"EFFECTIVENESS OFMODIFIED CONSTRAINT–INDUCEDMOVEMENT THERAPY COMPARED TO HAND ARM BIMANUAL INTENSIVE THERAPY ON QUALITY OF UPPER EXTREMITY FUNCTION IN HEMIPLEGIC CEREBRAL PALSY CHILDREN – AN EXPERIMENTAL STUDY "

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ABSTRACT

BACKGROUND : Cerebral palsy (CP) is the most frequent cause of physical disability in children.Hemiplegic cerebral palsy is characterized by motor impairments largely confined to one side of the body. Nevertheless, even the "less-affected" upper extremity (UE) has subtle motor impairments and importantly, bimanual deficits can be seen when children with hemiplegia are asked to perform tasks that involve specific spatial-temporal demands between the two hands.

OBJECTIVES : To assess the significant difference of effectiveness of modified constraint induced movement therapy compared to ham arm bimanual intensive therapy on quality of upper extremity function in hemiplegic cerebral palsy children.

METHODOLOGY : An experimental study was conducted on 30 subjects of age group 4 - 8 years, fulfilling the inclusion criteria. The quality of upper extremity skill test was performed and score noted down. T test was used to examine the relationship between the parameter evaluation.

RESULTS : Pre post comparison in grip Group A & group B shows statistically significant with p value of 0.000, 0.000 respectively. Pre post comparison in PRTEE Group A & group B showsstatistically significant with p value of 0.000, 0.000 respectively.

CONCLUSION :From our study we conclude that majority of the group A & group B, both were shows improvement as compared with the control group c, but group A were more significant as compared with the group B.

KEY WORDS: CP, QUEST, motor skill etc.

INTRODUCTION

The term cerebral palsy refers not to a specific disease entity, but rather to a group of conditions with variable severity that has certain developmental features in common. The formal definition, delineated by an international panel in the mid2000s, is as follows: "Cerebral palsy describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances

that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication and behaviour, by epilepsy and by secondary musculoskeletal problems". The nuances of this definition are parsed in more detail elsewhere.[1]

What links all people with cerebral palsy are the clinical and functional onset of symptoms in early development, the high probability that the symptoms have an effect on the whole life course and the current lack of a definitive cure. Almost all children with cerebral palsy survive to adulthood. In fact, survival rates among even the most functionally compromised young people with cerebral palsy have remarkably improved over the past few decades, as demonstrated by population-based data from the California Department of Developmental Services[2,3], but remain lower than typically developing controls. Cerebral palsy has traditionally been identified as part of a spectrum of neuro disability, with the imperative to understand aetiological forces, potential primary prevention and early therapies that can mitigate the effects of brain impairment on function. However, given that cerebral palsy presents early in infancy and persists throughout an individual's lifetime, the disorder needs to be thought of and managed in the context of development, functioning and the family.[4] Interventions are necessary to promote and enhance child and family functioning and wellbeing to prevent secondary musculoskeletal impairments and to help families plot a successful life-course plan for their children (and themselves) in the face of developmental differences.

The past 25 years have been the most exciting and productive time in the field since William J. Little first described what we now call cerebral palsy.[4] However, despite neuroscientific breakthroughs described in this Primer, and discussed in detail elsewhere,[5] many unanswered questions remain. Among the most compelling challenges for the twenty-first century is the need to chart and understand the life course of adults who have grown up with a 'children's condition' and whose adult lives remain affected by the condition.[6] Hopefully this Primer on cerebral palsy will begin a new and fruitful dialogue, and stimulate a new generation of young practitioners and scientists to work towards answers to these basic clinical and scientific issues.

Cerebral palsy is the most common motor disability of childhood. Population-based registries of cerebral palsy, largely in Australia and Europe, have historically found cerebral palsy prevalence ranging from 1.5 to 2.5 per 1,000 live births.[7] However, recent studies in the United States,[8] Taiwan[9] and Egypt[10] have found prevalence rates above 3 per 1,000 live births in people 4–48 years of age. The increased survival of very premature infants has contributed to a modest increase in the prevalence of cerebral palsy in developed countries over the final quarter of the twentieth century that now appears to be levelling off.[11]

The earliest clinical description of children with cerebral palsy recognized that most patients had two factors in common: premature birth and difficult labour with neonatal asphyxia (or oxygen deprivation).[4] Both factors were considered direct causes of cerebral palsy, but are now considered reflective of factors operating earlier in development.[12] Infants who experience fetal inflammation, for example, are more likely to be born prematurely and to develop cerebral palsy; fetal inflammation probably contributes independently to both outcomes.[13] Indeed, although newborns with Down syndrome are five-times more likely to experience birth depression, as indicated by a low (< 6 out of 10) Apgar score (which evaluates the baby's condition based on skin colour, heart rate, reflexes, muscle tone and breathing rate and effort)
5 minutes after birth, we do not ascribe Down syndrome to birth asphyxia.[14]

Preterm birth is the most important risk factor for cerebral palsy. Risk increases steadily with declining gestational age at birth, with a modest increase in risk already detectable as early as
38 weeks of gestation.[15] The risk in infants born before 28 weeks of gestation is approximately 50times that of full-term births.[16] Among premature births, the most important risk factor is evidence of white matter damage on cranial ultrasonography or other brain-imaging modalities. Infants with evidence of persistent damage, such as single or multiple brain lesions (cystic or cavitary) or ventriculomegaly (dilatation of the lateral brain ventricles), have a roughly 50% risk of developing cerebral palsy.[17] Perinatal factors that have been associated with the development of cerebral palsy in premature infants include: chorioamnionitis (intra-amniotic infection) or other evidence of perinatal inflammation, especially when sustained postnatally[18]; transient hypothyroxinaemia (low maternal thyroid hormone levels)[19]; and hypocapnia (reduced carbon dioxide levels, which can induce cerebral vasoconstriction) in association with mechanical ventilation.[20] Some of these factors are also associated with the risk of developing white matter damage, but whether all of these associations are directly causal is unclear. The finding that intra-uterine growth retardation and postnatal inflammation have additive effects on the risk of cerebral palsy development in premature infants indicates that combinations of biological processes could also be involved in acquiring this condition.[21] Several recent trials have demonstrated that cerebral palsy is reduced by approximately 30% in premature infants whose mothers received magnesium sulfate during labour (see below).[22]

In full-term infants, who account for the majority of cases of cerebral palsy, signs of birth depression, such as low Apgar score, also correlate with an increased risk of developing cerebral palsy.[23] However, in the absence of birth depression, many other complications of labour probably do not raise the risk of cerebral palsy.[24] Imprecision regarding the proportion of cerebral palsy that is causally attributable to birth asphyxia in part reflects the difficulty of rigorously defining birth asphyxia[25], but only ≤10% of children who develop cerebral palsy clearly experienced major birth asphyxia. Various perinatal abnormalities

often attributed to birth asphyxia — such as meconium passage, need for caesarean section, neonatal seizures and respiratory difficulties after birth — are correlated with cerebral palsy, but may reflect other underlying biological processes that occur earlier in development. Birth defects outside of the brain, such as cardiac and skeletal abnormalities, are found with much greater frequency in cerebral palsy. A most important recent advance in cerebral palsy prevention is the discovery that 72 hours of brain or body cooling in full-term infants with birth asphyxia will reduce the prevalence of cerebral palsy.[26]

Other factors that are associated with a higher risk of cerebral palsy at term include placental abnormalities and fetal growth retardation.[27] Neonatal hyperbilirubinemia (excessive levels of bilirubin in the blood owing to red blood cell breakdown) can cause dyskinetic cerebral palsy at any gestational age, but is now fortunately very rare in developed countries as a result of preventive interventions, including exchange blood transfusion, phototherapy and, most importantly, Rho (D) immune globulin therapy (that is, maternal anti RhD immunoglobulin treatment to prevent Rhesus disease in the foetus or newborn).[28]

Approximately 10–15% of children with cerebral palsy have a brain malformation other than a brain lesion, which usually requires neuroimaging to detect.[29] A small percentage of cerebral palsy (< 5%) in full-term infants is a consequence of perinatal ischaemic stroke; this is mainly associated with hemiplegic cerebral palsy in which only one side of the body is affected.[30]

Given that socioeconomic status is strongly associated with preterm birth and low birth weight, one might expect that cerebral palsy shows a similar gradient, and it does seem to.[31,32] The prevalence of cerebral palsy seems to be higher in African-American infants in the United States, which may be explained by the higher rate of preterm birth in African-American women.[33]

Of seven population-based studies of the epidemiology of cerebral palsy in low-income and middle-income countries reviewed by Durkin[34], one study showed much lower prevalence than in developing countries, two were in the same range and four showed higher prevalence's, ranging from 4.4 to 10 per 1,000 live births or children. This observation hints to an increased risk of cerebral palsy in low-income and middle-income countries versus high-income countries despite the fact that many who experience perinatal brain-damaging events that might lead to cerebral palsy in developing countries do not survive infancy. In some regions of the world, children may be born with a neurological syndrome that strongly resembles spastic diplegia — a type of cerebral palsy — due to severe iodine deficiency. Neonatal jaundice caused by high levels of bilirubin remains a major risk factor for cerebral palsy in developing countries, as is perinatal infection.

