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Research Article

Evaluating the Use of Nutech Functional Score in Comparison to Gross Motor Function Classification System in Assessing Patients with Cerebral Palsy after Human Embryonic Stem Cell Therapy

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Abstract

The Gross Motor Function Classification System (GMFCS) is widely used to assess the extent of disabilities in patients with cerebral palsy (CP). However, its use is limited in assessing various symptoms of CP that are important. Our study aimed at evaluating the efficacy of a new scoring system, Nutech Functional Score (NFS) as compared to GMFCS in assessing patients with CP treated with human embryonic stem cell (hESC) therapy. The study included a total of 91 CP patients aged 16 months to 18 years. The patients were treated with hESC therapy for one treatment period. All the patients were scored with GMFCS and NFS at baseline and after hESC therapy. The patients showed an improvement in parameters (epilepsy, aggression, drooling etc.) associated with CP when evaluated with NFS. This improvement went unnoticed when the patients were assessed with GMFCS. hESC therapy is effective in treating patients with CP. NFS could be a suitable scoring system for patients with CP as it can assess the slightest improvements in the patients. Use in other settings would be helpful in assessing its utility.

Key words: *Cerebral palsy; Nutech Functional Score (NFS); Gross Motor Function Classification System (GMFCS); Human Embryonic Stem Cell (hESC) Therapy*

Introduction

Cerebral palsy (CP) is an abnormality or damage to the developing brain which results in disorganization of the brain that further leads to loss of the ability to regulate movement and co-ordination of the body [1]. The Centers of Disease Control (CDC) and the Autism Developmental Disabilities Monitoring (ADMM) reports that for 323 children, 1 child in the U.S. is born with CP [2]. The risk factors that have been recognized to be associated with CP involve the interruption of oxygen supply during birth [3], postnatal injuries [4], low birth weight and prematurity for instance new born of very low birth weight are 20-80 times more prone to have CP than infants of a birth weight >2500gm [5].

There is no effective cure for CP [6] but physical therapy helps in improving the patients' quality of life or slow down the progression of disease [7,8]. Ketelaar and colleagues in his study showed a significant improvement in patients with CP who were receiving functional therapy. The improvement in therapy was measured by means of two systems; GMFM (Gross Motor Function Measure) and PEDI (Pediatric Evaluation of Disability Inventory). The GMFM system was designed to detect change in gross motor functions of children with CP while, PEDI measures both capability and performance of functional activities by means of three ways, *i.e.*, self-care, mobility and social function [9]. However, with GMFM the children with contrasting ability within and between the dimensions can get a same total score [10].

The other is Gross Motor Function Classification System (GMFCS) that was established to characterize the gross motor functions in children with CP. This system relies on self-initiated movement, especially in sitting and walking of CP patient [11]. The GMFCS scoring system is widely used but, the system does not assess certain parameters (epilepsy, hearing, drooling, writing, mathematical skills, communicating, playing) that are needed to be gauged in patients with CP [12].

Redi *et al*, in his study indicated that there is a greater classification uncertainty found between level I and II of the GMFCS. The author also reported enormous limitations in registries during assignment of GMFCS levels [13] GMFCS provides a lot of data which is complicated and time consuming for staff and also for the practitioners. In addition to these limitations, it is not a numeric system (*i.e.* cannot add or subtract the grades) [14].

We have reported an improvement in 101 patients with CP who were treated with human embryonic stem cell therapy (hESC) and assessed with GMFCS before and after the therapy [15]. We have also developed a new functional, directional and positional scoring system, Nutech Functional Score (NFS) to assess the patients with CP [16] and statistically validated it for these patients who underwent hESC therapy (Unpublished data communicated to the journal). Here, we compare the two scoring systems, *viz.,* NFS and GMFCS in the patients with CP who underwent a single session of hESC therapy

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at our institute.

