hypoxic- ischemic insult leads to cellular necrosis, neuronal inactivation and cerebral white matter injury are the most common causes of severe neurological handicaps in children with CP (Efrati and Ben- Jacob, 2014).

Children with cerebral palsy typically receive physiotherapy therapy to facilitate motor development and to enhance their independence in motor skills, Self- care, play, and leisure activities. Over the years, many systems of treatment have been developed that differ in their specific treatment strategies, but aim to lead children with cerebral palsy toward the greatest degree of independence possible.

In our study, as regards the age, there was no statistical significant difference between the mean value of the 4 studied groups A, B, C& D Which was 5.90± 1.16, 5.90± 1.20, 5.90± 1.20, and 5.90± 1.20 years respectively.

In our study, as regards the gender, there was no statistical significant difference between the percentages of the 4 studied groups. Group A was 12 (40%) female and 18 (60%) male, Group B was 4 (40%) female and 6 (60%) male, Group C was 5 (50%) female and 5 (50%) male and Group D was 6 (60%) female and 4 (40%) male.

In our study, there was no statistical significant difference pre treatment between the 4 studied groups A, B, C& D regarding Gait Parameters (Step length, Stride length, Step width, and Foot progression angle) and Modified Ashworth Scale.

In group A (Control) there was statistical significant improvement in gait parameters and Modified Ashworth scale. There was high statistical significant difference between pre and post treatment regarding Step length, Stride length, Step width, Foot progression angle and Modified Ashworth scale.

In group B there was statistical significant improvement in gait parameters. There was high statistical significant difference between pre and post treatment regarding Step length, Stride length, Step width and Modified Ashworth scale.

In group C there was statistical significant improvement in gait parameters. There was high statistical significant difference between pre and post treatment regarding Stride length, Step width, Foot progression angle.

In group D there was statistical significant improvement in gait parameters. There was high statistical significant difference between pre and post treatment regarding Step length, Stride length, Step width, and Foot progression angle.

In our study, In Comparison between the post treatment of studied groups A, B, C, and D according to Step length there was more improvement in groups Band C.

In our study, In Comparison between the post treatment of studied groups A, B, C, and D according to Stride length there was more improvement in group B.

In our study, In Comparison between the post treatment of studied groups A, B, C, and D according to Step width there was more improvement in group B.

In our study, In Comparison between the post treatment of studied groups A, B, C, and D according to Foot progression angle there was more improvement in group B.

In our study, there was no statistical significant difference post treatment between the 4 studied groups A, B, C& D regarding Modified Ashworth Scale. There was more improvement in groups A and B.

In agreement of our study, hyperbaric oxygen therapy (HBOT) is an interesting therapeutic modality defined as the use of oxygen at greater than atmospheric pressure as a drug to treat basic pathophysiologic processes and the associated diseases (Lacey et.al., 2012).

As HBOT can initiate vascular repair and improve cerebral vascular flow, induce regeneration of axonal white matter, stimulate axonal growth, promote blood- brain barrier integrity and reduce inflammatory reactions as well as brain edema (Huang and Obenaus, 2011).

At the cellular level, HBOT can improve cellular metabolism, reduce apoptosis, relieve oxidative stress and increase levels of neurotrophins and nitric oxide through improving mitochondrial function in both neurons and glial cells and may even promote neurogenesis of endogenous neural stem cells (Lin et.al., 2012).

Efrati and Ben- Jacob (2014), who mentioned that some weeks would be necessary for brain tissue regeneration and angiogenesis and they also reported that the brain of the child with cerebral palsy suffered from neurological insult since birth, so it would take time for the brain repair to become clinically apparent.

The sooner the ozone therapy is started the better, because there is no hope of reviving dead neurons. Controlled administration of ozone can be helpful (Bocci, 2007).

Acupuncture treatment for cerebral palsy is still considered relatively new. Only a few in- depth studies have been done, but the results so far have been positive. (Neoh Choo et.al., 2017).

Western medical science so far has not found a proven explanation for the success of Chinese scalp acupuncture in treating central nervous system disorders and specifically with treating cerebral palsy. There is a growing amount of clinical evidence that scalp acupuncture can improve or remove symptoms in patients with cerebral palsy (Lin et.al., 2012).

Conclusion:

1. Hyperbaric oxygen therapy HBOT have the best results in this study followed by ozone followed by acupuncture.
2. Physiotherapy (PT) and occupational therapy (OT) are very important methods in management of children with cerebral palsy.

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Ethical issues:

Written informed consents were obtained from parents after explanation of the aim of the study and its benefits for their children.

Data Analysis:

The data obtained was statistically analyzed. The mean and standard deviation were calculated for each variable, for all groups A, B, C and D before and after the application of management programs.

Results:

[1]Table (1) Comparison between the studied groups A& B according to Gait Parameters and Modified Ashworth Scale after applying protocols

		Group A	Group B	Test Value	P- Value	Sig.
		No. = 30	No. = 30			
Step Length Post	Mean± SD	25.25± 1.14	26.55± 1.01	- 3.198	0.003	HS
	Range	23.5- 27	25.5- 28			
Stride Length Post	Mean± SD	55.00± 1.35	56.25± 1.36	- 2.538	0.015	S
	Range	53- 57	54.5- 58.5			
Step Width Post	Mean± SD	10.75± 0.83	10.45± 0.76	1.011	0.318	NS
	Range	9.5- 12	9.5- 12			
Foot Progression Angle Post	Mean± SD	16.17± 0.97	14.37± 0.70	5.395	0.000	HS
	Range	15- 17.5	13- 15.5			
Modified Ashworth Scale Post	1	9 (30%)	4 (40%)	0.659	0.719	NS
	1+	15 (50%)	5 (50%)			
	2	6 (20%)	1 (10%)			

Table (2) Comparison between the studied groups A& C according to Gait Parameters and Modified Ashworth Scale after applying protocols

		Group A	Group C	Test Value	P- Value	Sig.
		No. = 30	No. = 30			
Step Length Post	Mean± SD	25.25± 1.14	26.55± 2.83	- 2.092•	0.043	S
	Range	23.5- 27	23.5- 34			
Stride Length Post	Mean± SD	55.00± 1.35	55.15± 1.40	- 0.303•	0.764	NS
	Range	53- 57	53- 57			
Step Width Post	Mean± SD	10.75± 0.83	10.65± 0.82	0.332•	0.742	NS
	Range	9.5- 12	9.5- 12			
Foot Progression Angle Post	Mean± SD	16.17± 0.97	16.00± 0.94	0.483•	0.632	NS
	Range	15- 17.5	15- 17.5			
Modified Ashworth Scale Post	1	9 (30%)	2 (20%)	0.416*	0.812	NS
	1+	15 (50%)	6 (60%)			
	2	6 (20%)	2 (20%)			

Table (3) Comparison between the studied groups A& D according to Gait Parameters and Modified Ashworth Scale after applying protocols.

		Group A	Group D	Test Value	P- Value	Sig.
		No. = 30	No. = 30			
Step Length Post	Mean± SD	25.25± 1.14	25.60± 1.02	- 0.859•	0.396	NS
	Range	23.5- 27	24.5- 27.5			
Stride Length Post	Mean± SD	55.00± 1.35	55.41± 1.00	- 0.882•	0.383	NS
	Range	53- 57	54- 57.5			
Step Width Post	Mean± SD	10.75± 0.83	10.60± 0.77	0.504•	0.617	NS
	Range	9.5- 12	9.5- 11.5			
Foot Progression Angle Post	Mean± SD	16.17± 0.97	15.60± 0.93	1.625•	0.113	NS
	Range	15- 17.5	14.5- 17.2			
Modified Ashworth Scale Post	1	9 (30%)	3 (30%)	0.571*	0.751	NS
	1+	15 (50%)	6 (60%)			
	2	6 (20%)	1 (10%)			

Table (4) Comparison of the studied cases in group A pre and post applying protocols

		Group A		Test Value	P- Value	Sig.
		Pre	Post			
Step Length	Mean± SD	24.70± 1.21	25.25± 1.14	-19.746**	0.000	HS
	Range	23- 26.5	23.5- 27			
Stride Length	Mean± SD	54.35± 1.42	55.00± 1.35	- 7.779**	0.000	HS
	Range	51.5- 56	53- 57			
Step Width	Mean± SD	11.65± 0.72	10.75± 0.83	9.893**	0.000	HS
	Range	10.5- 12.5	9.5- 12			
Foot Progression Angle	Mean± SD	16.93± 1.08	16.17± 0.97	9.583**	0.000	HS
	Range	15.2- 18.4	15- 17.5			
Modified Ashworth Scale	1	0 (0%)	9 (30%)	11.273**	0.004	HS
	1+	18 (60%)	15 (50%)			
	2	12 (40%)	6 (20%)			

Table (5) Comparison of the studied cases in group B pre and post applying protocols

		Group B		Test Value	P- Value	Sig.
		Pre	Post			
Step Length	Mean± SD	24.70± 1.14	26.55± 1.01	- 12.333	0.000	HS
	Range	23- 26.5	25.5- 28			
Stride Length	Mean± SD	54.50± 0.82	56.25± 1.36	- 4.341	0.002	HS
	Range	53.5- 56	54.5- 58.5			
Step Width	Mean± SD	11.95± 0.50	10.45± 0.76	9.000	0.000	HS
	Range	11.5- 12.5	9.5- 12			
Foot Progression Angle	Mean± SD	15.36± 5.00	14.37± 0.70	0.572	0.582	NS
	Range	1.4- 18.4	13- 15.5			
Modified Ashworth Scale	1	0 (0%)	3 (30%)	11.273*	0.004	HS
	1+	6 (60%)	5 (50%)			
	2	4 (40%)	2(20%)			

Table (6) Comparison of the studied cases in group C pre and post applying protocols

.		Group C		Test Value	P- Value	Sig.
		Pre	Post			
Step Length	Mean± SD	24.75± 1.23	26.55± 2.83	- 1.751**	0.114	NS
	Range	23- 26.5	23.5- 34			
Stride Length	Mean± SD	54.35± 1.47	55.15± 1.40	- 7.236**	0.000	HS
	Range	51.5- 56	53- 57			
Step Width	Mean± SD	11.65± 0.75	10.65± 0.82	5.071**	0.001	HS
	Range	10.5- 12.5	9.5- 12			
Foot Progression Angle	Mean± SD	16.89± 1.14	16.00± 0.94	5.870**	0.000	HS
	Range	15.2- 18.4	15- 17.5			
Modified Ashworth Scale	1	0 (0%)	2 (20%)	3.377*	0.185	NS
	1+	5 (50%)	6 (60%)			
	2	5 (50%)	2 (20%)			

Table (7) Comparison of the studied cases in group D pre and post applying protocols.

		Group D		Test Value	P- Value	Sig.
		Pre	Post			
Step Length	Mean± SD	24.70± 1.14	25.60± 1.02	- 7.216**	0.000	HS
	Range	23- 26.5	24.5- 27.5			
Stride Length	Mean± SD	54.20± 0.79	55.41± 1.00	- 4.549**	0.001	HS
	Range	53.5- 56	54- 57.5			
Step Width	Mean± SD	11.65± 0.75	10.60± 0.77	6.034**	0.000	HS
	Range	10.5- 12.5	9.5- 11.5			
Foot Progression Angle	Mean± SD	17.13± 1.09	15.60± 0.93	4.915**	0.001	HS
	Range	15.2- 18.4	14.5- 17.2			
Modified Ashworth Scale	1	0 (0%)	3 (30%)	4.800**	0.091	NS
	1+	6 (60%)	6 (60%)			
	2	4 (40%)	1 (10%)			

Discussion:

CP is generally considered as a nonprogressive condition resulting from neurological injury in the antenatal or perinatal period. Perinatal

NS: Non significant; S: Significant; HS: Highly significant, *: Chi- square test; •: Independent t- test, **: paired t- test.