Little is known of the distinct epidemiology of the different subtypes of cerebral palsy. Hemiplegic cerebral palsy, as noted above, at times represents the effects of a perinatal ischaemic stroke, but can occur in premature infants who have unilateral porencephalic cavities
(or cysts in the cerebrum filled with cerebrospinal fluid) following white matter damage. Spastic diplegia, which is usually accompanied by periventricular white matter loss, is linked to both preterm birth and fetal growth retardation at term. The combination of spastic quadriplegia with dyskinesia in term infants has been associated with severe birth asphyxia.

Dyskinesia accompanied by sensorineural hearing loss is the form of cerebral palsy most often seen with kernicterus (a form of brain damage due to high levels of bilirubin). The rarest form of cerebral palsy, ataxic cerebral palsy, sometimes indicates the presence of a cerebellar malformation.

Cerebral palsy is a clinical entity that implies much heterogeneity in terms of aetiology and pathophysiology.[1] Our understanding of the pathways leading to cerebral palsy has gained much from epidemiological, neuroimaging and post-mortem studies and animal models. However, a comprehensive understanding of the mechanisms that underlie the many features and profound phenotypic variations of cerebral palsy to enable specific strategies for management and primary and secondary prevention is yet to emerge.

Cerebral palsy is associated with various motor defects, which largely depend on the location of the brain lesion. Disruption of cortico– striatal–thalamic–cortical and cortico–cerebellar– cortical networks impairs motor planning, coordination, muscle strength regulation, motor learning and fine motor skills. Additional disruption of descending motor pathways that project to the brainstem and spinal relays, and retention of circuits that normally disappear with maturation result in persistent or poorly inhibited 'primitive' reflexes, abnormal organization of movement and posture, hyperactive reflexes and abnormal muscle tone, including spasticity. The motor impairments, with poor motor repertoire, hypertonia, progressive muscle changes related to neuronal, nutritional and mechanical factors, lead to musculoskeletal deformities.

Whereas cerebral palsy results from a primary injury in the central nervous system (CNS), clinical symptoms are observed in the peripheral neuromuscular system — skeletal muscles in particular. Indeed, muscle contractures, defined as limited joint movement that results from high passive muscle force, are common complications of cerebral palsy. Our understanding of the tissue-level adaptations — both functional and structural — in muscle contractures has dramatically improved in recent years.

The most consistent mechanical change observed in the muscles of patients with cerebral palsy is hypertrophy of the extracellular matrix (ECM), which leads to increased muscle

stiffness.[35,36] Increased amounts of ECM can be quantified in various ways[37], with the most common being biochemical measurement of collagen content38. In most studies to date, collagen content is increased in muscle obtained from patients with cerebral palsy, as is the relative volume of the extracellular space compared to the cellular mass. Although increased collagen content and extracellular space volume correlate with increased stiffness, they do not correlate well with biomechanical tissue properties such as the Young modulus or stiffness measured in the same samples.[38] The structure of the ECM (collagen organization and crosslinking), as well as other non-collagenous constituents, such as hyaluronic acid, decorin, biglycan and uronic acid, may also influence biomechanical properties.[37]

Spasticity is a clinical phenomenon in which muscles overreact to rapid stretch. By contrast, dystonia is defined as a movement disorder characterized by sustained or intermittent muscle contractions or co-contractions (that is, simultaneous activation of muscle groups across one or more joints) causing abnormal and repetitive movements and/or postures. Dystonia and spasticity have distinct pathophysiological features that require different management strategies. The physiological scheme of motor dysfunction is summarized in. Each component — that is, the movement, posture and stretch reflex disorders and the trophic changes in muscles — has distinct operational definitions set in a framework of electromyographic activity or inactivity, influenced by sleep and vestibular inputs. Many medical and surgical options for managing the movement disorders associated with cerebral palsy have been described.[39,40] Up to 17% of people with cerebral palsy have normal MRI brain scans, a figure that rises to 50% for those with dyskinetic cerebral palsy. Genetic and metabolic disorders, such as the doparesponsive dystonias, aromatic l-amino acid decarboxylase (AADC) deficiency as well as glucose transporter (GLUT1; also known as SLC2A1) deficiency may mimic cerebral palsy owing to the early onset of movement disorders, including dystonic features and motor delay. Dystonia. Dystonic movements are typically patterned or twisting and can be tremulous, interfering with voluntary movements. Dystonia is often initiated or worsened by voluntary action, the intention to move and nonspecific stress, emotion or sensations.[41] Dystonia can be developmental, task dependent and pathological. In young children, the presence of tonic labyrinthine postures produce the typical picture of scissoring, which is exaggerated when lying supine, in vertical suspension and is reversed when held upside down, but is always abolished by sleep. In all cases of cerebral palsy, the influence of sleep, which transiently switches off dystonia and tonic labyrinthine postures, should be considered.[42]

The currently accepted physiological definition of spasticity was framed by James Lance[43] and highlights the importance of the velocity-dependent stretch reflex. Indeed, the stretch reflex response increases approximately linearly with the increase in the velocity of stretch. The reflex component of the increased tone might, therefore, be measured in terms of the threshold velocity required to evoke reflex activity and the slope of the electromyography–

velocity relationship. Spasticity only partially explains poor gross motor function (floor skills, standing and walking) in those with cerebral palsy.[44] Important positive relationships were found between strength, gross motor function and functional outcomes, indicating that weakness accounts for more disability than spasticity.[44] This prompted a call for activity-based rather than impairment-based interventions.[44] Velocity-dependent stretch reflexes can be reduced by oral baclofen (a γaminobutyric acid agonist used as a centrally acting muscle relaxant) and by biofeedback methods, but such spasticity reduction does not necessarily improve functional gains.45 Cocontraction in dystonia of the quadriceps and hamstring muscles may not be suppressed with small doses of oral baclofen, despite a reduction in the velocity-dependent stretch reflexes.[45] Spasticity is not the cause of the typical equinus posture (toe walking) typically seen in children with cerebral palsy.[46] Elegant pharmacological studies on baclofen receptor distribution in the Rexed layers of the spinal cord explain why dorsal rhizotomy cannot alter postures but baclofen may, indicating that dorsal rhizotomy should not be considered as a cheaper alternative to intrathecal baclofen. However, baclofen can also induce floppiness, postural relaxation, drooling, drowsiness and, in high doses, may provoke coma and respiratory depression that can be life-threatening. Stretch reflexes in individuals with cerebral palsy change over time and after interventions.[47] Exercise, immobilization, surgery or disuse alter the stretch reflex excitability, clonus (rhythmic muscle twitches)[47] and the visco-elastic properties of muscle[48,49] even though the cerebral lesion remains unchanged.[47] In a review of 15 studies in children with cerebral palsy[50], spasticity remained poorly defined and measured.

The development of methods to distinguish neural from non-neural resistance to muscle stretch continues.

CIMT is a deviation from traditional treatments, used to treat hemiplegia. Its aim is to stimulate the functional use of the affected limb and reverse the process developmental is disregard.[51] In this method, the unaffected or less affected limb is restrained, so the person has to use the affected limb. This method has risen up out of the intersection of behavioral brain research/learning hypothesis and disclosures in neuroscience with respect to neuroplasticity. CIMT is a kind of paradigm shift in rehabilitation of central nervous system injuries. It changes the paradigm from emphasis on compensatory skills to a desire for partial restoration.[52] CIMT is the most convincing clinical treatment to improve sensory and mobility functions in hemiplegic CP children.[53] Two possible mechanisms may lead to more use of the affected limb (Overcoming developmental disregard). These two are a) Overcoming the learned non-use of the more affected arm (for example increased use of the more affected arm) and b) usedependent cortical reorganization. By using Trans cranial Magnetic Stimulation (TMS), motor cortex mapping before and after CIMT were studied and the increase of motor output area size and MEP amplitudes were noticed. It shows enhanced neuronal excitability in the damaged hemisphere and the target muscles. With the use of FMR activation of the motor cortex changes after CIMT.[54]

METHODOLOGY

This Experimental study was conducted in patients of hemiplegic cerebral palsy fulfilling the criteria, referred by specialists for physiotherapy, from tertiary hospitals.

The study population was selected by convenient sampling method. The study was conducted over a period of one year.

Inclusion criteria for the study were:

- Subjects were age group of 4 – 8 years.
- Subjects with hemiplegic cerebral palsy.
- Both gender.
- Children with score III or less on MACS.
- Spasticity range between 1, 1+, 2 on modified Ashworth scale.
- Ability to achieve minimum of 10 degrees of active wrist extension, 10 degrees finger extension.
- Able to understand and follow commands.

  Subjects were excluded if:
- Subjects with severe spasticity i.e. grade 3 or 4.
- Subjects with visual and auditory impairment that would prevent them from carrying out the intervention or testing task.
- Subjects having history of previous orthopaedic surgery in affected upper limb.
- Subjects with fixed upper limb deformities.
- Botulinum toxin injections in upper limb within last 6 months.