Materials and Methods

The NFS scoring system assesses a symptom based on five ordinal grades that runs in a direction of GOOD → BAD. The NFS system is also helpful in conducting probability based studies and these scores have been converted into numeric values. It is a numeric scale that scores all the known symptoms for patients with CP. NFS for CP is a 32-point positional (*i.e.*, symptoms were sub-graded with a specific score) and directional (*i.e.*, from level I - V) scoring system that can be used to assess or validate the diagnosis of patients with CP [16].

In this study, a total of 91 CP patients were assessed with NFS, who were previously assessed with GMFCS after a single treatment session with hESC [15]. The NFS/GMFCS scores of the patients before and after therapy were compared to assess which scoring system is better in evaluating the patients treated with hESC therapy. All the patients provided written informed consent prior to start of the study. The study was conducted in accordance with Declaration of Helsinki [17] and approved by an institutional Independent Ethics Committee (IEC).

Results

NFS has 32 parameters; of which we describe the results of some key symptoms that are left out in GMFCS. We observed aggression in 86 patients (85%) with CP. At baseline (BL), 50 patients were at NFS score of 1, 17 patients at NFS score of 2, 18 patients at NFS score of 3, 1 patient was at NFS score of 4 and no patient was at NFS score 5. After the end of the session, all the patients showed an improvement with only 4 patients at NFS score of 1, 17 patients at NFS score of 2, 36 patients at NFS score of 3, 12 patients at NFS score of 4 and 17 patients at NFS score of 5. Overall, 50% patients with NFS score 1 at BL, *i.e.,* in bad condition moved to higher grades after a single treatment session with hESC therapy. Table 1 describes the overall movement of patients from lower grades at BL to higher grades after treatment session.

Drooling was observed in 71 patients (70%) with CP. At BL, 45 patients were at NFS score of 1, 9 patients at NFS score 2, 12 patients were at NFS score 4 and no patient at NFS score 5. After treatment session, there was a significant improvement in the NFS scores, only 3 patients at NFS score of 1, 19 patients at NFS score of 2, 23 patients at NFS score of 3, 12 patients at NFS score of 4 and 14 patients at NFS score of 5. Overall, 45% patients with NFS score 1 at BL, *i.e.,* in bad condition moved to higher grades after a single treatment session with hESC therapy (Table 1).

Similar improvement was observed after treatment for the parameter epilepsy in 57 patients (56%) with CP. At BL, 8 patients were at NFS score of 1, 15 patients at NFS score 2, 20 patients were at NFS score 4. After the treatment session with hESC therapy, an improvement in the NFS scores was observed with no patient at NFS score of 1, 6 patients at NFS score of 2, 9 patients at NFS score of 3, 22 patients at NFS score of 4 and 20 patients at NFS score of 5. Overall, 8% patients with NFS score 1 at BL, *i.e.*, in bad condition moved to higher grades after a single treatment session with hESC therapy. NFS scores for all the parameters at BL and at the end of treatment phases are presented in Table 1. It also shows the movement of patients from lower grades at BL to higher grades after treatment session.

Discussion

In our previous study, we reported an improvement in the GMFCS scores of these 91 patients with CP (Before [1=1, 2=12, 3=15, 4=21 and 5=42]; End of treatment session [1=6, 2=32, 3=37, 4=17 and 5=1]) [15]. Overall, 37 (37%) patients transitioned from GMFCS score of 5 to lower scores by the end of one treatment session It was also found that 42 patients had a GMFCS score of 5 at the beginning of T1; of which 41 (40%) moved to lower scores at the end of treatment session. We observed an improvement in the scores of patients when assessed using NFS. An overall assessment of patients with NFS is presented in Table 1. Every patient who received hESC therapy showed a change in NFS scores for better between BL and end of treatment session. The improvement in NFS scores by the end of session were compared with the scores obtained with GMFCS presented in Table 2. Though, both the scoring systems help in assessing the improvement in patients with CP, but NFS seems to be more beneficial as it helps in highlighting even the slightest improvement in the condition of the patient either with epilepsy, drooling, head control, aggression, toilet training, trunk control, kyphosis, problem solving, recognition awareness, writing *etc*.

