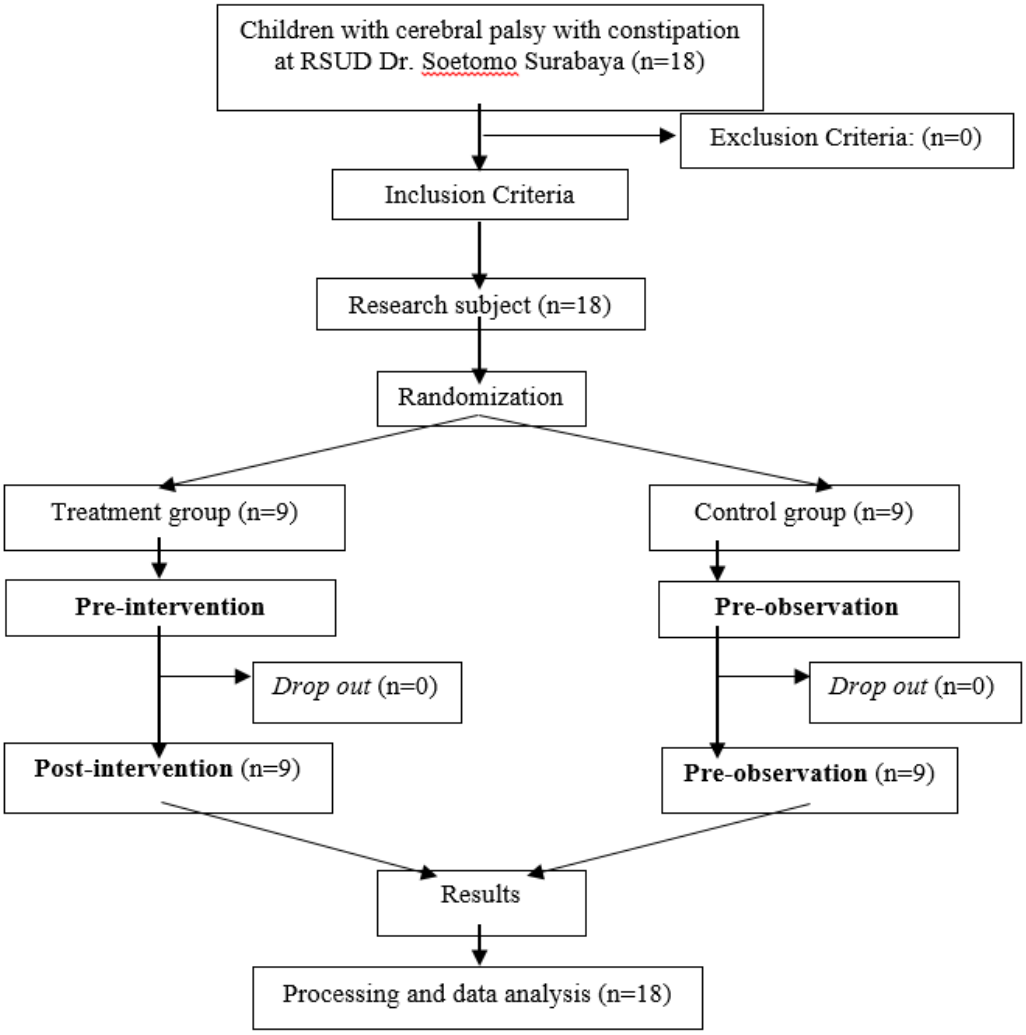

Figure 1. Subject recruitment flow

Table 2. Normality and Homogeneity Test of the Characteristics of Research Subjects in Pre-treatment for Both Groups

Variable	Treatment (n = 9) Means ± SD	*p-value* (Normality)	Control (n = 9) Means ± SD	*p-value* (Normality)	*p-value* (Homogeneity)
Age (year)	7.89 ± 3.23	0.091	5.78 ± 1,39	0.348	0.091
Sex (L/P)	4L.5P		7L, 2P		0.165
Weight (kg)	16.61 ± 7.70	0.001	17.44 ± 6.89	0.449	0.812
Height (cm)	107.78 ± 16.78	0.166	100.22 ± 14.91	0.655	0.328
BMI (kg/m^2)	13.88 ± 2.50	0.492	16.86 ± 3.53	0.120	0.056
CSS pre (score)	13.11 ± 2.57	0.053	10.22 ± 3.66	0.088	0.071

Table 3. CSS in Both Groups (Pre and Post-Treatment)

	Treatment (n=9)			Control (n=9)		
	Pre	Post	*p-value*	Pre	Post	*p-value*
CSS (score)	13.11±2.57	7.44±4.09	0.002*	10.22±3.67	7.66±4.74	0.014*

* Significant if p-value < 0.05

Table 4. CSS Post Administration of Therapy in Both Groups and Delta CSS

	Treatment (n=9)	Control (n=9)	*p-value*
CSS post (score)	7.44 ± 4.09	7.67 ± 4.74	0.917
Δ CSS (score)	4.67 ± 2.00	3.11 ± 1.90	0.11

* Significant if p-value < 0.05

A normality test was performed on the basic characteristic data using the Shapiro-Wilk test before statistical analysis. The normality test results showed that all the basic characteristic data had a normal distribution except for body weight in the treatment group, followed by homogeneity test with parametric statistical test (independent sample t-test) (Table 2). There was no significant difference between the mean values of each initial characteristic of pre-treatment in the two groups ($p > 0.05$). This means the group is homogeneous.