This study involved minimal equipment

1. Demographic data sheet
2. Data collection sheets
3. Pen
4. Consent form
5. Mat
6. Sling
7. Peg board
8. Therapeutic ball
9. Weight cuffs

PROCEDURE:

Subjects will be selected as per inclusion and exclusion criteria. Demographic data like name, age, sex, with contact no. of parents will be taken. Children will be randomly divided into three groups a control group and experimental group.

QUEST:

The QUEST was developed to measure quality of upper limb movement and function in a clinical trial of therapy and upper limb casting for children with CP aged 18 months to 8 years.

The QUEST aimed to evaluate movements that, according to neurodevelopmental theory, were the basis of upper limb use and function. It is a 34-item criterion-referenced measure consisting of 186 item categories, which are scored, summed, and then converted to a percentage total score. There are four domains: dissociated movement, grasp, protective extension, and weightbearing.

Experimental group A:

Subjects unaffected extremity will be restraint using sling and then they will be engaged in unimanual activities like board games, card games, puzzles, art & crafts etc. and conventional therapy for 2hrs per day along with rest periods. The sling will be strapped to the subject's trunk and the distal end will be shut to prevent the use of hand as an assist. Toys will be openly displayed so that subjects are free to make choices of activities. The task will be made progressively more difficult as child improves in performance by increasing speed/accuracy, repetition. The training will be carried out for 6 times a week for 4 weeks.

Subjects will not carry sling at home because of safety concerns.

Experimental group B:

Bimanual activities that require use of both hands like clay activities, ball activities, cube activities, bottle & marble activities etc. will be selected by considering the role of the involved limb in the activity, subject will be asked to use the involved limb in the same manner as that of the non- dominant limb of a typically developing child. Demonstration of each task performance and how each hand will be used will be clarified to the subject before the start of each task to prevent use of compensatory strategies. The subject will be engaged in the activities and conventional therapy for 2hrs/day along with rest periods.
The task will be made progressively more difficult as subject improves in performance by increasing speed/accuracy, repetition.
The training will be carried out for 6 times a week for 4 weeks.

Control group C:

Control group will receive conventional PT treatment. The control group will receive 2-hour physiotherapy interventions, according to NDT approach, for facilitation and inhibition techniques using bolster, therapy balls and wedges, 6 days a week for 4 weeks. Stretching for the tight muscles will be givenAlso they will receive functional training like sit to stand activities, balance training, reach out activities, Gait training.

DATA ANALYSIS

- The collected information will be summarized by using, mean, standard deviation (Descriptive statistics).
- If the data is normally distributed, parametric test that is one-way analysis of variance will be applied. If the data is not normally distributed non-parametric test that is
  Kruskal-Wallis analysis of variance by ranks will be applied.
- The p value <0.05 will be considered significant

SAMPLE SIZE ESTIMATON

Towards estimation of sample size for this cross sectional study, the following guidelines were used:

$n = Za^2 pq/E^2$ n = Number of sample size Za = 1.96 at 95% confidence level p = 70% Percentage of prevalence (80 % of power) q = 30 %(100 – p) E = 20 % error of p

With 95% Confidence level & 80% power with reference to 70% sample size obtained was 30.

$n = (1.96)^2 \times (70\ \%\ of\ 80\ \%\ of\ power) \times 30\% [100 - (70\ \%\ of\ 80\ \%\ of\ power)]$

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20 % of (70 % of 80 % of power)

n = 3.84 x 70 x (100- 70) / 196 n = 3.84 x 70 x 30 / 196

n = 8067.36 / 196 n = 30

n = 30

RESULTS

MEAN AND STANDARD DEVIATION OF AGE IN 3 GROUPS

	N	Mean	Std. Deviation
Group A	30	4.8333	.69893
Group B	30	5.0000	.87099
Group C	30	5.0333	.88992
Total	90	4.9556	.81985

Table : Mean of Age

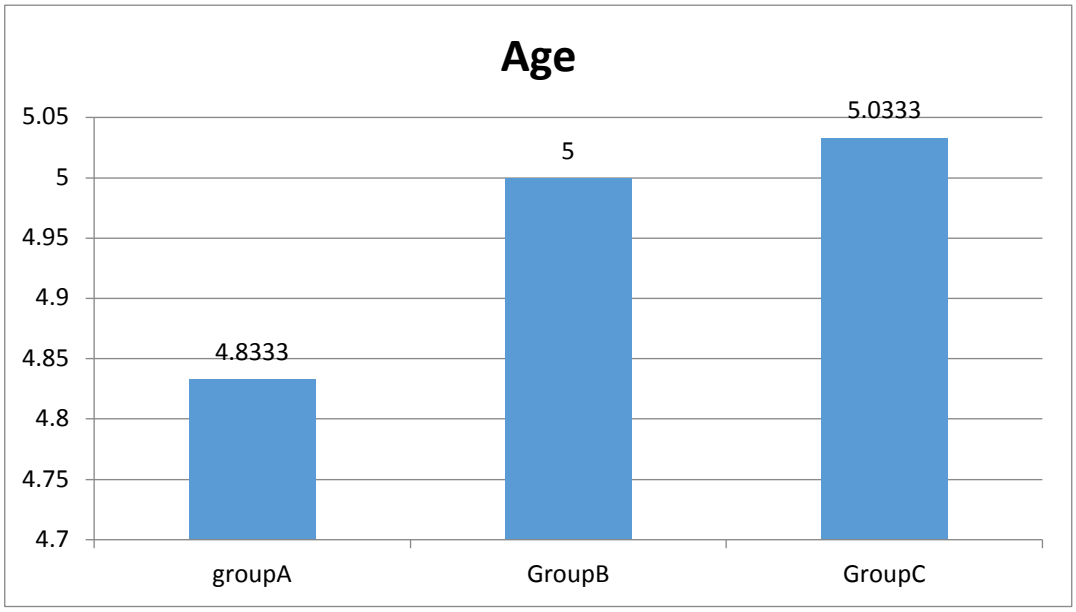

Figure : Mean of Age

PRE - POST COMPARISON BETWEEN IN GROUP A .GROUP B AND GROUP C

Pre post comparison between pre post in group A is statistically significant. Pre post comparison between pre post in group B is statistically significant. Pre post comparison between pre post in group C is not statistically significant.

		Mean	N	Std. Deviation	T value	P value	Result
Group A	Pre	37.7667	30	3.65479	19.357	0.000	P<0.05
	Post	57.0333	30	3.93467			
Group B	Pre	39.9667	30	2.18905	22.256	0.000	P<0.05
	Post	55.2667	30	4.44067			
Group C	Pre	39.9667	30	2.18905	1.027	0.313	p>0.05
	Post	40.7000	30	3.70601			

Table : Mean of Pre & Post QUEST OF GROUP A, B & C

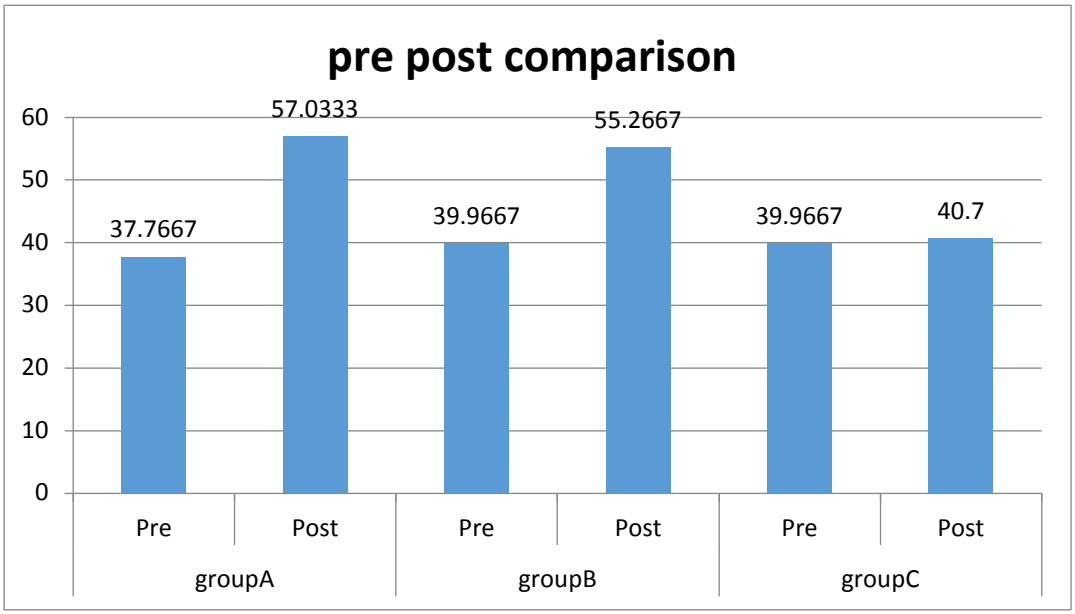

Figure : Mean of Pre & Post QUEST OF GROUP A, B & C

BETWEEN GROUP COMPARISON

There is sig diff between A and B ,there is sig diff between B and C, there is sig diff between A and C