Introduction:

Cerebral palsy (CP) describes a group of permanent disorders of development, movement and posture, resulting in activity limitation. Cerebral palsy (CP) is a nonprogressive disease that presents as a disorder of motion and posture following brain injury during a period of development (Asl et.al., 2015).

Also, CP is generally considered as a nonprogressive condition resulting from neurological injury in the antenatal or perinatal period. Perinatal hypoxic ischemic insult leads to cellular necrosis, neuronal inactivation and cerebral white matter injury are the most common causes of severe neurological handicaps in children with CP (Efrati and Ben-Jacob, 2014).

Cerebral palsy (CP) is a very common neural system development disorder that can cause physical disability in human (Zheng et.al., 2012).

Cerebral palsy is a major health problem caused by brain damage during pregnancy, delivery, or the immediate postnatal period. Perinatal stroke, intraventricular hemorrhage, and asphyxia are the most common causes of neonatal brain damage. Periventricular white matter damage (Periventricular Leukomalacia) is the predominant form in premature infants and the most common antecedent of cerebral palsy (Titomanlio et.al., 2011).

Hyperbaric oxygenation therapy (HBOT) has shown promise in clinical trials and is sought by many parents of children with cerebral palsy (CP). Evidence from around the globe is now accumulating providing strong support for the use of hyperbaric oxygen therapy (HBOT) as an approach to the actual underlying problem in children with cerebral palsy- a technique which actually targets the abnormalities of brain function. The use of hyperbaric oxygen therapy in cerebral palsy offers an exciting new therapeutic approach for the treatment of cerebral palsy (Lin et.al., 2012).

Hyperbaric oxygen therapy (HBOT) is an interesting therapeutic modality defined as the use of oxygen at greater than atmospheric pressure as a drug to treat basic pathophysiologic processes and the associated diseases (Lacey et.al., 2012).

Acupuncture with or without conventional therapy may have benefit in children with CP (Dabbous et.al., 2016).

Scalp Acupuncture, also known as Neuroacupuncture, is a treatment based on knowledge of traditional acupuncture and neurology. It is done by inserting acupuncture needles into the loose areolar tissue layer of the scalp to stimulate the brain neurons of the underlying area. It's a very safe treatment, since underlying area. It's a very safe treatment, since the skull protects the brain and there are no organs in the scalp to injure it. Scalp Acupuncture works by stimulating the brain cells that are related to the impaired functions. The mechanism is three- fold: to 'wake- up' the brain cells that are not dead but lacking in proper functioning, to encourage recruitment of healthy brain cells to perform the lost function and to promote a healthy reintegration of the brain system. (Neoh Choo et.al., 2017).

Aims:

The aim of this study is to compare different protocols management in cerebral palsy rehabilitation.

Subjects And Methods:

Type of the study: comparative study to compare different protocols management in cerebral palsy.

Subjects:

The study included 120 patients with CP of both genders, between 4 and 8 years of age, attending the Special Needs Care Center of the Faculty of Postgraduate Childhood Studies, Ain Shams University. The available patient's records used to select the sample, as well as written informed consents were obtained from parents. All The children in all groups received the same specific designed physiotherapy (PT) and occupational therapy (OT) program.

The children were classified into 4 groups: Group A: Included 30 children with cerebral palsy who received physiotherapy (PT) and occupational therapy (OT) as control group. Group B: Included 30 children with cerebral palsy who received physiotherapy (PT) and occupational therapy (OT) and hyperbaric oxygen therapy (HBOT). Group C: Included 30 children with cerebral palsy who received physiotherapy (PT) and occupational therapy (OT) and acupuncture. Group D: Included 30 children with cerebral palsy who received physiotherapy (PT) and occupational therapy (OT) and ozone. According to the protocol of each type of management.

Control Group: Who received a designed physiotherapy (PT) and occupational therapy (OT) program directed towards improving gait pattern and walking balance three times/ week for three hours/ day for eight successive weeks. The children in control group received a specific designed physiotherapy (PT) and occupational therapy (OT) program only. Study Groups: who received the same designed physiotherapy (PT) and occupational therapy (OT) program given to the control group in addition to the protocol of each type of management.

Inclusion Criteria:

1. Spastic Cerebral Palsy.
2. Ages between (4- 8) years.
3. Patients who signed the consent form.
4. The degree of spasticity ranged from grade 1+ to 2 according to Modified Ashworth Scale. (Bohannon, and Smith, 1987).
5. They were able to follow simple verbal commands or instructions in both evaluation and treatment procedures.

Exclusion Criteria:

1. Patients with any other co- morbid chronic illness.
2. Children with chronic illness affecting growth e.g. cardiac or renal disease.
3. Severe Mental Retardation.
4. Cerebral palsy with loss of vision or hearing loss.
5. History of Epilepsy.
6. Previously received any antispastic drugs and battox.

Comparative study of different treatment Methods of rehabilitation in cerebral palsy

Reda Mohmed Maged, Prof. Ghada Farag El-Dorry,and Prof. Ahmed Mohamed El-Kahky
Faculty of Postgraduate Childhood Studies

Summary

Background: Cerebral palsy is a major health problem caused by brain damage during pregnancy, delivery, or the immediate postnatal period. Cerebral palsy (CP) is generally considered as a nonprogressive condition. The goal of any treatment program for cerebral palsy is to maximize function and minimize the development of secondary problems.

Objective: The aim of this study is to compare different protocols management in cerebral palsy.

Subjects and Methods: The study included120 patients with CP of both genders, between 4 and 8 years of age, attending the Special Needs Care Center of the Faculty of Postgraduate Childhood Studies, Ain Shams University. The available patient's records used to select the sample, as well as written informed consents were obtained from parents. The children were classified into 4 groups. Group A: Included 30 children with cerebral palsy who received physiotherapy (PT) and occupational therapy (OT) as control group. Group B: Included 30 children with cerebral palsy who received physiotherapy (PT) and occupational therapy (OT) and hyperbaric oxygen therapy (HBOT). Group C: Included 30 children with cerebral palsy who received physiotherapy (PT) and occupational therapy (OT) and acupuncture. Group D: Included 30 children with cerebral palsy who received physiotherapy (PT) and occupational therapy (OT) and ozone. According to the protocol of each type of management. All The children in all groups received the same specific designed physiotherapy (PT) and occupational therapy (OT) program.

Results: Physiotherapy (PT) and occupational therapy (OT) are very important methods in management of children with cerebral palsy, hyperbaric oxygen therapy HBOT have the best effect in management children with cerebral palsy CP more than other management protocols such as ozone and acupuncture.

Conclusion: Hyperbaric oxygen therapy HBOT have the best results in this study followed by ozone followed by acupuncture.

Keywords: Cerebral palsy, hyperbaric oxygen therapy, ozone, acupuncture

دراسة مقارنة للطرق المختلفة لعلاج الشلل الدماغى

الخلفيه: الشلل الدماغى هو اضطراب تطور النظام العصبى ويمكن أن يسبب الإعاقة الجسدية فى الإنسان وهو مشكلة صحية كبيرة بسبب تلف فى الدماغ أثناء الحمل والولادة، أو فترة ما بعد الولادة مباشرة. تعتبر الولادة المبكرة ونقص الوزن عند الولادة أهم الأسباب التى تؤدى إلى حدوث الشلل الدماغى .والهدف من أى برنامج لعلاج الشلل الدماغى هو تحسين الوظيفة والحد من تطوير المشاكل الثانوية، وبالتالى تأخير أو تفادى الحاجة للتدخل الجراحي. وبرنامج العلاج الفعال يقلل ليس فقط الحاجة لإجراء عملية جراحية، ولكن يعزز قدرة المريض لتوازن أفضل، والمشاركة فى الأنشطة مع الأقران. استخدام العلاج بالأكسجين تحت الضغط فى الشلل الدماغى يقدم نهجا علاجيا جديدا لعلاج الشلل الدماغى ويؤدى إلى حدوث تحسن فى وظيفة الحركة وكذلك الوخز بالإبر والعلاج بالاوزون يعدا من الأمور المبشرة.

الهدف: الهدف من هذه الدراسة هو دراسة مقارنة للطرق المختلفة لعلاج الشلل الدماغى.

الأهمية: ان الشلل الدماغى كان دائما معضلة للوالدين جنبا إلى جنب مع المتخصصين فى العلاج فى محاولة للوصول لأفضل طرق العلاج. علاقة الدراسة باهداف القسم الوصول لأفضل اداء ممكن للأطفال المصابين بالشلل الدماغى هو من أهم أهداف القسم. حيث تهدف هذة الدراسة إلى التحقق من نتائج بعض الأساليب الحديثة فى علاج الشلل الدماغى.

نوع الدرسة: دراسة مقارنة.

الفرضية: يعتبر استخدام العلاج بالأكسجين تحت الضغط العالى أفضل من الوخز بالإبر والعلاج بالاوزون فى علاج الشلل الدماغي.

المرضى: شملت الدراسة على ١٢٠ طفلا مصابا بالشلل الدماغى التقلصى من الذكور والإناث المتابعين فى العيادة الخارجية بمركز رعاية الأطفال ذوى الأحتياجات الخاصة بكلية الدراسات العليا للطفولة، جامعة عين شمس. قد استمرت فترة العلاج لمدة ٦ شهور تبعا للبروتوكول الخاص بكل نوع من انواع العلاج.

النتائج: استخدام الأوكسجين بالضغط العالى حقق أفضل النتائج يليه استخدام الاوزون ثم الوخز بالابر، وان العلاج الطبيعى والعلاج الوظيفى مهم جدا فى علاج الأطفال المصابين بالشلل الدماغى.

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the ICU incubator department in kenayat- hospital in Zagazig.

6. In our study Neonatal Jaundie was treated by using probiotic substances by orally- taking with milk to reduce the number of days under the phototherapy in the incubator.
7. This study included 2 groups. Intervention Group (200 cases) Of jaundiced neonates of different gestational ages, weights, sexes, and total serum bilirubin levels The cases were given the probiotic (Lactobacillus) with milk during the photo therapy management, and Control group (200 cases) also with different Gestational ages, weights, sexes and total serum bilirubin levels.

   After blood sample analysis for bilirubin level and using statistical methods we found that.

   Total serum bilirubin were highly significantly lower in intervention group out more than in control group out by the effect of probiotic lactobacillus and the duration of phototherapy was shorter in the intervention group.

   Feeding intolerance was significantly lower in the intervention Group than in the control group.

   The dose of 250mg/ daily of lactobacillus is safe and effective for full-term and pre- term including VLBW neonates in the short term. (Demirel et.al 2013)
8. The effect of probiotic (lactobacillus) was through:
   a. Improving the feeding intolerance.
   b. Suppressing the reabsorption and degradation of bound bilirubin into the enterohepatic circulation. (LIG et.al 2012) (LIG et.al 2017)
   c. Facilitating the growth of normal bacterial colonies and vitamins in the intestinal tract of neontes. (Maldonado it al 2012)
   d. Forming metabolites corrected the alkaline environment thus weakening the activity of B- GA (B- glucuronidase) and preventing it form binding and hydrolyzing biliubin. (Ratu TN 2012) (Suganthi et.al 2016)
   e. Forming acids that lower the PH in the intestine thus/ Impeding the growth of bacterial pathogens. (Wang et.al 2006) (Tewarivv, et.al 2006)
   f. Enhancing the Immunity by forming a biological barrier in the intestinal epithelial calls and stimulate specific lymphocytes cytokines and IgG and IgA antibodies to fight infection.
   g. Improving a healthy micro flora and displace a harmful bacteria. (Wang et.al, 2006) (Zheng Sf, et.al, 2012)
   h. Stimulating intestinal peristalsis to eliminate bilirubin from Reducing the enterohepatic circulation. (LIG et.al, 2012) (Jia Hy, 2015)

Conclusion:

1. Probiotics were able to treat and lowered the serum bilirubin levels of neonates with jaundice, Rapidly, safely, and significantly,
2. Without discernible side effect and a ccelerated jaundice fading as on well. Thous reducing both need and duration of phototherapy with its burden related issues:

   Hence, this method is worthy of application in clinical practice.

