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Possible Role of Bee Venom Therapy in Children with Cerebral Palsy

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Abstract: Cerebral palsy (CP) is a non-progressive disorder of posture and movement caused by a defect or insult to the central nervous system. Impaired or altered growth patterns are very common in children with CP. This work aimed to evaluate the effect of bee venom therapy as an apitherapy in cerebral palsy. Forty children with CP were divided into two groups, Group I (20 cases), exposed to bee venom therapy and group II (20 cases) with no bee venom therapy. All cases were subjected to full clinical, neurological history and examination. Anthropometric measures were assessed, as well as biochemical analysis for Copper, zinc, alpha tochopherol,serum iron and levels of immunoglobulins at the start of the study then by the end of the study. Results revealed that cases of group I showed improvement in their posture, reflexes and reducing pain sensation as well as behavioral improvement as compared with cases of group II. Vertebral column deformity showed mild improvement in their angles of deviation, with better sitting position in cases of group I as compared with cases of group II. The nutritional intake shows that the energy intake zinc, copper, vit. E and iron were poor in both groups at the start of the study, but by the end of the study, cases of Group I showed mild improvement in their nutritional intake as well as levels of zinc, copper, alpha tochopherol, iron and immunoglobulins. In conclusion, Bee venom therapy can be considered as a part of apitherapy which utilizes bee venom in the treatment programs of children with CP.

Key words: Cerebral Palsy · Bee Venom · Child Health

INTRODUCTION

The most abundant active component of the venom is melittin. which has many useful properties, including powerful anti-inflammatory, anti-bacterial and anti-viral actions. However, bee venom is a complex mixture of a variety of peptides and proteins, some of which have strong neurotoxic and immunogenic effects. While, Apitherapy is the medical use of honey bee products [1, 2]. This can include the use of honey, pollen, bee bread, propolis, royal jelly and bee venom [3].

There is no standardized practice for the administration of bee venom. Some reported that the location of the sting is important, with the sting acting as a sort of acupuncture in combination with the effects of the venom, while others report the location is not important. The number of stings also varies widely from a few to hundred and they may be administered either by live bees or by injection [4]. This treatment can cause pain and even result in death if the subject has an allergy to bee venom, which can produce anaphylactic shock [5].

Cerebral palsy (CP) is general term for a group of permanent, non- progressive disorders that cause physical disability in human development, chiefly in the various areas of body movement [6]. It is a central motor dysfunction affecting muscle tone. posture and movement resulting from a permanent, non-progressive defect or lesion of the immature brain. CP is neither genetic nor a

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disease and it is not contagious. The vast majority of cases are congenital, arising at or about the time of birth and are diagnosed at a very young age rather than during adolescence or adulthood [7, 8].

Cerebral palsy's nature as a broad category means it is defined mostly via several different subtypes, especially the type featuring spasticity and also mixtures of those subtypes [9]. Aim of the work is to evaluate the effect of bee venom therapy in cerebral palsy.

MATERIALS AND METHODS

This study was carried on Fourty children with CP., spastic type, aged 3–7 years, of both sexes, all cases were under the same program of treatment, same physiotherapy exercise, training and stimulation therapy, from those attending the outpatient clinic of pediatric Neurology in Suzan Mubarak Hospital Egyptian Red Crescent, Mohandeseen, over a period about 3 and half years, from January 2008 till June 2011. Diagnosis was confirmed by complete history and clinical examination, Cases were divided into two groups, Group I (20 cases), exposed to bee venom therapy, treated with bee acupuncture 3 times weekly, for 12 months, started gradually by one sting then gradually increase up to 8 stings per session, in addition to their medical treatment.While group II remains on their ordinary medical treatment only, with no bee venom therapy. The study was submitted to and approved by the ethics rules. Informed consent for all cases were signed by the patients and their caregivers to participate in the study including the following:

Full general and neurological assessment, including full history and examination according to sheet prepared for the study, neurological examination on the beginning of the study to confirm the diagnosis then examination was repeated every two months and by the end of the study, to examine and detect the changes which may be happened for each case and recorded in the form of scores starting from 0 for normal with no abnormal signs up to 5 for complete disability.

Anthropometric measures assessment, including weight measurement to the nearest 100 grams, height measurement to the nearest millimeter and calculation of body mass index (BMI) using the hand held calculator in Kg/m2.[10] Mid arm circumference as well as mid thigh circumference were recorded using the standard method, mid arm and mid thigh muscle and fat areas were calculated [11].