	Mean difference	Std. Deviation	t value	p value	result
Group A Group B	19.267 15.300	5.452 3.715	3.293	0.002	p<0.05
Group A Group C	19.267 0.733	5.452 3.912	15.920	0	p<0.05
Group B Group C	15.300 0.733	3.715 3.912	14.291	0	p<0.05

Table : comparison of P value of QUEST Pre & Post QUEST OF GROUPS

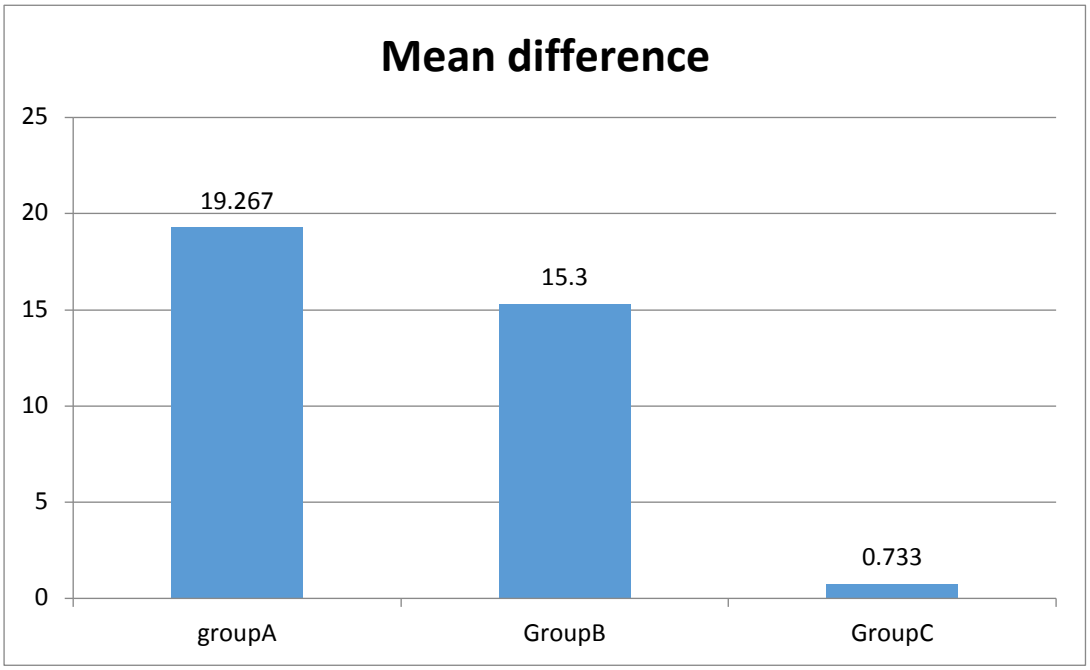

Table : comparison of P value of QUEST Pre & Post QUEST OF GROUP

DISCUSSION

CIMT for CP children has little to do with age. The age range for CIMT in the studies is between two years to 14 years and in all of them, CIMT had acceptable results. The therapeutic effect of CIMT was not age-related. They also confirmed the results of sung and DeLuca's study. There were no differences between boys and girls for this therapy and CIMT was equally

effective for both genders. Gender was reported as an ineffective factor in CIMT too.[97,98]

Articles reviewed in the study had used only two kinds of restrictions. Most of them had used a splint for restriction (12 of them) and three of them had used sling for restriction. For this reason, maybe the use of splints and slings are easier for children. Other kinds of restriction were reported too. Restrictions such as Short arm casts and Long arm casts, holding child's hand, using a glove or mitt and Slings. CIMT effect on the left or right side is the same because no study mentioned to affected side.[99]

For concerning the effect of CIMT on muscle tone the result of four articles about the impact of CIMT on muscle tone was inconsistent. CIMT had an influence on muscle tone. CIMT was considered as an ineffective method on muscle tone. CIMT was considered as an ineffective way of reducing muscle tone. However, this study did not find definite conclusion about the impact of CIMT on muscle tone. This issue requires further studies in the future.[100]

CIMT has a good effect on protective extension. It was not effective on protective extension; however, it was effective on protective extension. CIMT was effective on protective extension, however, in another study; CIMT was not effective on protective extension. In this case, literature are not unified and more studies are needed.[101]

There were no significant adverse effects for CIMT in the studies. Nevertheless, early implementation of CIMT for children who are in the stages of development of bilateral hand can cause a negative effect on the growth of bilateral hand development. Therefore, CIMT should be used with caution for children under twelve months. In addition, restriction of the non-affected hand for a long time (e.g. plastering) had negative effects on the development of motor skills.[102]

Results showed statistically significant difference in QUEST and COPM for both group A & B after 2weeks of intervention with (p = 0.001). Children with hemiplegic cerebral palsy as also known as unilateral cerebral palsy learn to use only unaffected hand for daily tasks which leads to behavioural suppression of use of affected hand and is termed as developmental disregard.[103] Thus therapy must create experience that should change the behavioral suppression of developmental disregard and must reward the use of affected limb in simpler tasks like stabilizing an object. CIMT is considered as one of the method of achieving this experience.

Various modified and distributed form of CIMT has been proposed. One of them which were used in this study was to constraint hand for 6 hours per day with 2 hours of unimanual activities for 2 weeks. This modified way was used to make the protocol more child friendly. There is insufficient evidence to support the use of a specific type of constraint over another.[104]

Constraint used in this study can be considered as key point to make it childfriendly as it was a gentle restraint in order to reduce frustration, discouragement in using constraint and reduces fall. Results from present study are consistent with other studies in showing a significant improvement in upper limb function after mCIM therapy in children with unilateral impairments.

Morris and Taub has proposed two mechanisms to be responsible for increased use of the more affected extremities, overcoming learned non-use and inducing use-dependent cortical reorganization.[105,106] which basically works on motor learning principle to strengthen new motor pattern to perform an activity more efficiently. HABIT was implemented on the basis of the experience with CIMT for children with unilateral impairments, mainly to focus on an area that leads to activity limitation and participation restriction. HABIT uses principles of specificity of training in form of repetitive practice and plasticity. Neurophysiology literature specifically motor behaviour states that practicing active bilateral movements may result in a facilitation effect from the non-paretic arm to the paretic arm. Thus both arms work as coordinated unit in the brain.

In his research, Gordon asserts HABIT as name suggest is 6 hour intensive training of bimanual activities that helps in shaping of motor cortex ,motor planning, coordination and in turn improves quality of use of U/E. Moreover results shows there is no significant

difference in effect of MCIMT and HABIT on quality of upper extremity skills with (p=0.753). Both the intervention works on motor learning principle with shaping of motor task with intensive practice which might leads to plasticity. Similarly as a child engages in intense practice using their affected extremity it is thought that the neural connections in their brain change. The altered neural connection can create new pathways (sprouting) or change pre-existing pathways
(unmasking) in order to enhance functional movement (occupational performance) (Pendleton & Schultz-Krohn, 2006), that is what occurs with intensive therapy of HABIT as supported by Nichole Hayes.[107]

Our result is even supported by study done by Sakzewski where it was postulated that both the therapies found to be equally effective in improving hand functions in children with congenital hemiplegia. Results showed significant improvement within both groups A and B in COPM for performance and satisfaction with (p = 0.001). Traditional management for children with hemiplegic cerebral palsy works mainly at impairment level to reduce tone, increase range of motion and to increase strength of the limb for function. However MCIMT and HABIT both of this technique works on activity limitation and participation restriction and not on impairment level. COPM for performance and satisfaction is goal based subject's perception about their performance and satisfaction related to their activity. [108]

Training focusing on specific goal that are meaningful to child and can be transferred to the daily functioning leads to significant change in parental perception of their child performance regardless to type and intensity of training. Moreover, major part of intervention (50 hours for each group) was implemented as home program to make it more feasible for parents, increase parental participation and provide natural environment for intensive practice. Compliance was found to be 78.2% and 82.4% for mCIMT and HABIT group respectively at home. Home based therapy for CIMT and Bimanual OT were investigated with effective results as quoted in a meta- analysis. Compliance achieved in bimanual training was 85% as compared to 70 % of CIMT which suggest home practice sounds to be easier for bimanual group and supports the finding present in this study.109

Post intervention carry over effect of mCIMT and Habit were investigated which showed the significant difference for both the group after 1month of intervention. There was drop out of total 11 subjects secondary to distance of center, school got started, patient got shifted or due to family issues. These changes seen after constraint therapy can be attributed to change in efficiency, ease and facilitation of use in the environment. Along with that a study showed that Functional magnetic resonance imaging showed bilateral sensory motor activation before and after therapy and a shift in the laterality index from ipsilateral to contra lateral hemisphere after therapy. mCIMT is creating a window of opportunity where children learn to use affected limb more efficiently in everyday activities which is supported by study, where effects were maintained for 1 month and 6 month after intervention

respectively. HABIT is a form of functional training mainly targeted on coordination of the two hands using structured task practice embedded in bimanual play and functional activities with key concept of repetitive intensive practice. Studies done in adult stroke shows significant cortical reorganization after bimanual training.[110]