Recommendation:

This study recommended that that we can use aprobitic substances within a plane of management of neonatal hyperbilirubinemia.

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common cause was ABO, Rh in compatibilities.

- In our study, TSB (out) of intervention Group was 9.39± 1.35 of control Group was 9.82± 0.91. we found that (TSB) were highly significant lower in intervention group out only as (P= 0.00) this was agree with demirel et.al (2013) who reported that the good impact of probiotic on the course of indirect hyperbilirubinemia and phototherapy duration in full term and very law birth weight infant through his study in reducing (TSB) level. and Liu et.al (2015) who reported that the good therapeutic effect on neonatal Jaundice through his study to reduce (TSB) level.
- In our study, (TSB) out was decreased in Both groups by the effect of phototherapy but more derease in intervention group. This agree with jia Hy (2015) through his study of effect of oral probiotics on treatment of jaundiced neonates by its influence on Immune function and suganthi et.al (2016) who reported through his study the important role of probiotic in reduction of neonatal hyperbilirubinemia and Mu-xue et.al (2003) who reported that (TSB) in intervention group was 33.33% while it was 57.14% in the control group when given aprobiotic as aprophylactic treatment and this was against (Zahed et.al 2017) who reported by his study that: oral probiotics in neonates with jaundice have no significant effect on (TSB) and the duration of phototherapy. As follows:

  The mean (TSB) before intervention in the intervention and control groups was 16± 1.9 and 16.9± 1.9 mg l dl Respectively as (P > 0.05), and on Exit after 72 hours it decreased to 10.25± 1.32 in intervention group 9.09± 1.38 in control group with no significance as (P >0.05).
- In Our Study: The days needes to stay under the phototherapy treatment in the ICU are:
- Mean of intervention group: 4.84± 0.62 and of control group: 5.785± 0.801

  We found that the days needed are highly significantly lower in intervention group as (P= 0.00).

  This agree with Demirel et.al (2013) who reported from his study that: the median duration of phototherapy in the intervention group was (18 hrs) and that of control group was (24 hrs) was significant as (P= 0.027) with probiotic therapy.

  and agree with wenbin et.al (2015) who reported from his study that in the treatment group, the probiotic therapy exerted effects on (1.0± 0.5) days and jaundice faded on (3.8± 1.7) days.

  Which were (2.6± 0.6) day and (5.3± 2.1) days respectively in the control group as (P <0.05) in addition, the two groups had significantly different numbers and times of phototherapy as (P <0.05).

  But this was against with yadallah zahed posha et.al (2017)

  Who reported from his study that the duration of phototherapy in the intervention group and the control group was. 3.61± 1.17 days and 3.72± 1.18 day respectively with probiotic therapy.
- This means that there in no significant difference between (TSB) in both groups after exposure to probiotic therapy.
- This was agree with demirel et.al (2013) who reported that in his study the effect of probiotic therapy to reduce the duration of phototherapy in very low birth weight (VLBW) newborns of GA ≤ 32 weeks and also Suganth et.al (2016) who reported that significant differences in (TSB) levels between intervention group and control group in full-term and pre- term newborns treated with probiotic for the first few days of life.
- In our study: (TSB) out was significantly lower in the intervention group in physiological cases than other two hemolytic and infection cases and infection lower than hemolytic cases as distribution was 8.61± 1.2, 9.15± 1.4 and 9.62± 1.44 respectively and in the control group as 9.44± 0.91, 9.65± 0.93 and 9.97± 0.89 respectively,

  This Was Agree With Tewari et.al (2015) who reported in his study that the proper effect of Bacillus clausii probiotic for prevention and treatment of late onset sepsis in preterm infant.

  and agree with Zheng et.al (2012) who reported that the proper effect of probiotic treatment in neonatal necrotizing enterocolitis and LiG et.al (2018) who reported that the propr effect of bifid triple viable on immune function of newborn of with infection.

  But against zahed pasha et.al (2017) who reported that he could not evaluate the neonates for colonization of probiotic bacteria and not a significant difference in (TSB) in the two groups may be associated with this fact that the selected probiotics may not colonize the neonates intestine.
- In Our Study: In control group there were significant positive correlation between (TSB) IN and GA and weight also between T. bilirubin OUT and weight and there were significant negative correlation between days needed and G. A and weight.

  Regard intervention group there were significant positive correlation between (TSB) IN and OUT with GA and weight also between, (TSB) in and out there were significant negative correlation between days needed and GA and weight.

Summary:

1. Neonatal Jaundice or hyperbilirubinaemia is a common neonatal problem in a bout 60% of full- term and 80% inpre- term in fants in the first week of life. (Rennie at al 2011).
2. Extreme neonatal jaundice occurs in frequently but carries a high risk of permanent sequelae (Kernictrus)
3. Rapid therapeutic intervention has the potential to reduce this Risk in some infants, like phototherapy and exchange transfusion: (Hansen, 2011) (American Academy of ped. 2014)
4. The aim of this study was to assess the effectiveness of the probiotic substance as lactobacillus in reducing the total serum bilirubin level, reducing the number of days needed for phototherapy treatment to decrease its common side effects and to reduce the need of exchange transfusion with its complication. (Alizadeh et.al 2014), (Uatlah, et.al 2016)
5. The study was carried out during one year from 5/ 2017 to 5/ 2018 in

increase the number of anaerobic bactenal colonies promotes the recovery of intestinal microflora balance, and resist infection in some cases, on the other hand, intestinal probiotics affect the amount of bilirubin in the enteroheptic circullation by reducing the degradation of bound bilirubin, Meanwhile they are able to stimulate intestinal peristalsis, which also benefits the elimination of bilirubin, it has been reported that oral administration of probiotics showed markedly better effects than those of routine blue light photo therapy.

- Probiotic enhance the healthy microbiota of the gastrointestinal tract of the new born. (Raju, TN, 2012, Wang x 2006)
- They produce lactic, acetic, and other acids that lower the PH in these environments, thus impeding the growth of bacterial pathogenes on mucosal surfaces of the intestine. (Wang x, chowdhury JR 2006)
- Probiotics used also to enhance immunity by regulating bacterial colonies, they can form a biological barrier by specifically binding intestinal epithelial cells through techoic acid. (LiG et.al, 2012)
- Probiotics are thought to work synergistically with the host immune system to stimulate specific lymphocytes cytokines and IgG and IgA antibodies to fight infection. (Chen CH 2011) (LiG et.al, 2012)
- Probiotic also appear to stimulate the production of numerous substances that work together to improve healthy microflora and displace harmful Bacteria. (Wangx, chowdhury JR 2006)
- These substances inclued vitamins, bacteriocins, and enzymes that alter the surface tension and reduce pathogen adherence to the mucosa. (Zheng sf 2012) (LIG et.al, 2012)
- In our study we aimed to assess the therapeutic effects of probiotic substances on neonatal (Jundic to reduce the need and duration of phototherapy and hospitalization duration.
- In our study we have 400 neonates having a jaundice classified into (2) groups.
  1. Group 1: intervention group: 200 cases who received intensive phototherapy with getting oral probiotic substance as lactobacillus powder with milk feeding as 250 mg/ day (one sachet) divided in 2 doses.
  2. Group 2: Control Group: 200 Cases Who Received Intensive Phototherapy Only.

	Group 1 (Control Group)	Group 2 (Intervention Group)
Hemolytic	43 Cases	33 Cases
Infectious	36 Cases	35 Cases
Physiological	121 Cases	132 Cases

- In our study we have 400 cases of jaundiced newborns Males and females, Males were 58% and females were 42%, Here, percentage of Males is greater than females,

  This is supported by the study of Paul et.al, (2010), where jaundiced Males were significantly higher than females and was in agreement with (Abdel fatah et.al, 2014) who had studied two groups with severe neonatal jaundice and found that malas were 58.8%.
- In our study the Ages of the newborn varies between (1 day to 7 days),

  Mean Age in days of admission of intervention group was 3.24± 1.1 and in control group was 3.33± 1.08 and we found that, there was no significant difference between groups regards Age as (P= 0.411)
- This was higher than mean age of admission in sivanandan et.al (2009) study who reported the average postnatal age of jaundiced new borns beginning phototherapy was 2.7± 1.03 and 3.04± 1.83 days in groups.

  But less than reported in Abdel fattah et.al (2014) study, who, reported that the average age was 4.7± 2.7 and 5± 3.1 days in groups
- In Our Study:

  Mean Gestational age of cases of intervention group was 36.85± 2.18, of control group was 37.01± 2.54, we found that, there was no significant difference between groups regard GA as (P= 0.061).

  Because we did not select between neonates having a jaundice to put them in any group.

  This agree with Abd el fattah et.al (2014) study who reported that Mean GA was 36.12± 1.04 and 37.09± 8.92.
- In our study:

  Mean weight in groups was in intervention group was 3239.5± 456.07, in control group was 3306± 463.18, we found that, there was no significant difference between groups regard weight as (P= 0.149).

  That was similar to reported in Abdel fattah et.al (2014) study, who found Mean weight at time was 2989± 395 and 2967± 417. statistical analysis revealed that all of the pre- treatment parameters were well balanced between the two groups of jaundiced neonates,

  There were no significant differences between groups regarding their gender, Age, gestational age, weight, days of admission and family history of other jaundiced sibling.
- In our study, there was no significant differences between groups regarding laboratory parameters as hematological indices, reticulo cytic count, blood group and Rh of the Baby and mother and (TSB) levels at the time of application.

  This was in agreement with Abdel Fattah et.al (2014) who found no significant differences between studied groups regarding laboratory parameters.
- In our study about 30% of included neonates had appositive family history of other jaundiced siblings, that was higher than reported in (Abdel fattah et.al, 2014) Study who found that 20% of included neonates with appositive history of other Jaundiced siblings this may be due to difference in numbers of first babies in the two studies.
- In our study, the most common cause for hyperbilirubinemia is physiologic (4.8595/ 5.7348) more than (hemolytic) mean (4.8837/ 5.7273) and (infectious) mean (4.7222/ 6.0289) this was similar with Begum et.al (2012) study who performed that the physiological jaundice was 50%, ABO, Rh in compatibility was 30% and infections was 20%. and we found that the most common cause for hemolytic jaundice was ABO, Rh in compatibilities,
- This agree with Annagur et.al (2014) who found that the most

Table (10) Comparison among types in intervention group

Group			N	Mean	SD	Minimum	Maximum	F	P
Intervention Group	Day	Hemolytic	43	4.8837	0.54377	4.00	6.00	0.790	0.455
		Infectious	36	4.7222	0.70147	4.00	7.00		
		Physiological	121	4.8595	0.63647	4.00	6.00		
	Tbilirubinout	Hemolytic	43	9.6279	1.44788	7.00	12.00	6.512	0.004*
		Infectious	36	9.1556	1.45297	6.00	10.00		
		Physiological	121	8.6132	1.27586	6.00	10.00		
	Tbilirubinin	Hemolytic	43	19.1256	2.11256	11.00	22.00	1.581	0.189
		Infectious	36	17.7222	2.64695	11.00	22.00		
		Physiological	121	17.8231	2.18513	12.00	22.00		

Bilirubin out significantly lower in physiological than other two groups and infection lower than hemolytic type as distribution was 8.61± 1.2, 9.15± 1.4 and 9.62± 1.44 respectively

Table (11) Total bilirubin distribution between groups in hemolytic

	Intervention Group (N= 200)	Control Group (N= 200)	t	P
Tbilirubinout	9.62±1.44	9.97±0.8	- 2.685	0.02*
Tbilirubinin	19.1±2.11	19.15±1.6	- 1.018	0.234

Total bilirubin were high significantly lower in intervention group out ONLY, P= 0.02* as distributed were 9.62± 1.44 and 9.97± 0.8 respectively, but no significant regard T bilirubin in P= 0.234 as distributed were 19.1± 2.11 and 19.15± 1.6 respectively

Table (12) Total bilirubin distribution between groups in infection

	Intervention Group (N= 200)	Control Group (N= 200)	t	P
Tbilirubinout	9.15±1.45	9.65±0.93	- 3.878	0.00**
Tbilirubinin	17.72±2.6	17.28±1.6	- 1.754	0.068

Total bilirubin were high significantly lower in intervention group out only, P= 0.00 as distributed were 9.15± 1.45 and 9.65± 0.93 respectively, but no significant regard T bilirubin in P= 0.068 as distributed were 17.72± 2.6 and 17.28± 1.6 respectively

Table (13) Total bilirubin distribution between groups in physiological

	Intervention Group (N= 200)	Control Group (N= 200)	t	P
Tbilirubinout	8.61±1.27	9.44±0.91	- 4.547	0.00**
Tbilirubinin	17.82±2.18	18.28±5.68	- 1.841	0.061

Total bilirubin were high significantly lower in intervention group out only, P= 0.00 as distributed were 9.44± 0.91 and 8.61± 1.27 respectively, but no significant regard T bilirubin in P= 0.061 as distributed were 17.82± 2.18 and 18.28± 5.68 respectively.