Based on table 3, in the treatment group, the mean CSS before being given IFC therapy was 13.11+2.57, and the mean after being given IFC therapy was 7.44+4.09. Based on the parametric statistical test (paired t-test), there was a significant improvement in CSS in the treatment group ($p = 0.002$). In the control group, the mean CSS at the initial assessment was 10.22+3.67, and the mean at the final evaluation was 7.66+4.74. Based on the parametric statistical test (paired t-test), there was a significant improvement in CSS in the control group ($p= 0.014$).

Based on Table 4, the CSF in the treatment group after giving standard therapy plus IFC for 1 month (12x) was 7.44 + 4.09, while the control group after giving

standard therapy was 7.67 + 4.74. Based on the independent sample t-test statistical test, there was no significant difference between CSS in the two groups (p = 0.917).

Based on Table 4, the mean CSS delta in the treatment group given standard therapy plus IFC for 1 month (12x) was 4.67 + 2.00, while the control group was 3.11 + 1.90. Based on the independent sample t-test statistical test, there was no significant difference in the difference in CSS improvement between groups (p = 0.11).

The magnitude of the effect size after IFC therapy for one month was calculated by Cohen's d. The result of effect size in the treatment group is 1.66, which indicates that therapy in this group has a significant effect on improving CSF, while the effect size result in the control group is 0.60, which indicates that therapy in this group has a moderate effect on improving CSF.

Discussion

In this study, there was no significant difference in the sex characteristics of the research subjects between the treatment and control groups with p = 0.165. The proportion of men compared to women is more with a ratio of 11:7. In Brazil, the prevalence of CP with constipation in men is 59.7% and in women is 40.3% (Ferreira *et al.*, 2019). Another study stated that the prevalence in males was 47.1% and 52.9% in females (Veugelers *et al.*, 2010). In Pakistan, the prevalence of cerebral palsy with constipation is higher in women than in men (42.9% vs. 39.3%) (Nadeem & Awan, 2019). Both sexes had the same brain volume, but females showed larger cortical folds, evidence of sexual dysmorphism. Genetic polymorphisms cause CP boys to be more susceptible to worsening conditions related to the underlying disease or current conditions (Ferreira *et al.*, 2019).

The mean age of the subjects in the treatment group was 7.89 + 3.23 years with an age range of 4.5-13 years, while the control group was 5.78 + 1.39 years with an age range of 4-8 years. There was no significant effect between the age of the subjects in the treatment and control groups, p-value = 0.091. Research by Park et al. obtained a mean age of 5.0 ± 2.9 years in the subject of spastic type CP (Park *et al.*, 2004). Other studies show a greater mean age, namely 7.00 ± 5.09 years and 7.33 ± 5.24 years (Tarsuslu *et al.*, 2009). The mean age of children with CP is 9 years 6 months ± 4 years 6 months (Veugelers *et al.*, 2010).
Body Mass Index (BMI) is still used to assess growth, body composition, and nutritional status in the CP population. According to WHO, the expected target BMI ranges from 18.5-24.9 kg/m2 (Ferreira et al., 2019). BMI used for 137 CP children (2-18 years) and found in ambulated children (GMFCS level I, II, III) showed a trend towards a higher prevalence of obesity, while underweight was more common in non-ambulated children (GMFCS level IV and V) (Hurvitz et al., 2008). In this study, the mean BMI of the treatment group was 13.88 + 2.50 kg/m2 with a BMI range of 10.4-19.2 kg/m2, while the control group was 16.86 + 3.53 kg/m2 with a BMI range of 13-22.3 kg/m2. The BMI characteristics of the subjects of this study were not found to be significantly different between the two groups with p = 0.056 and the mean BMI of the two groups was below the normal range or underweight. This is in accordance with the proportion of non-ambulated

subjects who were more than ambulated subjects in this study with a ratio of 11:7.

Oropharyngeal dysfunction, difficulty in swallowing and chewing are some of the disabilities of children with CP (Mulyadi et al., 2020). This contributes to low food intake, which can lead to malnutrition (Nadeem dan Awan, 2019). Diet counseling should be given to parents and caregivers by prioritizing fiber such as vegetables, whole grains, and whole grains, which can reduce constipation (Ferreira *et al.*, 2019).