Reorganization of corticocerebellar circuits with inclusion of contralesional motor cortex and ipsilesional cerebellum may be a key mechanism of bimanual therapy. Bleyenheuft states that improvements in upper extremity function are believed to be associated with neuroplastic changes, presenting differential corticospinal developmental reorganization (ipsilateral and contralateral). Moreover, intensive practice can increase in activation and size of motor area controlling the affected hand as quantified by imaging techniques. As HABIT focuses primarily on functional activities which help to improve bimanual coordination thus significant improvement is seen in quality of U/E skills as well as activities of daily living which would have led to carry over change in perception of child's performance. These results are supported by a study that showed the significant increase in functional use of affected upper extremity remained same after 1 month of intervention.[111]

Theories of motor learning and neural plasticity are the key principle for both: unimanual as well as bimanual approach, where mCIMT approach works on use dependent reorganization by intensive training of impaired hand, while other uses bimanual use along with functional activities for relearning of motor control in impaired hand which justifies results in our study. Moreover, a systematic review was done to compare constraint induced movement therapy and bimanual training in children with unilateral cerebral palsy, which shows that both interventions produce similar improvements in unimanual and bimanual capacities and functional performance. An another study with approach of bimanual training with and without constraint on hand functions shows that both interventions were similarly effective for improving use of affected hand in bimanual tasks shows similar results as shown in our study.[112]

As there was no significant difference between the effect of two approaches so, effect size was calculated which came out to be large effect size with group mCIMT having larger effect as compared to HABIT group.113 This was supported by Sakzewski in a meta analysis that postulated that, studies comparing intensive unimanual therapy (CIMT, mCIMT) or hybrid therapy with standard care of a lesser dose have shown modest to strong treatment effects across most outcomes. whereas, trials comparing intensive unimanual therapy (eg, mCIMT) with an equivalent dose of bimanual training have reported weak to modest treatment effects on most outcomes. There were few limitations in our study such as the restraint of the unaffected arm for mCIMT and intensive training for HABIT were accurately controlled during the practice in therapist's presence where as it was difficult to control at home during intervention in both groups. Moreover, none of the tests measured the bimanual coordination or unimanual / bimanual ability individually. Proper accurate methods of

restraining and applying intensive training at home for both mCIMT and HABIT should be incorporated. Future implications to be incorporated are to assess effect of unimanual capacity over bimanual performance should be measured after intervention. Effect of mCIMT followed by HABIT should be assessed on quality and bimanual coordination for activities of daily living.[114]

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REVIEW OF LITERATURE

PREVALENCE AND PATHOLOGY OF HEMIPLEGIC CP

The prevalence of this disability is different in parts of the world, spastic hemiplegia is the most common subtypes of CP. Cortical and additionally subcortical lesions caused by asymmetrical periventricular leukomalacia, middle cerebral artery stroke, or intraventricular hemorrhages, happened within motor areas of the contralateral hemisphere to the affected limb are the main causes of this type of CP.[55]

Paradox: Very strong relationship between prematurity and risk of cerebral palsy versus the fact that most patients with cerebral palsy are born at term". Children born before 28 weeks´ gestation, and all preterm children with additional risk factors, such as intracranial haemorraghe, encephalitis, meningitis, seizures and other conditions leading to care in the neonatal unit, are included in the Swedish neonatal society's high risk group. These children are offered **a** follow up at the neonatal clinic according to the Guidelines from Swedish neonatal society 2015.[56] Children born at 28–32 weeks are considered an intermediary risk group**.** For term infants, low birthweight, especially infants being small for gestational age (SGA), is a significant risk factor.[57]

Cerebral palsy has long been associated with congenital cytomegalovirus (CMV) infection.[58] More recent reports have been published, where CMV-DNA was assessed by PCR in the

neonatal screening card.[59] In a study from 2017, 31 (9, 6%) of 401 children with cerebral palsy, tested positive for CMV- DNA.

In approximately 90% of cases, cerebral palsy results from destructive processes that injure healthy brain tissue rather than from abnormalities in brain development. Hypoxia and ischaemia have traditionally been proposed as causes of brain injury. Pathological and imaging studies of cerebral palsy have demonstrated varying combinations of lesions in the cerebral cortex, the hemispheric white matter, the basal ganglia and the cerebellum. The stage of brain maturation during which pathogenetic events occur defines the type and site of lesions, as well as the specific response to injury.[60]

Early in maturation (that is, in the foetus and the preterm infant) blood vessels in the brain have limited capacity for dilatation, which enhances ischaemia and leads to diffuse injury. Diffuse injury during the second trimester of pregnancy leads to liquefaction necrosis (a type of necrosis that transforms tissue into a viscous liquid mass), resulting in porencephalic cysts. The astrocytic response to injury (including biochemical activity and morphological changes), which might lead to gliosis, is limited during the second trimester of pregnancy (<15% of the level observed in the mature brain) and gradually increases during development. Astrocytic response leads to cysts with increasing components of astroglial proliferation and septation observed for insults up to the neonatal period and astrogliosis without cysts for lesions sustained later.[61]

The localization of brain lesions following diffuse insult markedly varies with gestational age. In preterm infants, deep periventricular white matter, which is a site of active proliferation of oligodendrocytes, is the most vulnerable. Maturation-dependent metabolic and molecular factors further enhance the susceptibility of the periventricular white matter in the preterm brain. Consequently, periventricular leukomalacia (necrosis of white matter near the lateral ventricles) is the characteristic lesion pattern seen in cerebral palsy associated with preterm birth; it can be diffuse, focal or multifocal, cystic or non-cystic. By contrast, insults occurring in full-term infants primarily affect the cerebral cortex and underlying subcortical and periventricular white matter as a result of other maturation-dependent factors and probably factors affecting vascular supply with changes in intervascular boundary (watershed) zones (that is, border-zone regions in the brain supplied by major cerebral arteries where blood supply is slightly reduced).[62]

The link between perinatal respiratory difficulties leading to hypoxia or ischaemia and cerebral palsy has been recognized clinically since the original description by Little, and it has served to design various animal models since the 1950s. Given that birth asphyxia does not account for the majority of cases of cerebral palsy, other mechanisms must play a part. Brain injury in response to hypoxia or ischaemia is suggested to involve several events,

including cellular energy depletion, excitotoxicity (that is, damage or death of nerve cells owing to excessive stimulation by neurotransmitters, particularly glutamate) and oxidative stress; oxidative stress leads to mitochondrial failure that further exacerbates this energy depletion. Ultimately, neurons and glial cells undergo apoptosis or necrosis.[4]

ATP depletion caused by mitochondrial failure disrupts cellular ATP-dependent processes, which may result in cell death. Among ATP-dependent processes, Na+/K+-ATPase disruption alters neuronal membrane potential, contributing to glutamatergic Nmethyldaspartate (NMDA) receptor-mediated excitotoxicity through massive Ca2+ influx into the cytoplasm, leading to necrosis and apoptosis. Understanding this pathway has led to the study of the potential neuroprotective effects of agents that block NMDA receptors, including magnesium sulfate.[63] Intracytoplasmic Ca2+ overload induces necrosis and apoptosis by inducing oxidative stress. Activation of Ca2+-dependent oxidases and inhibition of antioxidant activities48 generate excess reactive oxygen species that affect mitochondrial function, which further increases the rate of reactive oxygen species production, ultimately leading to cell death. This effect is particularly marked early in brain maturation (second trimester) owing to the limited efficiency of scavenging systems. This notion has led to the development of neuroprotective strategies based on free-radical-scavenging agents, such as melatonin. In addition, the use of high oxygen concentrations in resuscitation approaches in neonatal asphyxia are contraindicated on the basis of studies in animals50 and those showing adverse clinical outcome in humans.[64]

Various insults, not just hypoxia and ischaemia, can lead to necrosis and/or apoptosis. Necrosis occurs as an immediate response to injury and typically results in focal injury that involves nonspecific cell-type death. Conversely, apoptosis is more protracted, usually more diffuse and cell specific — preferentially targeting pre-oligodendrocytes if the process is triggered in the brain. These characteristics of necrosis and apoptosis are reflected in patterns of white matter injury, which occur in atterm birth but are typically associated with preterm birth. Necrosis results in focal lesions that can be microscopic and evolve into gliosis (a nonspecific reaction of glial cells in response to injury that involves proliferation and hypertrophy), which is the predominant neuropathological finding in non-cystic periventricular leukomalacia. Less commonly, necrosis can lead to macroscopic cysts, for example, in cystic periventricular leukomalacia. The consequence of pre-oligodendrocyte apoptosis is hypomyelination. The pathways underlying these two cell death mechanisms offer potential targets for anti-necrotic or anti-apoptotic intervention.[65]