Discussion:

- Neonatal hyperbilirubinemia is diagnosed when the total serum bilirubin is higher than accepted with respect to weight and age of the newborn. (American Academy of pediatrics, 2004)
- Neonatal Jaundice, which is common in clinical practice, can mainly be classified as physiological and pathological ones. The former does not need special treatment but the later which originates from vaxious factors, easily lead to bilirubin encephalopathy and even brain damage or death. (Maisels et.al, 2012)
- The lack of bacteria in the gut during the newborn period has an impact on the enterohepatic circulation of conjugated bilirubin.
- The low bacterial load during this first week of life results in decresed conversion of conjugated bilirubin to stercobilin.
- The resultant high levels of conjugated bilirubin get converted to un conjugated bilirubin in the intestine by the enzyme beta-glucoronidase.
- The resultant high levels of un conjugated bilirubin gets absorbed and reaches the Blood stream resulting in un conjugated hyperbilirubinemia during this period.
- Neonatal Jaundice is caused by enhanced intestinal- hepatic circulation of bilirubin owing to high content and activity of B-glucuronidase (B- GD). (Raju TN, 2012)
- B- GD can hydrolyze the bound bilirubin into unbound one and glucuronide, and the unbound bilirubin boost intestinal hepatic circulation after being absorbed by intestinal cells. (wang x 2006)
- Enteral feeding is often delayed in preterm neonates which may limit intestinal flow and bacterial colonization resulting in further enhancement of the enterohepatic circulation and increase in serum bilirubin level. (Partner LMJ perinat al 2011)
- Very high total serum bifirubin (TSB) levels can injure the newborn central nervous system,
- For this reason, TSB levels in Jaundiced newborns are followed and treated with either photo therapy or exchange transfusion when they are at risk of rising or to have reached potentially dangerous level. (Newman et.al, 2012)
- In this study neonatal jaundice was treated by using lactobacilus that are normal microorganisms in the human intestinal tract. (Wang et.al, 2006)
- After being orally talken, they grew in the intestinal tract to produce vitamins and to help the proliferation of normal bacterial colonies.
- Accordingly, lactobacillus (delbrueki, fermentum), 10 billons units accelerated jaundice fading by rapidly lowering the bilirubin level, by facilitating the growth of normal bacterial colonies in the intestinal tract of neonates and the resulting metabolites effectively corrected the slightly alkaline environment thus weakening the activity of B- GD and preventing it from binding and hydrolyzing bilirubin. (Maldonado et.al, 2012)

  Furthermore, the activities of liver enzymes were also enhanced, which benefited the excretion of and binding of bilirubin.
- The Roles of probiotics in human body have been explained by different pharma cological mechanisms, for example, they can rapidly

There was no significant difference between groups regard GA P= 0.061 as groups distributed as 36.85± 2.18 and 37.01± 2.54 respectively

Table (3) weight distribution between groups

	Intervention Group (N= 200)	Control Group (N= 200)	t	P
Weight	3239.5±456.07	3306.0±463.18	- 1.447	0.149

There was no significant difference between groups regard weight P= 0.149 as groups distributed as 3239.5± 456.07 and 3306± 463.18 respectively.

Table (4) Total bilirubin distribution between groups

	Intervention Group (N= 200)	Control Group (N= 200)	t	P
Tbilirubinout	9.39±1.35	9.82±0.91	- 3.685	0.00**
Tbilirubinin	17.97±2.31	18.28±4.74	- 1.718	0.075

Total bilirubin were high significantly lower in intervention group out only, P= 0.00 as distributed were 9.39± 1.35 and 9.82± 0.91 respectively, but no significant regard T bilirubin in P= 0.075 as distributed were 17.97± 2.31 and 18.28± 4.74 respectively

Table (5) Change assessment in each group

Group		Mean± SD	Paired T	P
Control Group	T_Bilirubinin	18.28±4.74	25.114	0.00**
	Tbilirubinout	9.82±0.91		
Intervention Group	T_Bilirubinin	17.97±2.31	57.378	0.00**
	Tbilirubinout	9.39±1.35		

Both groups significantly decreased but more in intervention group

Table (6) Day before discharge distribution between groups

	Intervention Group (N= 200)	Control Group (N= 200)	t	P
Days	4.84±0.62	5.785±0.801	- 13.115	0.00**

Days needed highly significantly lower in intervention group P= 0.000 as day distributed as 4.84± 0.62 and 5.785± 0.801 respectively

Table (7) Correlations

Group			Tbilirubinin	Tbilirubinout	Day
Control Group	Tbilirubinin	r	1	0.014	-0.076-
		P		0.847	0.286
	Day	r	-0.076-	-0.081-	1
		P	0.286	0.256	
	GA	r	0.266**	0.070	-0.423- **
		P	0.000	0.328	0.000
	WT	r	0.201**	0.149*	-0.458- **
		P	0.004	0.035	0.000
Intervention Group	Tbilirubinin	r	1	0.529**	-0.121-
		P		0.000	0.087
	Day	r	-0.121-	-0.079-	1
		P	0.087	0.267	
	GA	r	0.558**	0.404**	-0.233- **
		P	0.000	0.000	0.001
	WT	r	0.540**	0.400**	-0.247- **
		P	0.000	0.000	0.000

** Significant + or- positive or negative correlation

In control group there were significant positive correlation between T bilirubin in and GA and weight also between T bilirubin out and weight, and there were significant negative correlation between days needed and GA and weight. Regard intervention group there were significant positive correlation between T bilirubin in and out with GA and weight also between T bilirubin out and in, there were significant negative correlation between days needed and GA and weight

Table (8) Type distribution between groups

			Group		Total	X^2	P
			Control Group	Intervention Group			
Type	Hemolytic	N	33	43	76	1.8	0.4
		%	16.5%	21.5%	19.0%		
	Infectious	N	35	36	71		
		%	17.5%	18.0%	17.8%		
	Physiological	N	132	121	253		
		%	66.0%	60.5%	63.2%		
Total		N	200	200	400		
		%	100.0%	100.0%	100.0%		

No Significant Difference Between Groups

Table (9) Comparison among types in control group

Group			N	Mean	SD	Minimum	Maximum	F	P
Control Group	Day	Hemolytic	33	5.7273	0.83937	5.00	7.00	1.981	0.141
		Infectious	35	6.0286	0.98476	5.00	8.00		
		Physiological	132	5.7348	0.72953	5.00	8.00		
	Tbilirubinout	Hemolytic	33	9.9788	0.89294	8.00	12.00	4.214	0.023*
		Infectious	35	9.6571	0.93755	7.00	11.00		
		Physiological	132	9.4485	0.91205	8.00	11.00		
	Tbilirubinin	Hemolytic	33	19.1515	1.69781	16.00	22.00	1.403	0.248
		Infectious	35	17.2857	1.67282	14.00	22.00		
		Physiological	132	18.2848	5.68712	15.00	81.00		

Bilirubin out significantly lower in physiological than other two groups and infection lower than hemolytic type as distribution was 9.44± 0.91, 9.65± 0.93 and 9.97± 0.89 respectively

Introduction:

1. Infantile Microbiota:
   - The mature GIT contains a large quantity of microbiota. that play a role in protecting infant and promoting health functionality.
   - The normal development of the human GIT depends on the presence of complex gastro intestinal microbiota.
2. Probiotic: It's a living friendly bacteria or micro- organism in the intestine.
   - Have health Benefit on the host.
   - It's a normal intestinal flora.
   - Controlls the growth of harmfull bacteria which, when administered in adequate amounts, confer a health benefit on the host, (Bjarnasdn I, MacPherson A, Hollander, 1995)
   - Most commonly available probiotic supplements contain Lactobacillus and/ or Bifidobacterium, which are part of the normal human microbiotic. (Bertini G, Dani C. Neonatol.; 2012)

Current recommendations for the management of hyperbilirubinemia in preterm infants have focused on determining age- specific bilirubin levels for initiating phototherapy. (Maisels MJ, Watchko JF, Bhutani VK, Stevenson DK. 2012)

However, there is concern regarding Potential adverse effects. of aggressive phototherapy in preterm infants.

Besides blue light phototherapy, and drugs, probiotics have also been used to enhance immunity mainly by regulating bacterial colonies. They can form a biological barrier by specifically binding intestinal epithelial cells through teichoic acid. Therefore, particular attention has- been paid to the use of probiotics in treating neonatal jaundice. (Tyson JE, Pedroza C, Langer J, et.al. 2012)

Probiotic microorganisms are typically members of the genera Lactobacillus, Bifidobacterium, anAstreptococcus. However, yeast such as Saccharomyces boulardii is also a probiotic microorganism.

Methods:

- This study was carried out in the Neonatal intensive care unit of kenayat- hospital in zagazig for all the cases of two groups
- Laboratory investigations were done in clinical pathology department in the same hospital.
- It was held in between May 2017 and May 2018.

Subjects:

Subjects included in the study: 400 of Jaundiced newborn cases included both full- term and pre- term.

1. Age: Ranges between 1st day of life the to the 7th day.
2. Sex: Both males and females.

The studied neonates were classified into 2 groups.

a. Group-1 intervention Group: included 200 neonates of high total serum bilirubin level which necessitated phototherapy treatment.
b. Group-2 Control Group: included 200 neonates of high total serum bilirubin level which necessitated phototherapy treatment.

Clinically significant indirect hyperbilirubinemia was defined according to data blotted on the chart of guidelines for phototherapy in hospitalized infants obtained from American Academy of pediatrics. Subcomitte On Hyperbilirubinemia.

3. Routine laboratory investigations:
   a. Completes blood count (CBC) before and after treatment by automated cell counter (cell dyne 1700).
   b. ABO, RH grouping for neonates and mothers. (Dacie and Lewis, 2012).
   c. Reticulocyte count (Dacie and lewis, 2012)
   d. Comb's test (Dacie and lewis, 2012)
   e. C- reactive protein (CRP) (Sonntag and Scholer, 2001)
   f. Special Laboratory Investigation:
      - Total and direct bilirubin levels.
      - On admission: before exposure to treatment.
      - Every 2 days: during treatment.
      - Before discharge: after treatment.
4. Analysis Procedure: Venous blood (3ml) were drawn from the newborn to detect serum bilirubin levels, After centrifugation at 3000 rlminutes for 10 minutes. The serum was collected and detected Automated by auto analyzer. (COBAS 6000)
   a. Automated by Bio chemical Analyzer with the oxidation method. (Salinas M, et.al, 2012) (Wolff M. , et.al, 2012)
   b. Comparison between the two groups was done according to:
      - Rate of decline TSB.
      - Duration of exposure to Phototherapy and Hospitalized Duration.
5. Intervention:
   a. All infants were fed with an initial dose of 70 ml/kg/day milk reaching to 150 ml/ kg/ day breast or artificial milk.
   b. Parenteral nutrition was gradually tapered as enteral feeding volume was in creased.
   c. The infants were randomly allocated into the probiotic intervention and controlled group, infants in the probiotic group received a supplementation of sterilized probiotic supplementation a safe for VLBW infants in the short term.
   d. All infants in both groups are investigated by blood sample to detect the percentage of total and direct serum bilirubin, in the 1st, 3rd, 5th, 7th, days in the incubator.