Biochemical analysis for Copper, Zinc according to the method of Homsher and Zac [12] and Abe *et al*. [13], respectively, Alpha tochopherol (Vitamin E) using the method of Desai and Machlin [14]. Serum iron Estimation of serum iron calorimetrically as described by Ceriotti and Ceriotti [15] and Serum IgE levels were estimated by using ELISA at the start of the study and the end of the study.

Apiacupuncture done by bee stings for regulating the immune system in the following points GB 20, Li4, GB 21, S36, Li 11, GB 34, B 11, B60, Li 3[16].

Physiotherapy: All cases were exposed to a program of none fatiguing strenthing exercises [17-20]. This program includes the Isometric muscles contraction and isotonic muscles contraction. By using Grip Dynamometer for hand power assessment for both upper limbs and using the tensiometer& tape measure for both lower limbs, for determination of the changes in the muscles efficiency (Quadriceps muscles) [21].

Statistical analysis: All data obtained were statistically analyzed using Microsoft Excel and SPSS 11.5 for windows software package including, “t test, non parametric Qui square, Mann witney and anova test” as Steel and Torrie [22].

RESULTS

In this study,40 cases with CP, 26 females and 14 males with a ratio 1.86:1. Table (1) shows clinical findings of the cases of both groups at the start of the study. Clinically at the start of the study the cases of group (I) "exposed to bee venom therapy"include "13 cases with diplegia, 1 case with hemiplagia and 6 cases with quadriparesis", while cases of group (II) "not exposed to bee venom therapy"were clinically included 10 cases with diplegia, 4 cases with hemiplegia and 6 cases with quadriparesis.

Table (2) showed that by the end of the study, cases of group (I) showed improvement in their posture, spasticity, reflexes by and reducing pain sensation, as compared with cases of group (II). Regarding vertebral column deformity showed mild improvement in their angles of deviation, with better sitting position in cases of group (I) as compared with cases of group (II). Regarding the hand grip power there was an improvement among cases of group II, while improvement was more among cases of group I. The percentage of improvement among cases with diplegia was 38.46% in group (I), as compared with cases with diplegia among group (II) which was 20% and improvement was 100% among hemiplegic cases in

Table 1: Shows the distribution of CP subtypes found in this study according to clinical findings at the start of the study:

	Group I (Exposed to bee venom therapy)			Group II (No bee venom therapy)		
Variables	Diplegia	Hemiplegia	Quadriparesis	Diplegia	Hemiplegia	Quadriparesis
Clinical Findings	Spasticity of both Lower Limbs + Average tone + average mentality	Unilateral Asymetrical spasticity + Partial Siezures + Headache	All extremities as well as trunk spasticity + Impaired Bowel and/or bladder control + autonomic dysreflexia + Breathing troubles	Spasticity of both Lower Limbs + Average tone	Unilateral Asymetrical spasticity + Partial Siezures	All extremities as well as trunk spasticity + Impaired Bowel and/or bladder control + autonomic dysreflexia +Breathing troubles
Sex distribution (M:F ratio)	4 M / 9 F (1:2.25)	0 M / 1 F (0: 1)	2 M / 4 F (1: 2)	3 M/ 7 F (1: 2.33)	1 M / 3 F (1: 3)	4 M / 2 F (2: 1)
Number Of Cases and their Percentage %	13 cases (65%)	1 case (5%)	6 cases (30%)	10 cases (50%)	4 cases (20%)	6 cases (30 %)
Total Percentage %	20 cases (50%) 6 M & 14 F			20 Cases (50%) 8 M & 12 F		

Table 2: Shows the distribution of CP subtypes found in this study according to clinical findings by the end of the study:

	Group I (Exposed to bee venom therapy)			Group II (No bee venom therapy)		
Variables	Diplegia	Hemiplegia	Quadriparesis	Diplegia	Hemiplegia	Quadriparesis
Clinical Findings	Spasticity of both Lower Limbs + Average tone + average mentality	Unilateral Asymetrical spasticity + Partial Siezures + Headache	All extremities as well as trunk spasticity + Impaired Bowel and/or bladder control + autonomic dysreflexia + Breathing troubles	Spasticity of both Lower Limbs + Average tone	Unilateral Asymetrical spasticity + Partial Siezures	All extremities as well as trunk spasticity + Impaired Bowel and/or bladder control + autonomic dysreflexia +Breathing troubles
Sex distribution (M:F ratio)	4 M / 9 F (1:2.25)	0 M / 1 F (0: 1)	2 M / 4 F (1: 2)	3 M/ 7 F (1: 2.33)	1 M / 3 F (1: 3)	4 M / 2 F (2: 1)
Number Of Cases and	8 cases	0 case	3 cases	8 cases	3 cases	5 cases
their Percentage %	(40%)	(0%)	(15%)	(40%)	(15%)	(25 %)
% of Improvement	38.46%	100%	50%	20%	25%	16.67%