Animal findings suggest that the hypoxia– ischaemia hypothesis has the most relevance in the case of perinatal asphyxia in the full-term newborn, as opposed to pre-term newborns. At term, the vulnerability to a deficit in oxygen supply is higher than earlier in development. The highest metabolic requirements involve the grey matter, chiefly the basal ganglia, the thalamus and parts of the cerebral cortex. This metabolic demand is reflected in patterns of

brain damage at term, with lesions to these structures and clinical signs of dyskinetic, spastic or mixed-type cerebral palsy. The notion of failure to meet the metabolic demand has been the focus of studies of animal models preparing the development of therapeutic hypothermia as the standard of care for full-term newborns with moderate or severe perinatal asphyxia.[66]

In addition to these advances, much progress has been achieved based on clinical, epidemiological, experimental and pathological evidence of the implication of maternal and neonatal inflammation, whether infective or non-infective. The inflammatory pathway may also be a target of strategic therapies. Although the role of pro-inflammatory cytokines has mostly been studied in relation to periventricular leukomalacia and cerebral palsy associated with preterm birth, hypoxia–ischaemia at term also triggers the release of pro-inflammatory cytokines, mostly from astrocytes, leading to damage to neighbouring neurons. Indeed, inflammation has been suggested to be a final pathway in cerebral palsy pathogenesis common to hypoxia–ischaemia, brain infection, systemic maternal infection, or fetal or infant infection, and other conditions in which they are produced, including trauma, inflammation and autoimmunity. These pro-inflammatory cytokines can induce the expression of adhesion molecules in brain parenchymal and vascular endothelial cells and can promote microglial activation and demyelination.[67]

The clinical symptomatology can be directly attributable to brain abnormalities or can occur in the course of development as a secondary consequence of activity limitations1 during critical periods for activity-dependent and use-dependent plasticity. For example, in addition to motor impairment components ascribed to lesions along motor pathways, restricted sensorimotor experience (less neural stimulation owing to fewer or less-complex movements) impedes motor learning. Similarly, visual impairment can result from a combination of lesions to visual pathways and poor perceptual development experiences. These reinforcing attributes would be a strong argument for early intervention as a means of secondary prevention.

The developmental aspect of cerebral palsy implies a special focus on neuroplasticity. For example, the corticospinal tract from the less affected hemisphere can project bilaterally on spinal relays, particularly if damage occurred before 24 weeks of gestation56. Evidence from adaptive, partially compensatory plasticity driven by experience has influenced therapy programmes. Moreover, a lack of physiological pruning (that is, postnatal synapse elimination) of early neural connectivity can also impair motor control.[68]

Among non-motor features, mechanisms underlying visual dysfunction have been well documented. Cerebral visual impairment, in particular attentional and perceptual deficits, has been related to lesions in ventral and dorsal streams. The ventral stream leads from the occipital lobe through to the temporal lobe to process object identification and recognition;

the dorsal stream terminates in the parietal lobe and is involved in processing the spatial location of an object relative to the viewer. These notions have become an important focus in management strategies. Similarly, there has been increasing interest in understanding other cognitive outcomes, with respect to, for example, communication, executive functions and arithmetic performance.[69]

Muscles from children with cerebral palsy are shorter and smaller and contain fibres of reduced diameter. Human skeletal muscles have different fibre-type distributions, meaning that muscles contain a mixture of fast-contracting and slow-contracting fibres. Numerous descriptions of altered fibre-type distribution in cerebral palsy muscle have been reported. However, some studies report fibre transformation in the slow-to-fast direction, whereas others report fibre transformation from the fast-to-slow direction. These inconsistent results are mainly because fibre type varies widely among the muscles sampled and sampling is extremely unreliable. Overall, it seems that muscle fibre types are not uniformly affected by cerebral palsy. Thus, decreased fibre diameter, which leads to a muscle with smaller force-generating area, partially explains decreased strength in these children.[70]

The most dramatic and unprecedented change that has been documented in the muscles of children with fixed contractures (that is, contractures that are present all the time, even when the muscle is relaxed) are the sarcomeres that are almost twice the normal length and fewer in number. The sarcomere — the functional unit of contraction of the muscle — is highly lengthened even though the muscle is highly shortened. These long sarcomeres in short muscles are a paradoxical muscle adaptation that has now been observed in contractures due to cerebral palsy in wrist flexors, hamstrings and plantar flexors. The extremely long sarcomeres are thought to generate relatively low active force and could also contribute to the weakness observed in children with cerebral palsy in addition to the size changes mentioned above. Longer sarcomere lengths are also associated with high passive muscle forces (that is, muscle force borne by the tissue in the absence of any neural activation). To date, the mechanistic basis for the extremely long sarcomeres observed in individuals with cerebral palsy is not known.
However, the transcriptional profiling studies and tissue-level analyses described below may provide insights.[71]

In addition to the changes in the ECM, increased stiffness of single fibres has been reported in the wrist flexors and calf muscles of individuals with cerebral palsy, but not in the hamstrings, compared with cells of the same muscle type obtained from age matched typically developing children. The structural basis for these cellular changes is not known, although the giant intramuscular protein titin, which extends half the length of the sarcomere, does not seem to be involved.[71]

Transcriptome analysis of the muscle of children with cerebral palsy (of upper extremity wrist extensors and one of the hamstring muscles) points to several abnormalities. For example, muscle from typically developing children does not express any of the developmental myosin heavy-chain isoforms (a type of myosin normally found in neonates or young children), but muscle of individuals with cerebral palsy does, suggesting that cerebral palsy is associated with a more immature type of myosin. Similarly, within the ECM, there is a paradoxical increase in both the matrix metalloproteinases (MMPs) and their inhibitors (tissue inhibitors of MMPs), which may indicate a large increase in ECM turnover. Another dramatic change observed in cerebral palsy muscle transcription is the considerable increase in the expression of parvalbumin (a Ca2+-buffering protein). Although parvalbumin regulation is poorly understood in mammalian muscle, this seems to indicate that the muscle is subjected to chronically increased Ca2+ loads.[72]

Another fundamental change in muscles affected by contracture, which may have direct therapeutic implications, is a decrease in the number of muscle stem cells — known as satellite cells. The muscle satellite cell is widely regarded as the precursor cell that is responsible for the majority of the growth in skeletal muscle and is crucial for muscle regeneration. Specifically, flow-assisted cell-sorting (FACS) methods have shown that the number of satellite cells is reduced by approximately 70% in muscles of children with contractures compared with age-matched typically developing controls. However, FACS technologies may be vulnerable to the physical condition of the tissue; satellite cells of healthy muscle are more likely to be released by enzymatic digestion methods than cells from muscle of those with cerebral palsy owing to the excess ECM. Independent studies that identify satellite cells based on a surface marker, co-localization with the nucleus and sub-sarcolemmal location were recently reported and supported the FACS finding, therefore, the results are not dependent on measurement method.[73]

However, if the number of satellite cells is indeed reduced, it would suggest some type of developmental or maturation defect in muscles that develops in the context of cerebral palsy. Indeed, the decreased number of satellite cells could explain the reduction in fibre size, with impaired muscle growth as a consequence. Increased sarcomere length could result from a decreased ability of cerebral palsy muscle to add sarcomeres in series, which normally allows a healthy muscle fibre to grow in length while maintaining a near-constant sarcomere length. Finally, the excess ECM observed in individuals with cerebral palsy may in part be caused by the decreased number of satellite cells, which has been shown to lead to excess muscle ECM in other experimental models through the activation of the WNT signalling pathway. The findings in this area seem to be converging on an understanding of the growth and regulation of satellite cells and tissue fibrosis; given that this is an active area of research, the future bodes well for treatment of these devastating consequences of cerebral palsy. It is easy to envision therapies that involve small-molecule activation of satellite cells, inhibition of some or all of the WNT pathway, direct injection of myogenic

precursors or even direct injection of appropriate genes in conjunction with or instead of orthopaedic surgery. Future studies are required to determine if and how CNS lesions alter muscle satellite cells.[74]

EFFECTS OF MCIMT ON QUALITY OF UPPER EXTREMITY FUNCTION IN CP

This systematic review was conducted using the electronic databases such as Medline PubMed, CINAHL, etc. performed from 1990 to 2016. Iranian and foreigner famous journals in the fields of pediatrics such as Iranian Journal of Pediatrics (IJP), Iranian Rehabilitation Journal (IRJ) and Google scholar with some specific keywords such as CP, CIMT, and occupational therapy were searched. Overall, 43 articles were found, from which, 28 articles were removed because of lack of relevancy. Ten article were omitted because of duplication and exclusion criteria, so finally 15 articles were included. CIMT is effective compared to no intervention but there are some inconsistencies regarding some parts of CIMT effectiveness such as its effectiveness on muscle tone and protective extension.[75]