Result:

Table (1) Age distribution between groups

	Intervention Group (N= 200)	Control Group (N= 200)	t	P
Age	3.24±1.1	3.33±1.08	- 0.812	0.411

There was no significant difference between groups regard as age distributed 3.24± 1.1 and 3.33± 1.08 respectively

Table (2) Gestational age distribution between groups

	Intervention Group (N= 200)	Control Group (N= 200)	t	P
GA	36.85±2.18	37.01±2.54	- 1.904	0.061

Probiotics for the management of Neonatal hyperbilirubinemia

Nasser Ramzy Rofail
Prof.Dr.Khaled Hussien Taman
Professor Of Pediatrics Faculty Of Post Graduate Childhood Studies Ain Shams University
Prof.Dr.Rehab Abd- Elkader Mahmoud
Professor Of Pediatrics Faculty Of Post Graduate Childhood Studies Ain Shams University

Abstract

Background: In recent years, the tendency to use drugs has been increasing in the treatment of neonatal jaundice. Several drugs have been used since then, but the effect of probiotics on serum bilirubin level (SBL) is not so clear. This study was conducted to evaluate the effect of probiotics on SBL and the duration of phototherapy in term neonates with hyperbilirubinemia.

Objective: The aim of the work: To evaluate and assess the therapeutic effects of the probiotic substance on neonatal jaundice.

Subjects and Methodes: In this Experimental Randomized clinical trial study we studied 400 newborns with jaundice hospitalized for phototherapy in kenayate Hospital in zagazig during 5/ 2017 to 5/ 2018- Eligible neonates were Randomly divided into two groups: Intervention (n= 200), and control (n= 200) Both groups receive standard conventional phototherapy but the intervention group received 250mg lactobacillus powder with milk as a probiotic substance until hospital discharge. The out come variable were. TSB and the duration of phototherapy. The data were analyzed by (SPSS version 20.0) and p value was at (<0.05) for significant, (<0.01) for high significant.

Results: TSB (out)/ on discharge after hospitalization of intervention group was a mean: 9.39± 1.35 and of control group was a mean: 9.89± 0.9, (TSB) was highly significant lower in intervention group/ on discharge with aprobiotic substance than the control group/ on discharge without aprobiotic substance. Duration of hospitalized days needed to stay under the phototherapy treatment are of intervention group is a mean of: 4.84± 0.62 and of control group is a mean of 5.785± 0.801.

Conclusion: Probiotics lowered the serum bilirubin levels of neonates with jaundice and decrease the duration of hospitalized days under phototherapy treatment Recommendation: This study recommended that we can use a probiotic substance within a plane of management of neonatal hyperbilirubinemia. Key words: total serum bilirubin, phototherapy, probiotics.

دور مادة البروبيوتيك في علاج صفراء الدم بالأطفال حديثي الولادة

مقدمة: تمثل نسبة حالات الصفراء فى الدم فى الأطفال حديثى الولادة حوالى ٦٥% منهم وتزداد النسبة فى الأطفال ناقصى النمو والعمر الجنينى وناقصى الوزن. من الناحية الوظيفية، تعرف صفراء الدم بأنها زيادة فى نسبة مادة البيليروبين فى الدم والتى تنتج عن نقص فى عملية ارتباط البيلروبين مثل حالات الصفراء الفسيولوجية وبعض المتلازمات المرضية. تحتوى أمعاء الطفل على بكتيريا تقوى مناعته ضد البكتيريا الضارة تسمى (بروبيوتيك).

فكرة الدراسة فى هذا البحث هو إدخال مادة خارجية تسمى البروبيوتيك وهى متواجدة فعلا فى أمعاء الطفل ولكن بنسبة قليلة أو غير ناضجة نتيجة نقص العمر الجنينى للطفل، أو نقص الوزن الحاد، مما تؤدى هذه المادة بروبيوتيك إلى تقليل نسبة صفراء الدم عن طريق عدة طرق إكلينيكية ستوضح فى العمل بالتفصيل.

قد اشتملت هذه الدراسة على ٤٠٠ طفل حديثى الولادة مصابا بالصفراء مقسمين إلى مجموعتين، المجموعة الضابطة مكونة من ٢٠٠ طفل مصابا بالصفراء تخضع للعلاج بالأشعة الضوئية (الفوتوثيرابي) فقط، والمجموعة التداخلية مكونة من ٢٠٠ طفل مصابا بالصفراء تخضع للعلاج بالأشعة الضوئية (الفوتوثيرابي) بالإضافة إلى مادة البروبيوتيك تضاف مع رضعات اللبن الصناعى للطفل، وقد تم قياس مستوى صفراء الدم لكل طفل مع بداية دخوله فى المحضن وكل ثانى يوم أو كل يوم حسب شدة حالته. تم عمل جداول إحصائية لهذه القياسيات وبعد التحليل الإحصائى باستخدام برنامج كمبيوتر ١س بى اس اس ٢٠١٢ وتبين منها الآتي وجود انخفاض ملحوظ فى نسبة صفراء الدم لأطفال المجموعة التداخلية الذين خضعوا للعلاج بمادة البروبيوتيك بنسبة انخفاض أعلى من أطفال المجموعة القابضة الغير خاضعة للعلاج بمادة البروبيوتك.

الهدف من العمل: إن الهدف من هذا العمل هو: تأثير مادة البروبيوتيك على صفراء الدم للأطفال.

الخلاصة: تستخلص من الدراسة أنه يمكن استخدام مادة (البروبيوتيك) فى علاج صفراء الأطفال حديثى الولادة والوقاية منها فى أيام عمرهم الأولي.

التوصيات: توصى الدراسة بإمكانية استخدام مادة (البروبيوتيك) لعلاج صفراء الأطفال حديثى الولادة بدون مضاعفات كعلاج مساعد مع العلاج بالأشعة الضوئية وكوقاية للأطفال فى أيام عمرهم الأولى من الإصابة بالصفراء.

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hyperactivity index scores ($p \leq 0.001$), impulsivity/ hyperactivity scores ($p \leq 0.001$) and learning scores ($p \leq 0.001$) occurred after following the diet.

That comes in agreement with Henríquez- Henríquez et.al. (2015) who measured S1P in ADHD children and their unaffected relatives and found that serum S1P in ADHD patients (1.55± 0.38 μM) was higher than their unaffected relatives (1.44± 0.38 μM). Also, Wu et.al. (2018) found that pharmacological decrease of S1P level associated with improvement of learning problems and memory impairment.

In this study, there was strong positive significant correlation between protein intake before diet modification and serum S1P level during baseline period ($r= 0.665$, $p \leq 0.001$). In accordance, Kunisawa and Kiyono (2016) found that high level of dietary proteins and thermally processed high protein food impaired S1P lyase activity that analyse sphingosine 1 phosphate to ethanolamine phosphate and hexadecenal leading to increase of S1P.

Narayan et.al. (2011) and Schnider et.al. (2017) found that emerging role of sphingolipids in disease pathogenesis in psychiatric disorders including neurodevelopmental disorders.

Asherson et.al. (2007) and Rommelse et.al. (2008) showed that regions containing genes encoding key enzymes in the sphingolipid metabolism i.e., serine- palmitoyl transferase and sphingomyelinases have been mapped in association with ADHD.

Another hypothesis that that S1P is involved in the development of intestinal immune diseases including food allergies and intestinal inflammation as it is involved in various aspects of inflammatory cell function (T and B lymphocytes, as well as endothelial cells) that express distinctive profiles of sphingosin 1 phosphate receptors (S1PRs) as reported by Goetzl and Rosen (2005), Rivera, et.al. (2008) and Gohda, et.al. (2008) so gluten restriction was associated with decrease serum S1P.

A study of Naviaux et.al. (2014) revealed that cell danger response (CDR) encountered with chemical, physical, or biological threats produces a cascade of changes in cellular electron flow, oxygen consumption, whole body metabolism and the gut microbiome are disturbed, behavior is changed, and chronic disease results as ADHD, asthma, atopy, gluten and many other food and chemical sensitivity syndromes, with stimulation of sphingosin 1 phosphate synthesis.

That can be the explanation for why serum sphingosin 1 phosphate levels decreases after diet protein and gluten restriction with the decrease of serum S1P level led to improvement of behavioral symptoms as assessed by CPR, so there is relation between ADHD, diet protein intake and serum S1P.

Conclusion:

The study revealed that serum S1P decreased significantly after diet protein restriction in ADHD patients with concomitant improvement in behavior.

Recommendations:

1. Further studies on larger samples to emphasis the conclusion.
2. Clarification of diet planning importance for ADHD patients.
3. Encouraging gluten free products industry and advising patients to use it.

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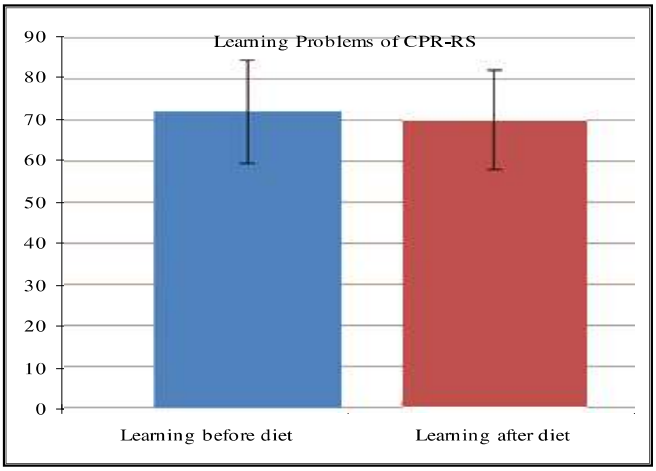

Figure (5) learning problem score before and after diet protein restriction

Table (4) S1P serum levels before and after diet protein restriction

	S1p Levels Before Diet Modification	S1p Levels After Diet Modification	Z*	P Value
Number Of Cases	46	46	- 3.737	0.000 HS
Median(IQR)	200(90- 485) ng/L	65(45- 140) ng/L		
Range	(45- 1536)	(25- 2280)		

Z: Wilcoxon test ng/ l: nanogram per liter HS: highly significant

That table shows statistically significant reduction in serum S1P after following diet protein restriction and gluten elimination from foods.

Figure (6) S1P serum level before and after diet protein restriction

Table (5) Correlation between serum S1P level and protein intake before diet protein restriction

		S1P serum level before diet modification	Protein Intake Before Diet Modification
Sphingosin-1- Phosphate	r	1	0.665**
	P Value		0.000
	N	47	47

**strong positive correlation r: Pearson correlation

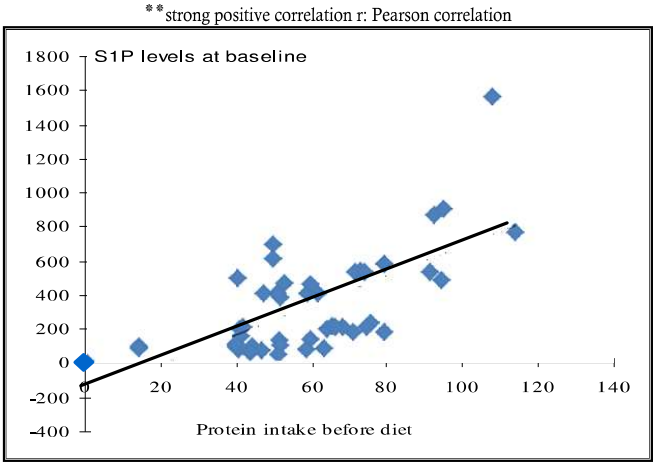

Figure (7) Correlation between hyperactivity index scores of CPR scale and protein intake before following the diet.