The Constipation Scoring System experienced a statistically significant improvement in the treatment group (p-value 0.002). The results of this study are in line with the study conducted by Azam, in children subject to myelomeningocele, there were significant improvements in bowel control seen from CSS after being given IFC therapy with a beat frequency of 5-10 Hz, duration of 200 microseconds, and repeated within 6 seconds with an amplitude of 0-20 mA, for 60 minutes per session 3 times a week for 12 weeks of therapy (Azam, 2017). In this study, the duration of therapy for 4 weeks, with a frequency of 3 times a week, was able to improve CSS. This is in accordance with previous research by Chase et al., which provides IFC 3-4 weeks in children with chronic constipation (Chase et al., 2005).

Sacral reflex modulation occurs when the differential stimulation technique is used to improve bowel control (Kajbafzadeh *et al.*, 2012). The colon is activated by parasympathetic innervation (via the vagus and pelvic nerves originating from the sacral segments S2-S4) (Varma, 1992). To facilitate defecation, the parasympathetic innervation transports motor nerves to the colon, rectum, and relaxation of the internal anal sphincter, followed by the external anal sphincter and puborectalis (Dubrovsky dan Filipini, 1990).

Stimuli are applied via surface electrodes to T9–L2, which is a sympathetic flow. Most children reported an urge to defecate following the intervention, indicating that sensory (afferent) fibers have been activated (Chase *et al.*, 2005). Electrical stimulation may facilitate neuroplasticity and motor learning by increasing afferent input synchronized with motor and sensory information (Roni et al., 2020). The enteric nervous system, located in the myenteric plexus or submucosa, sends signals to the gastrointestinal tract's muscle layer, causing the neurotransmitter serotonin 5-hydroxytryptamine to be released (Andrews dan Storr, 2011; King *et al.*, 2010). Interstitial cells, also known as Cajal cells, are critical for the normal movement of the colon and mediate the transmission of signals from nerves to muscles (Frattini dan Nogueras, 2008). By observing the effect of IFC, which appears to increase gradually and clearly persists for months after therapy is stopped, it is clear that the cellular system, which includes Cajal cells, is expanding (Yik *et al.*, 2013). The effects of IFC can last up to one month in five out of six children and three months in three out of six children (Chase, 2005).

Constipation Scoring System before and after therapy showed statistically significant improvement in the control group (p-value 0.014). According to a previous RCT study conducted by Cao and Liu with subjects of 100 children aged

2-6 years with chronic constipation who were given lactulose therapy at a dose of 5 ml/day (n=50) and placebo (n=50) for six weeks, lactulose showed better results in defecation frequency (P<.01) and stool consistency (P<.01) but not abdominal pain (P=.24) and flatulence (P=.44) compared to placebo (Cao & Liu, 2018). Lactulose, a synthetic disaccharide that cannot be absorbed, will be 100% metabolized by colonic bacteria to form fatty acids that stimulate colonic peristalsis by pulling water osmotically into the intestinal lumen, causing water retention, keeping stools soft, and increasing the frequency of defecation (Sullivan, 2008).

Both groups showed a positive effect in improving CSF, but there was no significant difference in CSF after treatment between the two groups (p-value after CSF = 0.917). The same conclusion was also obtained on the difference in CSS before and after therapy between the two groups (p-value Δ CSS = 0.11). However, if using the effect size calculation, it appears that the total value in the treatment group (1.66) is higher than the control group (0.6). This indicates that the addition of IFC therapy to standard therapy results in a better clinical response. This is similar to the results of previous studies by Chase et al., which showed that chronic constipation in children who failed laxative therapy improved after IFC therapy (Chase et al., 2005). Similarly, in the study of Kajbafzadeh et al., IFC in myelomeningocele patients with constipation who had failed conventional therapies such as diet modification and laxatives resulted in 73% of symptoms diminishing immediately after IFC and 53% of the effect lasting up to 6 months (Kajbafzadeh et al., 2012). In the larger cohort, the IFC was also able to improve quality of life scores, Holschneider and Templeton (Clarke et al., 2009).

Since constipation is frequently chronic, the outcome must be evaluated over the medium to long term. Only one study assessed outcomes after three months in the Cochrane systematic review, and half of the studies assessed outcomes after one month or less. If the research period is brief, it is difficult to conclude that the efficacy of PEG or lactulose can be sustained over time (Gordon et al., 2012). Additionally, lactulose is more likely to cause adverse reactions such as flatulence, abdominal pain, or cramping. Chronic use can also result in electrolyte imbalances (Gordon et al., 2012; Koppen et al., 2015). PEG also has similar side effects, namely vaginal incontinence (especially during disimpaction), flatulence, abdominal pain, and nausea (Koppen et al., 2015). This complicates the long-term use of lactulose and PEG.

Conclusion

This study indicates that when IFC therapy is added to standard therapy, the clinical response is improved, and there are no adverse effects, implying that IFC can be used as supportive therapy in cerebral palsy with constipation. Suggestions for future research include the need to monitor the effects of IFC over a longer period in order to ascertain their resilience.

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Conflict of Interest
All authors declared no conflict of interest.

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