Hemiplegic Cerebral palsy (CP) impairs hand function leading to inability or difficulty to perform activities of daily living (ADLs). Beside traditional therapies several new techniques like mCIMT & HABIT are in practice which focuses on precise and appropriate targeted results. There is a need to include a treatment protocol which is effective, easy and can be done under parents' guidance in home setting. Purpose of this study was to find and compare the effect of mCIMT & HABIT on the quality of upper extremity function in children with hemiplegic cerebral palsy. Objectives: To study the effects of mCIMT, HABIT and conventional therapy on quality of upper extremity function in hemiplegic cerebral palsy children and to compare the effects of mCIMT, HABIT & conventional therapy on quality of upper extremity function in hemiplegic cerebral palsy children. Material & Methods: The study included 20 children who were diagnosed cases of hemiplegic CP. The experimental groups were given mCIMT and HABIT with conventional therapy and the control group received only conventional therapy. Quality of upper extremity skills test (QUEST) was used as an outcome measure. All groups were evaluated with the QUEST before and after 4 weeks of treatment. Results: The results showed statistical difference in the final QUEST scores(p=0.001) between all the groups as well as difference in dissociated movement, grasp & weight bearing. There was however no difference in protective extension (p=0.704) domain. Also, there was statistically no significant improvement in weight bearing and protective extension within the group while dissociated movement, grasp and QUEST Score showed improvement. Conclusion: This study concluded that mCIMT is more effective than HABIT & CT alone in improving quality of upper extremity function in hemiplegic cerebral palsy children.[76]

In order to improve the affected upper limb "non-use", Constraint-Induced Movement Therapy (CIMT) is used, which consists of constraining the healthy upper limb with a whole or partial containment (glove), thus promoting the use of the affected upper limb in activities of daily living. The programmed tasks integrate the repetition of the motor action with a variety of exercises. The use of CIMT has spread in recent years among physiotherapists and
occupational therapists, due to the large number of studies that support the effectiveness of this intervention compared to traditional interventions that do not restrict the use of the healthy side.[77]

McConnell et al. found that a less intensive treatment (63 h of treatment over 21 days) produced similar benefits compared to a more intensive approach (126 h of treatment over 21 days). Functional gains may be feasible for some children with a less intense program adjusted to 20 h of therapy in more than two consecutive weeks. According to Schweighofer et al., the existence of a "functional threshold" would be necessary for the maintenance of functionality after therapy, below which the use of the upper limb decreases while the benefits to the individual remain above such threshold. It would be useful to determine the specific doses of therapy in each patient.[78]

McConnell et al. applied mCIMT for 2 weeks with two hours of dose per day in a clinical setting, designed for children aged 8–15 years, and the therapist increased the dose to continue with the use of the affected upper limb for 30 min at home. The children executed 20 h of total dose with functional changes. We proposed to apply 50 h of total dose, with the same distribution per day according to this study, although increasing the dose by 30 h, since the participants in our study were younger than those in McConnell et al. and the therapy was performed at home, thus the children and their families needed more time to obtain significant results. Thus, we decided to assess the children at Week 2 of treatment (20 h) in order to verify whether the changes would be the same at Week 5 (after treatment with a total dose of 50 h).[78]

The systematic review included 31 papers, each of which applied different doses per day, total doses, measurement tools, etc. All 31 studies were compared, with the main difficulty being that the children had different manual ability levels, and it would be ideal to know the correct dose for each level. In this systematic review, the manual ability levels were assessed with the
Manual Classification System, MACS; some studies show Levels I–III, I–IV or I–V. We could consider a moderate hand ability level for children classified as Level I–II in MACS. These levels reflect that the children are independent in the execution of activities using one or two hands or including compensation strategies (neck, trunk, mouth, etc.) to complete the

bimanual task; they also show that the movement restrictions do not impede the complete use of the affected upper limb.[79]

The deterioration of hand functionality causes a weakness present in the execution of activities of daily living in children with hemiplegia. There is an alteration compared to the healthy upper limb that manifests in the general slowness of movement, discontinuous movements, variability in the trajectory of the hand with compensations of the trunk and the presence of inadequate coordination in the grasp strength of the affected hand.[80] The improvement in grasp strength and stability occurs from the third to the fourth measurement due to an increase in hand strength. The increase was observed only in the last measurement, which could be due to the need for a longer treatment time (5 weeks of intervention). These children with impaired fine motor adjustment, a lack of finger dissociation and deficient proprioception in their affected hand had greater experience (trial–error) to adapt the grasp to the shape, texture and weight of the object, allowing the execution of a previous thinking strategy (anticipatory control) to achieve precision in the grasp and adjustment of the strength to grasp the object adequately.

The improvement of grasp stability and strength allows a functional grasp when picking up objects of different characteristics and holding them while performing selective and precision activities, such as throwing a small ball at a target, keeping a fork steady with the affected hand and bringing food to the mouth during the feeding phase. Most children with unilateral brain injury do not develop adequate grip strength in the affected upper limb to coordinate onehanded activities. There is a pathological pattern or an immature state of grasp for their age, leading to an inadequate synergy of the coordination strength that is related to the deterioration of the manual ability of the affected hand depending on the level of injury.[81]

Eliasson et al., who showed better rates of parental competence among those who had applied low doses of treatment. Likewise, some children showed higher levels of frustration or low tolerance was shown by both the child and the family with higher doses of treatment. To minimize such feelings, some authors have proposed adapting the original protocol, suggesting the use of the containment only during the intervention period, reducing the dose and using a protocol that is "child friendly" and enhances children's engagement.[82]

Chen et al. (2016), since the younger children with cerebral palsy responded better to homebased CIMT on some areas of upper limb functions than older children. When the child does not receive treatment, the choice of using the upper limbs to carry out a unimanual action will depend on the characteristics of the injury, levels of disability, experience and level of frustration and motivation in carrying out activities, among other factors. Learning "not to use" the unaffected upper limb by means of mCIMT intervention

can provide an increased spontaneous participation of the affected upper limb in unimanual and bimanual tasks.[83]

on mCIMT, which showed positive results for the assessment of the quality of movement of motor skills (measured through the QUEST scale) using an intervention protocol of 3 weeks of treatment with an intensity of 6 h per day of restriction and repetitive work. This study demonstrated the effectiveness of the intervention, as it had a larger sample and a control group
(18 children with hemiplegia, nine children in the experimental group and nine children in the control group). In 2011, a different study, conducted exclusively with a girl with hemiplegia, used mCIMT for one hour per day for two weeks.[84]

Children with unilateral spastic CP with Manual Ability Classification System (MACS) scores I, II, or III and aged 2.5 to 8 years were recruited and randomly allocated to either the mCIMTBiT group (three 3-hour sessions per week: 6 weeks of mCIMT, followed by 2 weeks of taskspecific training in goal-directed bimanual play and self-care activities) or to 1.5 hours of more general physical or occupational weekly plus encouragement to use the affected hand for the
UC group. Primary outcome measures were the Assisting Hand Assessment and the ABILHAND-Kids. Secondary outcomes were the Melbourne Assessment of Unilateral Upper Limb Function, the Canadian Occupational Performance Measure, and the Goal Attainment Scale. Twenty-eight children were allocated to mCIMT-BiT and 24 to UC. Except for the Melbourne, all primary and secondary outcome measures demonstrated significant improvements in the mCIMT-BiT group. mCIMT followed by task-specific training of goaldirected bimanual play and self-care activities is an effective intervention to improve the spontaneous use of the more affected upper limb in children with relatively good baseline upper extremity function.[85]

EFFECTS OF HABIT ON QUALITY OF UPPER EXTREMITY FUNCTION IN CP

systematically review the effectiveness of Hand-Arm Bimanual Intensive Training (HABIT) on upper limb function in children with cerebral palsy. Among 646 studies, 15 fulfilled the inclusion criteria. Eleven studies were RCTs, 64% of which were rated as having a high risk of bias; one was a quasi-RCT, one was a retrospective study, and two were longitudinal studies.
Nearly half of the included studies used HABIT for 6 h a day for three consecutive weeks (totaling 90 h), and some studies used different doses/schedules or added training components to HABIT. Synthesis of the results demonstrated a significantly small effect size (d = 0.36, P = 0.017) for improving upper limb function immediately after the interventions, and the improvements were maintained at follow-up. Similarly, significantly moderate or large effect sizes were found for self-care function (d = 0.52, P = 0.003) and goal

improvements (d = 1.782.28, P < 0.001). This review supports the effectiveness of HABIT as an intervention for improving upper limb function in children with cerebral palsy.[86]

A computerized database search yielded 468 studies. After meticulous scrutiny and screening of these studies according to the selection criteria, 4 full-text articles were included in the metaanalysis. All 4 studies underwent a methodological quality assessment according to the Physiotherapy Evidence Database Scale (PEDro), with a score of greater than 8. Five comparisons were then made involving the 4 selected randomized controlled trials (RCTs). The effect size was measured using the correlation coefficient (*r* value). The effect sizes of the individual studies were 0.006, 0.03, 0.04, 0.22, and 0.15. The total effect size was 0.06. This meta-analysis determined that there is a trivial benefit using HABIT when compared to constraint-induced movement therapy or structured and unstructured bimanual therapy in pediatric patients with unilateral spastic CP. More RCTs are needed to substantiate our evidence.[87]