Table (5) and figure (7) show significant strong positive correlation between diet protein intake and serum S1P level.

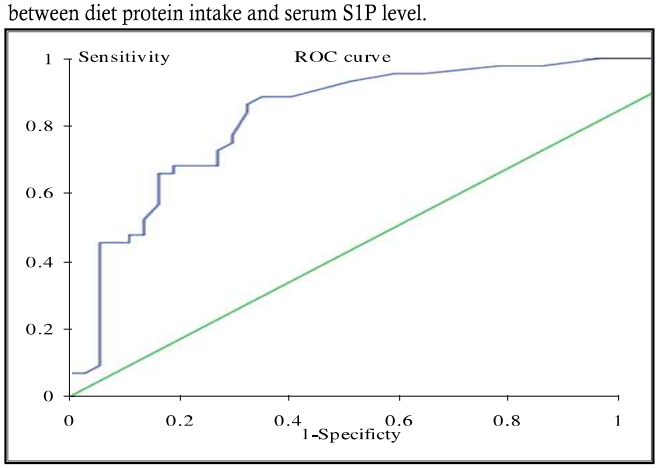

Figure (8) ROC curve for S1P serum level before and after diet protein restriction

Table (6) Diagnostic accuracy (Area under the curve AUC), sensitivity, specificity, and cut- off value of S1P before and after diet protein restriction

Cut- Off Point	AUC	sensitivity	specificity
47.5/L	0.842	0.977	0.727

The previous receiver operating characteristic curve (ROC) shows that serum S1P level of 47.5 ng /l was found as the best cut off point with sensitivity 84.2% and specificity 72.7% and area under the curve (AUC) 0.842%. Increased serum S1P level above this cut- off point associated with worsening of behavioral symptoms as measured with CPR.

The prognostic ability of S1P for detecting worsening in symptoms of ADHD was reliable. So increased serum S1P above this cut off value could be considered as a potentially marker of worsening symptoms.

Discussion:

Patients of the study were between the ages of (6- 9) years with a mean of 7.5. Number of males were 34 (72.3%) and females were 13 (27.7%) going with the male sex predilection in ADHD in a study of Biederman et.al. (2002).

In this study, 40.5% of children were normal weight, 40.5% were overweight and 19% were obese. That means that more than half of patients are either overweight or obese.

That is going with the systematic review and meta- analysis by Cortese and Vincenzi (2012), and Corteases and Tessari (2016) showed a clear association between attention deficit hyperactivity disorder (ADHD) and obesity in more than 700,000 children and adults, of whom 48.161 had ADHD. The explanation is that excess eating is one of impulsivity manifestations, also difficult planning as a result of inattention leads to skipping breakfast and lunch resulting in obesity as fitted with Kooij (2016).

In comparison to Tong et.al. (2017) who concluded that there was no significant relationship between ADHD and BMI.

In this study, we measured serum S1P levels in ADHD patients before and after following diet (protein restriction and gluten elimination). The median serum level of S1P before diet was 200 ng/l and after diet protein restriction 65 ng/l. There was statistically significant decrease after diet protein restriction (Z= -3.737 p= 0.000). Also, improvement in behavior as shown by statistically significant reduction CPR- RS subscales scores as

were calculated according to acceptable macronutrient distribution range (AMDR) so protein intake was 25- 35% of EER with exclusion of gluten and any gluten containing food from the diet.

9. Measuring serum S1P before and after dietary protein restriction by ELIZA technique using kit supplied from Bioassay technology laboratory Cat. No. MBS163661. This kit used enzyme linked immune sorbent assay (ELISA) based on the biotin double antibody sandwich technology to assay the human sphingosine 1phosphate (S1P).

Results:

The study included 47 children; they were 34 (72.3%) males and 13 (27.7%) females, their ages ranged between (6- 9) years. 40.5% of children were normal weight, 40.5% were overweight and 19% were obese. Diet analysis after following the provided diet showed statistically significant reduction of protein intake with concomitant decrease in all scores of Conner's test subscales (improvement of behavioral symptoms).

Table (1) Distribution of children according to their BMI

BMI	No. Of Children	Percentage
Normal weight (within 5th- 85th) percentile	19	40.5%
Overweight(within 85th- 95th)percentile	19	40.5%
Obese (above 95th percentile)	9	19%

This table shows that more than half of the patients are overweight and obese.

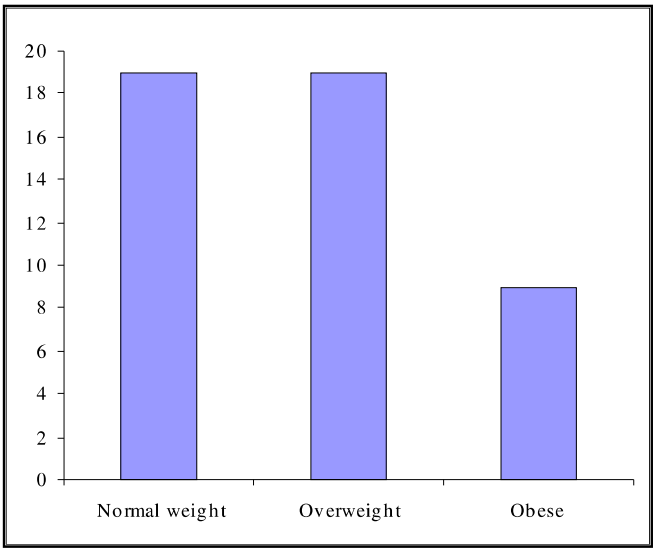

Figure (1) Distribution of children according to their BMI

This figure shows that 19 patients are normal weight, 19 are overweight and 9 patients are obese.

Table (2) protein intakes before and after dietary protein restriction

	Protein intake before diet protein restriction	Protein intake after following the provided diet	T- Test	P Value
Mean± SD	60±21.3 g	39.2±7.8 g	0.000	4.1 HS
Min. - Max.	38.7- 81.2	30.8- 47		

T- test: paired t- test HS: highly significant

Table (2) shows that protein intake of patients decreased significantly after following the diet

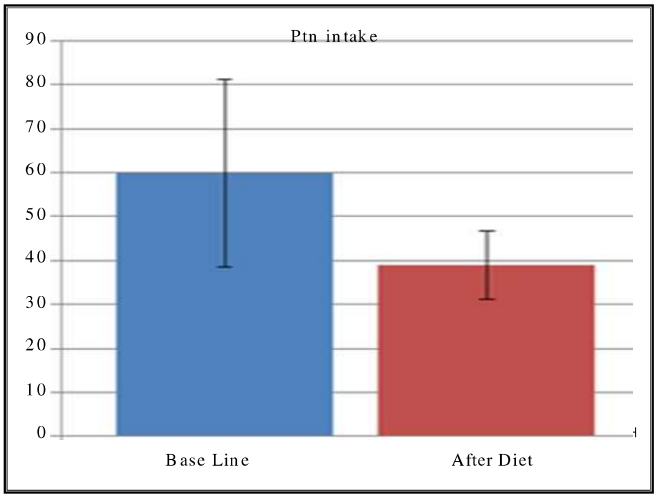

Figure (2) Protein intake before and after diet modification

Table (3) CPR- RS Scores Before And After Diet Protein Restriction

Conner's Subscales		Mean± SD	Min.	Max.	P Value	Z Value
Hyperactivity Index	Before Diet	69.38±14.19	83.57		0.000 HS	- 4.650
	After Diet	64±11.99	76	52		
Impulsive Hyperactive	Before Diet	65.94±7.36	58.58	73.3	0.000 HS	- 4.340
	After Diet	64.31±6.93	57.38	71.24		
Learning	Before Diet	71.85±12.58	59.27	84.43	0.000 HS	- 3.517
	After Diet	70.15±11.83	58.32	81.98		

*Wilcoxon test CPR- RS: Conner's parent rating scale- revised short form HS: highly significant

Table (3) shows improvement in behavioral symptoms as there is statistically significant reduction in CPR scores especially hyperactivity index.

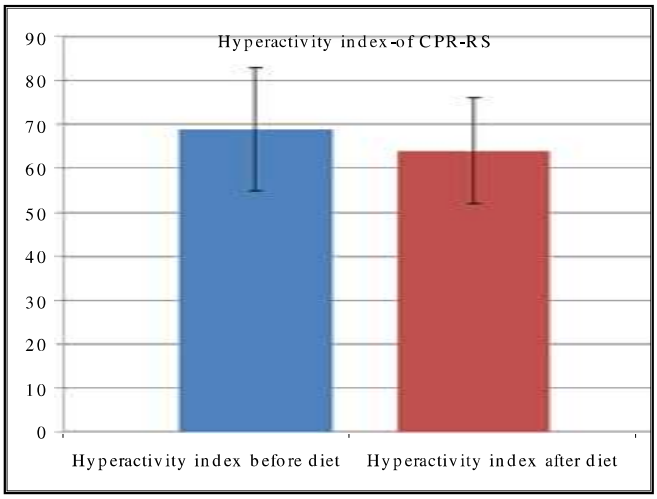

Figure (3) hyperactivity index score before and after diet protein restriction

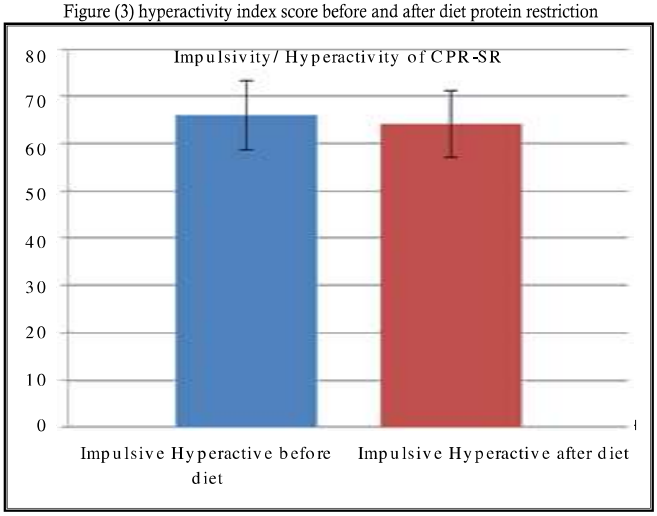

Figure (4) impulsivity/hyperactivity score before and after diet protein restriction

sIntroduction:

Attention- deficit hyperactivity disorder (ADHD) is a neuro-developmental disorder that affects 5% of children worldwide and is characterized by excessive and impairing inattentive, hyperactive, and impulsive behavior (DSM 5th ed. 2013). The pathophysiology of ADHD is unclear. Research on children with ADHD has shown a general reduction of brain volume especially in the volume of the left- sided prefrontal cortex (Krain et.al., 2006). Abnormalities in dopaminergic system either hypo- or hyperfunctioning are implicated (Congenit, 2003). Also abnormalities in the functioning of adrenergic, serotoninergic and cholinergic or nicotinergic pathways can be present and contribute to the pathophysiology of ADHD (Sikström& Söderlund, 2007). ADHD incidence and prevalence showed progressive increase over a period of 18 years worldwide. Several studies discussed the role of food as a precipitating and one of the risk factors for ADHD that could be targeted for intervention (Hill& Taylor, 2001). The effect of gluten intake on ADHD symptomatology was an era of research (Czaja- Bulsa et.al., 2015). Sphingosin- 1- phosphate (S1P) is a pleiotropic, bioactive, product of sphingomyelin metabolism; S1P signaling occurs via S1P receptors (S1PRs) and is involved in various aspects of inflammatory cell function. T and B lymphocytes as well as endothelial cells express distinctive profiles of S1PRs (Rosen& Goetzl 2004). Also, sphingolipids are highly abundant in nervous tissues; affect neuronal and glial proliferation, differentiation and apoptosis as well as membrane permeability to Ca and K relevant to the generation and propagation of nervous impulse and neurotransmitter release (Chaves& Sipione 2010). Emerging role of sphingolipids in disease pathogenesis in psychiatric disorders, including schizophrenia, bipolar, neurodevelopmental and major depression have been studied (Narayan et.al., 2017).