Harvey *et al* stated that the GMFCS is only a classification system and is not meant to be used as an assessment tool. The author agreed that the system does not assesses the relevant information emphasizing the need of other valid, reliable, evaluation and categorization tools to enthrall a wide range of clinical and research investigations [18]. Moreover, the practitioners and staff of our institute observed that all the levels (I-V) in GMFCS emphasize mainly on the walking motor abilities in a CP patient. The system is unable to assess other important parameters such as; breathing difficulty, constipation, defense mechanism, epilepsy, drooling, eye contact, feeding, head control, IT skills, aggression, kyphosis, problem solving, recognition/ awareness, rolling over scoliosis, smiling, toilet training, trunk control and writing that were important to gauge in a patient with CP. Therefore, it has been difficult for clinicians to make normative evaluation of children's motor potency with GMFCS levels [19]. However, NFS system is a functional and parametric system that assesses a patient with CP on the basis of all the parameters that were associated with CP.

Akbari and colleagues described that the GMFCS is complex and time consuming with interpretation in the total score. They stated that children who are initially scored (initial assessment whether high or low) at the beginning of the scale have a lesser potential to change the score than those who are scored in the middle of the scale. This is because of additional components which exist in the middle of the scale than at the extremes [14]. In other words, the probability of deflecting of the scores were more in the middle of the level, *i.e.,* (III-IV) than in the beginning because, the system limits in assessing other parameters that were associated in a patient with CP.

Let's take an example of a patient who showed slightest improvement when scored with NFS after hESC therapy whereas was placed in same level when assessed with GMFCS. It was found that the NFS score at baseline was 69 that changed to 82 after treatment session. However, on scoring with GMFCS, the patient scores 3 both before and after the end of treatment session (Table 3).

This signifies the usefulness of NFS in detecting even the minor improvement in patient's condition. In the present study, an improvement in functional limitations was observed in patients with CP after hESC therapy. No adverse events were seen in the patients with hESC therapy [15,20].

Use of hESC therapy has generally led to a concern because of clinical non-viability in culturing of cells in a xeno-free environment. However, our institution uses a patented methodology (Patent-WO 2007/141657A PCT/1B 2007, Published 13 December, 2007) for the extraction, isolation and maintenance of hESCs [21]. The ability of stem cell to proliferate and to reconstruct the damaged parts offers excellent possibilities [22]. Previous studies have shown the potential of stem cells to migrate at the injury site and commence host repair and healing *via* the direct or indirect cell-signaling. In the course of brain injury, stem cells initiate neuroprotection and neural repair by

inflammatory suppression, causing tissue reconstruction and averts cell damage. We have shown that hESC therapy is effective and safe in patients with CP [23].

The effect of GMFCS in clinical practices, administration or in education has not yet been effectively observed. However, there is a paucity of information that shows its effects on the research design of the study [24]. By restricted attributes of GMFCS, such kind of information is difficult to measure. Morris *et al*, in his study noticed that GMFCS is not able to describe the reliability in patients aged less than 2 years but shows a noticed capability in patients aged between 2-6 years. The author also stated that the system till now have not given any explanation in context with GMFCS in adolescents who moved into adulthood [24].

Table1: NFS Scores of All the Patients after the End of Session.