Thirty patients who fulfilled the inclusion criteria were randomly allocated into two groups. Group A-HABIT with Object Manipulation, Group B- HABIT without Object Manipulation with 15 patients in each group. All the patients were evaluated with Pediatric Motor Activity Log, Modified Ashworth Scale and Manual Ability Classification System at pre-and posttreatment level. There were significant decrease in spasticity MAS (p=0.001) & improvement in upper extremity function PMAL-R (p=0.001) & MACS (p=0.001) in both the groups post intervention. HABIT with object manipulation with different shape & size group had significant improvement on PMAL-R (p=0.002) & MACS (p=0.009) but no change in spasticity MAS (p=0.679) as compared to HABIT with object manipulation with similar shape & size group. From finding of this study conclude that HABIT with Object Manipulation with different shape and size have positive effect in improving upper extremity function in children with hemiplegic cerebral palsy but not in spasticity reduction after 4 weeks of intervention.
Cerebral palsy; Hand arm bimanual intensive training (HABIT); Manipulation; Object shape; Size; Weight.[88]

This international, multicentric study will include 50 pre-school children with CP from 12 to 60 months of age, comparing the effect of 50 h (2 weeks) of HABIT-ILE versus regular motor activity and/or customary rehabilitation. HABIT-ILE presents structured activities and functional tasks with continuous increase in difficulty while the child evolves. Assessments will be performed at 3 period times: baseline, two weeks later and 3 months later. The primary outcome will be the Gross Motor Function Measure 66. Secondary outcomes will include Both Hands Assessment, Melbourne Assessment-2, Semmes-Weinstein Monofilament Test, algometry assessments, executive function tests, ACTIVLIM-CP questionnaire, Pediatric Evaluation of Disability Inventory (computer adaptative test), Young Children's Participation and Environment Measure, Measure of the Process of Care,

Canadian Occupational Performance Measure, neuroimaging and kinematics. The results of this study should highlight the impact of a motor, intensive, goal-directed therapy (HABIT-ILE) in pre-school children at a functional, neuroplastic and biomechanical level. In addition, this changes could demonstrated the impact of this intervention in the developmental curve of each child, improving functional ability, activity and participation in short-, mid- and long-term.[89] Dysfunction in the upper limbs is one of the most common symptoms in children with cerebral palsy (CP), particularly children with hemiparetic CP which intern has the potential to limit the involvement of these children in life activities and cause distress and suffering for both children and their parents. The main purpose of the research was to compare the therapeutic impact among hand-arm bimanual intensive therapy (HABIT), modified constrained induced movement therapy (mCIMT) and taskoriented training (TOT) on upper extremity functions in children with hemiparetic CP. Sixty hemiparetic CP children of both genders with an age range from five to eight years were randomly divided into three equal-number groups. Group (A) received HABIT, group (B) received mCIMT and group (C) received TOT. Treatment was conducted for 30 minutes, three days per week for three successive months. Peabody
Developmental Motor Scale (PDMS-2) and Quality of the Upper Extremity Skills Test
(QUEST) were used to assess the function of the upper extremity for all groups. The Assessment was performed before as well as after the period of intervention. Significant improvement of the visual-motor integration and grasping subsets of PDMS-2 as well as a significant increase in dissociated movements and grasp subtests of QUEST in the three groups after intervention with a higher significant effect for the mCIMT. It could be concluded that all of the three physical therapy interventions (HABIT, mCIMT and TOT) could improve upper extremity functions for children with hemiparetic CP with a more significant effect on the mCIMT.[90]

Cerebral palsy (CP), which is the leading cause of motor disability during childhood, can produce sensory and cognitive impairments at different degrees. Most recent therapeutic interventions for these patients have solely focused on upper extremities (UE), although more than 60% of these patients present lower extremities (LE) deficits. Recently, a new therapeutic concept, Hand-arm Bimanual Intensive Therapy Including Lower Extremities (HABIT-ILE), has been proposed, involving the constant stimulation of UE and LE. Based on motor skill learning principles, HABIT-ILE is delivered in a day-camp setting, promoting voluntary movements for several hours per day during 10 consecutive week days. Interestingly, the effects of this intervention in a large scale of youngsters are yet to be observed. This is of interest due to the lack of knowledge on functional, neuroplastic and biomechanical changes in infants with bilateral CP. The aim of this randomized controlled study is to assess the effects of HABIT-ILE adapted for pre-school children with bilateral CP regarding functional, neuroplastic and biomechanical factors.[91]

In a randomized trial, 128 patients with acute stroke were assigned to the HABIT or the CRP groups. The primary endpoint was clinical motor functional assessment that was guided by the

Fugl-Meyer motor assessment (FMA) and outcomes of the action research arm test (ARAT). The secondary endpoint was an improved neurophysiological evaluation according to the motor-evoked potential amplitude (AMP), resting motion threshold (RMT), and central motor conduction time (CMCT) scores over the 2-week course of therapy. In both groups, scores were evaluated at baseline, 1 week from commencing therapy, and post-therapy. After 2 weeks, the HABIT group showed improved scores as compared the CRP group for FMA (51.7 ± 6.44 vs. 43.5 ± 5.6, *P*< 0.001), ARAT (34.5 ± 6.2 vs. 33.3 ± 6.3, *P* = 0.022), and AMP (1.1 ± 0.1 vs. 1.0 ± 0.1, *P*< 0.001). However, CMCT (8.6 ± 1.0 vs. 9.1 ± 0.6, *P* = 0.054) and RMT (55.3 ± 4.2 vs. 57.5 ± 4.1, *P* = 0.088) were similar when comparing between groups. HABIT significantly improved motor functional and neuro-physiological outcomes in patients with acute stroke, which suggested that HABIT might represent an improved therapeutic strategy as compared CRP.[92]

QUEST

The Quality of Upper Extremity Skills Test (QUEST) was developed to overcome limitations of currently available measures of hand function. This measure evaluates quality of upper extremity function in four domains: dissociated movement, grasp, protective extension, and weight bearing. It is designed to be used with children who have neuromotor dysfunction with spasticity and has been validated with children from 18 months to 8 years of age. Recently, a multi-centre trial evaluating the effect of neurodevelopmental therapy (NDT) and upper extremity casting on improvement of hand function in children with cerebral palsy was completed. Data collected during that study were analyzed to examine the validity and responsiveness of the QUEST. Consensus meetings were held with therapists who have used the QUEST, reliability testing was completed and a manual of test administration was written. The results of these studies indicate that the QUEST is a criterion referenced measure with good interobserver and test-retest reliability. The QUEST correlates strongly with another measure of hand function, the Peabody Developmental Fine Motor Scales. The QUEST is useful as a measure to describe upper extremity quality of movement and to use in planning intervention programs.[93]

Thirty-one QUESTs from 24 children with CP were rated once by two raters and twice by one rater. Internal consistency of total scores, inter- and intra-rater reliability findings for total, domain, and item scores were calculated. Total scores inter-rater reliability, Intra-class Correlation Coefficient (ICC) was 0.86, and for intra-rater reliability, ICC was 0.96. Domains had high reliability (ICC > 0.80) within raters and between raters except for grasp (moderate at ICC = 0.67). Item inter-rater reliability was moderate or better for 80% of items; item intrarater reliability was moderate or better for 87% of items. Total score

internal consistency was high (α = 0.97). The QUEST has proven reliability for children with CP aged 18 months to 8 years. This study demonstrates strong reliability for children aged 2-12 years.[94]

The QUEST and three existing tools designed to measure the quality of online health information were applied to two randomized samples of articles containing information about the treatment ($n = 16$) and prevention ($n = 29$) of Alzheimer disease as a sample health condition. Inter-rater reliability was assessed using a weighted Cohen's kappa (κ) for each item of the QUEST. To compare the quality scores generated by each pair of tools, convergent validity was measured using Kendall's tau (τ) ranked correlation. The QUEST demonstrated high levels of inter-rater reliability for the seven quality items included in the tool (κ ranging from 0.7387 to 1.0, $P < .05$). The tool was also found to demonstrate high convergent validity. For both treatment- and prevention-related articles, all six pairs of tests exhibited a strong correlation between the tools (τ ranging from 0.41 to 0.65, $P < .05$). Our findings support the QUEST as a reliable and valid tool to evaluate online articles about health. Results provide evidence that the QUEST integrates the strengths of existing tools and evaluates quality with equal efficacy using a concise, seven-item questionnaire. The QUEST can serve as a rapid, effective, and accessible method of appraising the quality of online health information for researchers and clinicians alike.[95]

In this paper, concerns are addressed regarding the reliability of the Quest scale introduced by Batson (1976) and Batson and Ventis (1982). After briefly reviewing the evidence, we have concluded that, although the Batson and Ventis (1982) six-item Quest scale seems to have acceptable test-retest reliability, it has poor internal consistency. To remedy this problem, a new 12-item version of the Quest scale is herein proposed. This 12-item version has satisfactory internal consistency (Cronbach's alphas in the .75 to .82 range) and, equally important, is highly correlated with the original six-item Quest scale (correlations in the .85 to .90 range). We recommend that both the new 12-item scale and the six-item version be used in future substantive research that seeks to assess the way in which a quest dimension of religion facilitates or inhibits personal adjustment and positive social behavior.[96]