Aim:

Aim of the study was to measure S1P level in a group of ADHD children before and after (dietary protein restriction and gluten elimination) and its relation to ADHD outcome

Sample:

The study included 47 children newly diagnosed with ADHD. Their ages ranged from (6 to 9) years. They were recruited from behavioral and psychological assessment clinic of, national research center. Parents are motivated and capable to follow 5 weeks' provided diet while not receiving any pharmacological or behavioral therapy. Any child with medical or metabolic condition interfering with the study (e.g. metabolic disorders, Diabetes mellitus, etc.) was excluded, also the desire to discontinue the study or refusing to participate, receiving drugs, behavioral therapy or already following diet. Patients with Intelligence quotient (IQ) below 70 or comorbid psychiatric diseases other than oppositional defiant disorder (ODD) or conduct disorder (CD) were excluded.

Ethical aspect of the study:

Written informed consent was obtained from the parents after explanation of the aim of the study, its benefits and expected risks for their children if they participate in the study. Informed verbal assent was taken also from all the patients as their age exceeds eight years after a simplified explanation of the aim and benefits of the study for them. Approval was taken to conduct this research from the Ethical Committee of faculty of Postgraduate Childhood Studies Ain Shams University and the Ethical Committee of the National Research Centre (NRC).

Methods:

1. Full history taking. Laying stress on Sociodemografic Data; name, age, sex and socio- economic class, Medical history of any medical condition interferes with dietary protein restriction (e.g. Diabetes mellitus or metabolic disorders).
2. Complete Psychiatric Examination: physical appearance, separation, manner of rating, orientation, soft neurological signs, reading difficulties, language and speech, self- esteem, affect, judgment and insight, problems solving.
3. Auxiological Examination: assessment of weight, height and body mass index (BMI) (CDC 2000).
4. They were diagnosed by DSM 5 (DSM 5th ed., 2013) Six or more of the inattentive symptoms, hyperactivity/ impulsivity symptoms or both have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/ occupational activities

   In addition, the following conditions must be met:

   a. Several symptoms are present in two or more setting (e.g., at home, school or work; with friends or relatives; in other activities)
   b. There is clear evidence that the symptoms interfere with, or reduce the quality of, social, school, or work functioning.
   c. The symptoms do not happen only during the course of schizophrenia or another psychotic disorder.
   d. The symptoms are not explained by another mental disorder (e.g. Mood Disorder, Anxiety Disorder, Dissociative Disorder, or a Personality Disorder).
5. Diet history (previous 24 hour recall and food records): by asking the caregiver to remember in detail all the food and drink the child consumed during the previous 24 hours. That was done for 3 days (1 day of weekend and 2 work days) with clarification of the description and preparation methods of foods and food portion sizes using household dishes and measures (e.g., Cups, Bowls, Glasses, and Spoons), Geometric shapes (e.g., Circles, Triangles, Rectangles) and Food labels.
6. Diet analysis was done using food composition tables of nutrition institute, Egypt (National Nutrition Institute, 2006).
7. Conner's parent rating scale- revised short form (CPR- RS) (Goyette& Conner, 1978). The Arabic form was used (Elbehery& Aglan, 2009). It consists of six subscales (conduct problems, learning problems, anxiety, and hyperactive- impulsive, psychosomatic, ADHD index).
8. Dietary protein restriction: The expected energy requirements (EER) were adjusted according to EER tables (USDA, 2002). Protein intakes

Sphingosin 1 phosphate (S1P) and dietary protein intake in a group of children with attention deficit hyperactivity disorder

Eman Mohamed Elsheikh,[2]Olweya Mohammed Abd El Baaki[1], Enas Raafat Abd El Hamid,[2]
Safaa Taha Zaki[2], Amani Salah El Din Alwakkad[3], Rania Nabil Sabry[2]
[1]Department of Medical Studies, Faculty of Postgraduate Childhood Studies, [2]Department of Child Health, National research centre,
[3]Department of physiology, National Research Centre

Summary

Background: ADHD is a neurodevelopmental disorder. There is increased prevalence of ADHD in children and adolescents in many countries and in Egypt. The specific causes for ADHD are unknown but there are several factors contribute or exacerbate ADHD as food. Sphingosin 1 phosphate (S1P) is a sphingolipid that is involved in inflammatory cell action and neuronal proliferation and differentiation and neurotransmitter release. S1P is involved in disease pathogenesis of psychiatric disorders including neurodevelopmental disorders.

Aim: To measure serum S1P level in a group of ADHD children before and after (gluten elimination and dietary protein restriction) and its relation to ADHD outcome.

Subjects and Methods: That interventional study was executed in behavioral and psychological assessment clinic of national research center from June 2014 to June 2017. The study was applied on 47 children newly diagnosed with ADHD not received pharmacological or behavioral therapy, their ages are from (6 to 9) years. Sphingosin1 phosphate (S1P) was measured before and after (diet dietary protein restriction and gluten elimination from food) for 5 weeks with the follow up with Conner's parent rating scale- revised short (CPR- RS).

Results: Sphingosin 1phosphate (S1P) decreased statistically significantly after diet protein intake restriction and gluten elimination. This decrease was accompanied by improvement in the behavior of children as confirmed by CPR.

Conclusion: Decrease of serum S1P level after dietary protein intake restriction in ADHD children with concomitant improvement in behavioral symptoms indicating the role of dietary proteins and S1P in the pathogenesis of ADHD.

Key Words: ADHD- Conner's parent rating scale- diet protein intake.

سفينجوسين ١ فوسفات والمتناول الغذائى من البروتين لدى مجموعة من الأطفال المصابين باضطراب نقص الانتباه وفرط الحركة

مقدمة: إضطراب فرط الحركة ونقص الانتباه هو اضطراب عصبى نمائي. هناك زيادة فى انتشار اضطراب فرط الحركة ونقص الانتباه لدى الأطفال والمراهقين فى العديد من البلدان وفى مصر. الأسباب المحددة لاضطراب فرط الحركة ونقص الانتباه غير معروفة ولكن هناك العديد من العوامل التى تساهم أو تفاقم اضطراب فرط الحركة ونقص الانتباه كما الطعام. سفينجوسين ١ فوسفات هو شحمى سفينغولييد الذى يشارك فى عمل الخلايا الالتهابية وانتشار الخلايا العصبية والتمايز والإفراز العصبى كما ان سفينجوسين ١ فوسفات له دور فى تطور الاضطرابات النفسيه والتى تشمل الاضطرابات العصبية النمائية.

الهدف: قياس مستوى سفينجوسين ١ فوسفات بالمصل فى مجموعة من الاطفال المصابين باضطراب فرط الحركة ونقص الانتباه قبل وبعد (تقييد البروتين الغذائى وإزالة الجلوتين) وعلاقته بنتيجة الاضطراب.

طرق إجراء البحث: أجريت هذه الدراسة التدخليه بعيادة التقييم السلوكى والنفسى بالمركز القومى للبحوث خلال الفترة من يونيو ٢٠١٤ حتى يونيو ٢٠١٧ وإشتملت على ٤٧ طفل حديثى التشخيص باضطراب فرط الحركه وتشتت الانتباه لم يتلقوا علاج دوائى أو سلوكى تتراوح اعمارهم من (٦- ٩) سنوات .تم قياس سفينجوسين ١ فوسفات فى مصل الدم قبل وبعد تقليص المتناول الغذائى من البروتين وإزالة الجلوتين من الطعام لمدة خمسة أسابيع مع المتابعة بمقياس كونورز- تصنيف الوالدين.

النتائج: أوضحت الدراسة انخفاض مستوى سفينجوسين ١ فوسفات فى مصل الاطفال المصابين باضطراب فرط الحركة ونقص الانتباه بعد (تقليص المتناول الغذائى من البروتين وإزالة الجلوتين) عن مستواه قبل ذلك وكان هذا الانخفاض مصحوب بتحسن فى سلوك الاطفال كما هو مؤكد بانخفاض درجات المقاييس الفرعيه من مقياس تصنيف الوالدين من اختبار كونورز.

الخلاصة: انخفاض مستوى سفينجوسين ١ فوسفات بالمصل بعد تقليص المتناول الغذائى من البروتين وإزالة الجلوتين فى الأطفال الذين يعانون من اضطراب فرط الحركه ونقص الانتباه مع تحسن مصاحب فى الاعراض السلوكيه مبينا دور سفينجوسين ١ فوسفات وبروتينات الطعام فى تطور اضطراب نقص الانتباه وفرط الحركه.

الكلمات المفتاحية: اضطراب فرط الحركه وتشتت الانتباه- مقياس كونورز للوالدين- المتناول الغذائى من البروتين.

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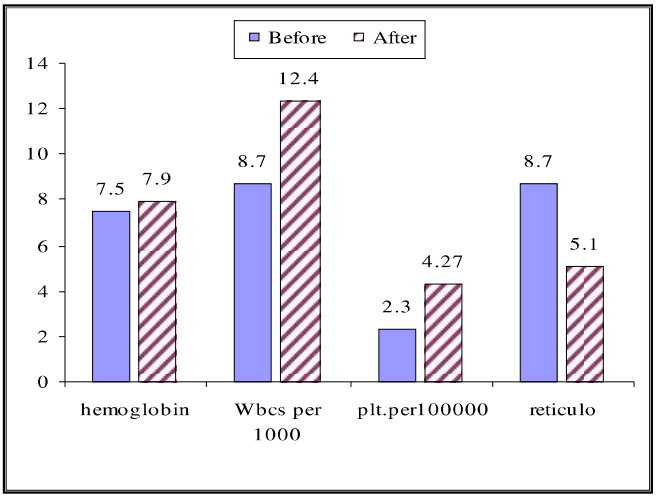

There is higher mean hemoglobin after splenectomy compared to presplenectomy level and the difference is statistically highly significant with 5.3% increase. There is a higher means increases in the mean WBCs 12.4 compared to 8.7 before surgery and the difference is statistically highly significant with 42.5% increase. This table shows higher mean platelets after surgery 427.6 compared to 203.5 before surgery with 110% rise in the mean platelet count and the difference is statistically highly significant. There is a lower mean reticulocytic count after splenectomy compared to pre- surgery level with a drop of 41% in the mean level of reticulocytes and the difference is statistically highly significant.

Discussion:

Forty patients 29 (72.5%) males and 11 (27.5%) females were included in our study. All were children aged 6 to 18 years with 12.5% of the patients are less than 10 years, 35% of the patients in the age range of 10 to less than 15 and 52.5% of the patients are 15 and above all with established diagnosis of β- Thalassemia Major, the previous studies were done on adults (Darzi et.al., 2014). To our knowledge, our study was the first to discuss the influence of splenectomy on different blood picture parameters in children with β- Thalassemia Major.

Regarding blood characteristics, the hemoglobin level is below the normal physiological level in all children with β- Thalassemia Major before and after splenectomy it is probably due to the fact that these patients are subjected to a state of chronic anemia that is caused by frequent hemolysis. On the other hand, there is higher mean hemoglobin after splenectomy was 7.9 g/dl compared to presplenectomy level 7.5 g/dl and the difference is statistically highly significant with 5.3% increase which agrees with previous studies (Ammar et.al., 2014).