Table 3: Shows the nutrient intake by all cases in the study (Both groups) at the start of the study and by the end of the study and the percentage of improvementas compared to the mean of RDA according to their ages

Nutritional Supply		Energy (k.cal)	Magnesium (mg/d)	Iron (mg/d)	Calcium (mg/d)	Zinc (mg/d)	Copper (mg/d)	Vit. D (IU/ d)	Vit. E (IU/ d)	Folate (mcg/ d)	Niacin (Vit. B_3) (mg/ d)
Mean RDA		105	200	12.5	700	13.5	2.25	400	2.25	400	20
GROUP (I)	Mean of the Intake At The Start	52.9±8	142.19±23	9.89±0.94	603.2±43	10.1±0.52	1.49±0.16	279.7±46	1.35±0.18	292±62.8	14.9±1.52
N= 20	Of The Study	50.38%	71.09%	79.12%	86.17%	74.81%	66.22%	69.93%	60%	73%	74.5%
	Mean of the Intake By The End	71.4±6	169.3±14	10.9±0.7	651.5±0.3	11.4±0.46	1.72±0.42	316.3±38	1.64±0.4	327.8±51	16.7±0.93
	Of The Study	68%	84.65%	87.2%	93.07%	84.4%	76.44%	79.08%	72.89%	81.95%	83.5%
Improvement %		17.62%	13.56%	8.08%	6.9%	9.59%	10.22%	9.15%	12.89%	8.95%	9%
GROUP (II)	Mean of the Intake At The Start	56.76±11	141.9±15	9.93±1.03	599.9±51	10.3±0.75	1.52±0.27	292.1±51	1.15±0.09	289±58.7	15.1±1.93
N= 20	Of The Study	54.06%	70.95%	79.44%	85.7%	76.29%	67.56%	73.03%	51.11%	72.25%	75.5%
	Mean of the Intake By The End	61.2±65	146.5±15	10.03±0.7	627±65	10.6±0.3	1.59±0.2	302.4±35	1.42±0.07	298±53.2	15.8±1.23
	Of The Study	58.29%	73.25%	80.24%	89.57%	78.52%	70.67%	75.6%	63.11%	74.5%	79%
Improvement %		4.23%	2.3%	0.8%	3.87%	2.23%	3.11%	2.57%	12%	2.25%	3.5%

Table 4: Mean levels of IgE for both groups at the start of the study and by the end of the study

Groups	Mean Levels of IgE levels At the start of the study (IU/ml)	Mean Levels of IgE levels by the end of the study (IU/ml)
Group (I)	491.42	1045.32
Group (II)	664.32	1031.14

Table 5: Shows the mean plasma and serum concentrations of micronutrients for both groups of CP at the start and by the end of the study with the percentage of improvement:

serum concentrations of micronutrients		Magnesium (mmol/l)	Iron (µmol/l)	Calcium (mg/dl)	Zinc (µg/dl)	Copper (µg/dl)	Vit. E (mg/dl)	Folate (nmcl/l)
Reference range	0.6 – 1	8 - 31	2.15 – 2.65	10.7 – 23	11 – 22	10 – 21	8 – 26	
GROUP (I)	Mean±SD Plasma levels At the start of the study (n= 20)	0.75±1.02	8.86±3.2	1.82±0.04	15.2±2.7	17.9±3.4	13.2±3.8	19.98±6.5
	Mean±SD Plasma levels By the end of the study (n= 20)	0.79±0.08	12.8±2.9	2.49±0.02	16.7±3.03	20.05±4.6	16.6±8.4	23.9±4.9
Improvement %		5.33%	44.47%	36.02%	9.87%	12.01%	25.76%	19.62%
GROUP (II)	Mean±SD Plasma levels At the start of the study (n= 20)	0.76±0.98	8.48±1.87	1.78±0.03	14.8±1.4	18.1±2.2	12.9±2.6	20.08±2.3
	Mean±SD Plasma levels By the end of the study (n= 20)	0.77±0.7	8.96±0.8	1.96±0.2	15.4±1.02	19.03±0.9	14.8±0.08	21.79±1.4
Improvement %		1.3%	5.66%	10.11%	4.05%	5.14%	1.29%	8.52%

group (I) as compared with hemiplegic cases of group (II) which was 25%, while improvement of cases with quadriparesis was 50% among group (I) as compared with cases of group (II) which was 16.67%.

Regarding nutritional intake (Table 3), the amount of the daily intake of all elements assessed were statistically low as compared with the RDA.The percentages of the nutritional intake shows that the energy intake, amount of magnesium, calcium, zinc, copper, Vit.D, Vit. E, Folate, iron and niacin were poor in both groups at the start of the study, but by the end of the study, cases of Group (I) showed more improvement in their nutritional intake as compared with group (II).

In this study the mean values of IgE in both groups of CP patients (Table 4)were low but with no statistical significance, while by the end of the study there were an elevation in the levels of IgE for both groups, which was statistically significant among those cases of group (I).

Regarding the serum levels of micronutrients (Table 5), the levels of all micronutrients assessed were low as compared with the reference ranges. The percentages of their levels showed that serum levels of magnesium, iron, calcium, zinc, copper, Vit. E and folat were low in both groups at the start of the study, but by the end of the study, cases of Group (I) showed more improvement in their nutritional intake as compared with the improvement among cases of group (II).

DISCUSSION

Cerebral palsy is a group of permanent disorders of the development of movement and posture, causing activity limitations 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 behavior, by epilepsy and by secondary musculoskeletal problems [23].

Spasticity refers to the muscle tone being unyielding and tight (hypertonia) with a decreased range of movement. If the person is only affected on one side of their body the term used to describe this is hemiplegia or unilateral cerebral palsy. If two limbs are affected (usually legs more than arms), the term is diplegia and if all four limbs are affected the term used is quadriplegia [24]. In this study we found 23 with diplegia, 13 in group (I) and 10 in group (II) and 5 cases with hemiplegia, 1 in group (I) and 4 in group (II), lastly 12 cases with quadriparesis 6 in group (I) and 6 in group (II).

In cerebral palsy secondary musculoskeletal problems and motor control are common. Often contractures of muscles of the spine or hip dislocation. A referral to a physiotherapist may be helpful [25]. In this study cases of both groups were exposed to a program of Non fatiguing strenthing exercises to manage postural defects as well as musculoskeletal problems and motor control which were present among cases in this study [26]. By the end of this study, cases of both groups (I&II) showed improvement in their posture, spasticity, reflexes by and reducing pain sensation which was more evident in group (I) and vertebral column deformity showed an improvement in their angles of deviation, with better sitting position among cases of group (I) and this confirms that bee venom had a role in these improvement as both groups were under same physiotherapy program, so these marked differences were because of the bee venom therapy and this may explain the improvement of bowel movement and reduction of constipation among this group (I). Feeding and GIS problems are frequent in children with CP and more marked in those with severe CP. Approximately one fourth of children with CP suffer from feeding dysfunction and more time has to be allocated to consume meals and poor appetite [27] and this is explained in this study as we found that the daily intake of all elements assessed at the start of the study were lower than the RDA, while by the end of the study the nutritional intake showed an improvement in their nutritional intake percentage which was markedly recognized among cases of group (I) under bee venom therapy as compared with group (II), this means that bee venom therapy improve appetite.

Serum levels of magnesium, iron, calcium, zinc, copper, Vit. E and folate were low in both groups at the start of the study, but by the end of the study, cases of Group (I) showed more improvement in their nutritional intake as compared with the improvement among cases of group (II), as well as levels of IgE which showed significant low levels among cases of both groups (I& II), while by the end of the study marked elevation of IgE levels was assessed and this can be explained by Nam *et al*. [27] who stated that bee venom is a mixture of many substances.In this study we found that there is a statistically significant improvement regarding their immunity and the improvement in their health and general conditions and this is explained byPark *et al*. [28] and Prado *et al*. [29] bee stings cause hemoconcentration which might be related to the marked edema induced by the venom. Following bee stings there is an increase in various cytokines like interleukin (IL)-1β, IL-6, tumor

necrosis factor-α, etc. In a mouse model using the subcutaneous route, rapid increases in serum alanine aminotransferase and aspartate aminotransferase transaminases, creatinine, urea nitrogen, uric acid, sodium and chloride electrolytes and creatine kinase were recorded [1, 28, 29]. The pain and swelling of the sting are caused by histamine, dopamine, serotonin and norepinephrine. Several toxins are also present, including apamin, melittin, monamine and mast-cell degranulating peptide. Lastly, the substances responsible for the allergic response include hyaluronidase and phospholipase-A2, enzymes that work to activate immune cells and produce immunoglobulin E [27].

It could be concluded that, this study give the chance for bee therapy to take a place among programs of management of CP. We concluded that although bee venom is not a curable therapy but it can be used to minimize the contractures occurred in CP. Bee venom therapy can be considered as a part of apitherapy which utilizes bee venom in the treatment programs of children with CP.

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