In our study there is higher mean platelets after surgery 427.6 compared to 203.5 before surgery with 110% rise in the mean platelet count and the difference is statistically highly significant and There is a higher mean increases in the mean WBCs 12.4 compared to 8.7 before surgery and the difference is statistically highly significant with 42.5% increase this may be explained by the fact that the spleen is the organ removing aging or abnormal RBC, foreign invaders, and other cells including platelets, WBCs from the circulation. Splenectomy raises circulating platelets and WBC, which may contribute to a high risk of thrombosis and certain infections including meningitis, pneumonia and sepsis which agrees with previous studies (Ruchaneekorn et.al., 2013, Cappellini., 2007 and Vento et.al., 2006).

It was reported in our study that there is a lower mean reticulocytic count after splenectomy compared to presplenectomy level with a drop of 41% in the mean level of reticulocytes and the difference is statistically highly significant, suggesting the role of spleen in reticulocyte pooling which comes in agreement with previous studies done by Ruchaneekorn et.al., 2013 and Khuhapinant et.al., 1994.

Conclusion:

There is an improvement of blood picture parameters includes increasing of hemoglobin level and platelet count with decreased the level of reticulocytic count. There is increase of total leucocytic count after splenectomy with the increased risk of sepsis and infection after splenectomy with the necessity of presplenectomy vaccination.

Recommendation:

We noticed that there was increase of total leucocytic count after splenectomy with the increased risk of sepsis and infection after splenectomy with the necessity of presplenectomy vaccination and to perform the ways of prevention of infection with early treatment of infection post splenectomy.

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Introduction:

Beta thalassemias are a group of inherited autosomal recessive hematological disorders spread in the Mediterranean region due to defects in synthesis of β chains of hemoglobin, caused by mutation in the HBB gene on chromosome 11 causing asymptomatic to clinically severe hypochromic microcytic anemia (Hayder and Ali, 2017).

Beta thalassemia major is a hereditary synthesis defect in beta chains of hemoglobin; it results in red blood cell destruction with symptoms of anemia. Red blood cell destruction, repeated blood transfusion and bad compliance to routine use of iron chelator lead to iron accumulation in the heart, liver and endocrine organs (Shodikin et.al., 2016).

Beta thalassemia major present in various shapes depending on the beta globin chains defect. The most severe form is beta thalassemia major which happens as a conclusion of inheritance of two beta globin chain mutations either in homozygous or compound heterozygous states. Patients with beta thalassemia major require recurrent blood transfusions for survival due to severe anemia. Clinical picture of this disease is microcytosis and hemolytic anemia that need repeated blood transfusion which may lead to irreversible damage to organs and tissues due to iron accumulation (Tolba et.al., 2015).

Splenomegaly in patients with thalassemia major is often huge and mainly associated with severe transfusion dependent anemia due to ineffective erythropoiesis and prolonged hemolysis due to RBC membrane affection associated with precipitation of unbound α globin chains., about 90% of patients with thalassemia had undergone splenectomy by age 15 years with a result in stoppage of transfusion requirement in most thalassemia intermedia patients and with a decrease in the need for red cell transfusions in thalassemia major patients. However, these improvements came at the expense of various splenectomy associated complications including sepsis from encapsulated organisms (although this risk has been overcome with new protein conjugate vaccines and antibiotic prophylaxis) (Neal et.al., 2013)

Aim of Study:

To study the effect of splenectomy on different blood picture parameters in children with β- Thalassemia Major.

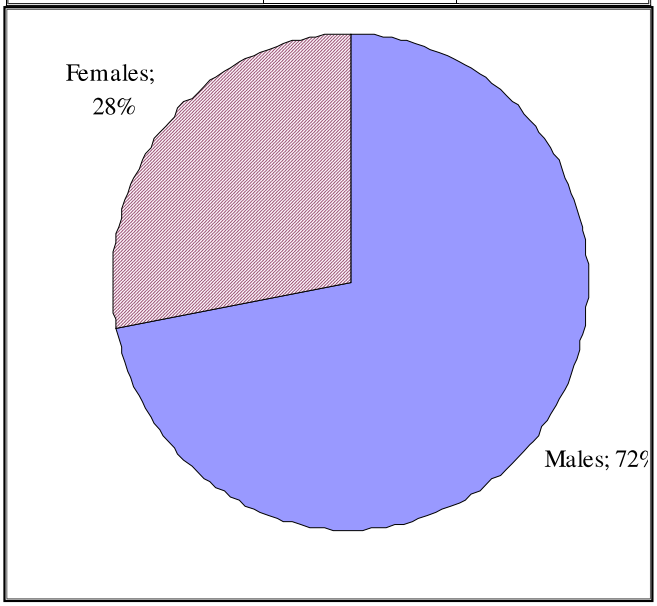
Patients And Methods:

This prospective study was conducted on 40 children (males and females) between (6- 18) years of age with confirmed homozygous β-thalassemia major diagnosis recruited from Hematology Clinic, Children's university hospitals; Ain Shams and Cairo Universities, Egypt, from December 2016 till December 2017, before and after splenectomy done to those patients. Informed consent was taken from all patients or their legal guardians. excluded patients with acute febrile illness within 72 hours prior to enrollment, serious concurrent illness, chronic renal failure and other hematologic disease comorbidity. Data were collected by reviewing medical records as well as by direct patient interviewing. Thorough history taking was obtained including age, sex, consanguinity, other affected siblings, similar family condition, history of disease related complications e.g. transfusion- related infections, allow sensitization, iron- overload, related cardiac, endocrine and liver disturbances… etc, history of concomitant medical conditions e.g. viral hepatitis (HBV, HCV), blood transfusion history including age of onset, duration and frequency of transfusion and history of drug therapy e.g. hydroxyurea, chelation. A complete physical examination was performed for all patients by assessing anthropometric measurements, vital signs, presence of pallor, jaundice, liver status. Complete blood picture with blood indices by Coulter Counter in addition to reticulocytes count. Patients' data were analyzed using SPSS 17.0 for Windows 7. Quantitative variables were expressed by mean and SD (Standard deviation), compared using unpaired t- student test and Mann- Whitney test. Spearman rank order test was used for correlating quantitative variables. P value was considered to be significant if less than 0.05.

Results:

Table (1) Distribution of gender and age of studied patients

N= 40		No	%
Gender	Male	29	72.5
	Female	11	27.5
Age	Less Than 10	5	12.5
	10-	14	35.0
	15>	21	52.5
		Mean SD	Range
Age (Years)		13.8 3.0	7.0- 17.0



This table shows that 72.5% of the studied patients are male and 27.5% are female with 12.5% of the patients are less than 10 years, 35% of the patients in the age range of 10 to less than 15 and 52.5% of the patients are 15 and above.

Table (2) Comparison between the mean level of blood picture parameters before and after splenectomy among studied patients

N= 40	Before Mean SD	After Mean SD	Paired T	P
Hemoglobin	7.5 (0.3)	7.9 (0.3)	13.8	0.000**
WBCs	8.7 (2.7)	12.4 (2.3)	11.5	0.000**
Platelets	203.5 (56.1)	427.6 (90.5)	20.4	0.000**
Reticulocytes	8.7 (3.0)	5.1 (2.3)	15.1	0.000**

** P<0.01 highly significant

Effect of Splenectomy on Blood Picture in Children with Thalassemia Major

Ahmed Adel Fathy Mohamed
Gamal Sami Ali (Professor of pediatrics at FPGS), M. Khaled El-Menabbawy (Professor at NRC),
Fatma A. Elzaree (Researcher at NRC), Reham Sabrey Abdel Aal(Lecturer of pediatrics at FPGS)

Summary

Background: Beta thalassemias are a group of inherited autosomal recessive hematological disorders, it results in red blood cell destruction with symptoms of anemia. Red blood cell destruction, repeated blood transfusion and bad compliance to routine use of iron chelator lead to iron accumulation in the heart, liver and endocrine organs, Clinical picture of this disease is microcytosis and hemolytic anemia that need repeated blood transfusion which may lead to irreversible damage to organs and tissues due to iron accumulation, about 90% of patients with thalassemia had undergone splenectomy by age 15 years with a result in stoppage of transfusion requirement in most thalassemia intermedia patients and with a decrease in the need for red cell transfusions in thalassemia major patients.

Aim of study: To study the effect of splenectomy on different blood picture parameters in children with β- Thalassemia Major.

Methods: A prospective study that was conducted on 40 confirmed homozygous β- thalassemia major patients before and after splenectomy with complete physical examination was performed for all patients by assessing anthropometric measurements, vital signs, presence of pallor, jaundice, liver status. Complete blood picture with blood indices by Coulter Counter in addition to reticulocytes count.

Results: After splenectomy there is higher mean level of hemoglobin with 5.3% increase, higher platelet count with 110% rise in the mean platelet count and higher total leucocytic count with 42.5% increase and decreased reticulocytic count with a drop of 41% in the mean level of reticulocytes with all results statistically highly significant.

Conclusion: There is improvement of blood picture parameters after splenectomy which includes increasing of hemoglobin level and platelet count with decreased level of reticulocytic count. The increase of total leucocytic count after splenectomy is explained by the increased rate of infection.

Key words: Thalassemia Major- Blood parameters– children- Splenectomy.

تأثير استئصال الطحال على صورة الدم لدى الأطفال المصابين بأنيميا البحر الأبيض المتوسط

الخلفية: أنيميا البحر الأبيض المتوسط هى مجموعة من الاضطرابات الوراثية الجسمية بسبب عيوب فى تخليق سلاسل الهيموجلوبين، ينتج عنها تدمير خلايا الدم الحمراء مع أعراض فقر الدم، وعمليات نقل الدم المتكررة والامتثال السيئ للاستخدام الروتينى للأدوية الطاردة للحديد إلى تراكم الحديد فى القلب والكبد وأجهزة الغدد الصماء . وفى حوالى ٩٠% من مرضى الثلاسيمية يخضعوا لعملية استئصال الطحال عند بلوغهم عمر ١٥ سنة مما يؤدى إلى توقف متطلبات نقل الدم فى معظم مرضى الثلاسيميا الوسطية مع انخفاض الحاجة إلى نقل خلايا الدم الحمراء فى مرضى الثلاسيميا الكبرى.

الهدف من البحث: دراسة تأثير استئصال الطحال على عناصر صورة الدم المختلفة لدى الأطفال المصابين بأنيميا البحر الأبيض المتوسط .

المرضى والاجراءات: تم إجراء دراسة استطلاعية أجريت على ٤٠ مريض مصابا بأنيميا البحر الأبيض المتوسط بعد تأكيد التشخيص وتماثل الجينات المرضية قبل وبعد استئصال الطحال. وتم عمل صورة الدم الكاملة مع مؤشرات الدم بواسطه الفحوصات وأجهزة التحليل المعملى بالإضافة إلى عدد الخلايا الشبكية.

النتائج: بعد استئصال الطحال هناك مستوى أعلى من الهيموجلوبين مع زيادة بنسبة ٥,٣% وارتفاع فى عدد الصفائح الدموية بنسبة ١١٠% فى متوسط عدد الصفائح الدموية وزيادة عدد كريات الدم البيضاء مع زيادة ٤٢,٥% وانخفاض عدد الخلايا الشبكية مع انخفاض بنسبة ٤١% فى المتوسط مستوى الخلايا الشبكية وجميع النتائج ذات دلالات احصائيه عاليه.

التوصيات: لوحظ من خلال الدراسة زيادة فى عدد كرات الدم البيضاء الكلى بعد استئصال الطحال ووجود خطورة بالاصابه بالعدوى وذلك فينصح باخذ التطعيمات اللازمة قبل استئصال الطحال والأخذ بسبل الحمايه من العدوى.

الخلاصة: يوجد تحسن بمعظم عناصر صورة الدم وتشمل زيادة مستوى الهيموجلوبين وعدد الصفائح الدموية مع انخفاض مستوى عدد الخلايا الشبكى وهناك زيادة فى عدد كريات الدم البيضاء الكلى بعد استئصال الطحال ويمكن تفسير ذلك من خلال زيادة خطر الأصابه بالعدوى.

الكلمات الدالة: أنيميا البحر الأبيض المتوسط– عناصر صورة الدم– الأطفال– استئصال الطحال.