NFS Parameters	NFS Scores at *BL (n)	End of Treatment Session				
		1	2	3	4	5
Aggression	1 (50)	4	17	20	1	8
	2 (17)	0	0	11	2	4
	3 (18)	0	0	5	9	4
	4 (1)	0	0	0	0	1
Total	86	4	17	36	12	17
Breathing Difficulty	3 (2)	0	0	1	1	0
	4 (1)	0	0	0	0	1
Total	3	0	0	1	1	1
Climbing Stairs	1 (44)	8	20	12	3	1
	2 (15)	0	3	8	3	1
	3 (12)	0	0	2	8	2
	4 (6)	0	0	0	4	2
Total	77	8	23	22	18	6
Commands	1 (74)	7	21	32	4	10
	2 (9)	0	0	7	0	2
	3 (5)	0	0	2	2	1
	4 (1)	0	0	0	0	1
Total	89	7	21	41	6	14
Constipation	1 (6)	0	2	3	0	1
	2 (6)	0	2	3	1	0
	3 (13)	0	0	3	7	3
	4 (4)	0	0	0	2	2
Total	29	0	4	9	10	6
Crawling	1 (45)	3	18	18	1	5
	2 (15)	0	0	10	3	2
	3 (6)	0	0	2	2	2
	4 (9)	0	0	0	3	6
Total	75	3	18	30	9	15
Daily living skills	1 (52)	4	25	14	7	2
	2 (18)	0	3	9	3	3
	3 (10)	0	0	1	7	2
	4 (9)	0	0	0	5	4
Total	89	4	28	24	22	11
Defense mechanism	1 (27)	3	11	8	3	2
	2 (26)	0	8	13	1	4
	3 (23)	0	0	8	12	3
	4 (6)	0	0	0	3	3
Total	82	3	19	29	19	12
Drooling	1 (45)	3	19	15	3	5
	2 (9)	0	0	6	1	2
	3 (12)	0	0	2	5	5
	4 (5)	0	0	0	3	2
Total	71	3	19	23	12	14
Epilepsy	1 (8)	0	3	2	0	3
	2 (15)	0	3	4	4	4
	3 (20)	0	0	3	11	6
	4 (14)	0	0	0	7	7
Total	57	0	6	9	22	20
Eye contact	1 (49)	1	20	17	3	8
	2 (14)	0	1	10	1	2
	3 (8)	0	0	1	6	1
	4 (6)	0	0	0	2	4
Total	77	1	21	28	12	15
Feeding	1 (20)	1	7	8	2	2
	2 (22)	0	3	15	2	2
	3 (26)	0	0	4	16	6
	4 (8)	0	0	0	3	5
Total	76	1	10	27	23	15
Grip	1 (16)	1	7	4	3	1
	2 (36)	0	2	26	2	6
	3 (17)	0	0	5	11	1
	4 (11)	0	0	0	6	5
Total	80	1	9	35	22	13
Head control	1 (21)	0	9	9	1	2
	2 (18)	0	1	15	1	1
	3 (10)	0	0	2	5	3
	4 (8)	0	0	0	3	5
Total	57	0	10	26	10	11
Hearing	1 (1)	0	0	1	0	0
	2 (2)	0	0	0	0	2
	3 (2)	0	0	0	2	0
	4 (1)	0	0	0	1	0
Total	6	0	0	1	3	2
I.T. skills	1 (43)	10	17	12	3	1
	2 (25)	0	4	17	1	3
	3 (12)	0	0	3	5	4
	4 (5)	0	0	0	4	1
Total	85	10	21	32	13	9
Indication	1 (31)	5	13	8	2	3
	2 (28)	0	2	18	5	3
	3 (23)	0	0	7	9	7
	4 (4)	0	0	0	3	1
Total	86	5	15	33	19	14
Kyphosis	1 (4)	3	1	0	0	0
	2 (2)	0	2	0	0	0
	3 (1)	0	0	0	1	0
	4 (2)	0	0	0	2	0
Total	9	3	3	0	3	0
Solving problem	1 (56)	10	25	14	6	1
	2 (9)	0	0	8	1	0
	3 (4)	0	0	1	1	2
	4 (3)	0	0	0	2	1
Total	72	10	25	23	10	4
Recognition/ awareness	1 (23)	2	7	11	0	3
	2 (12)	0	0	4	4	4
	3 (26)	0	0	5	14	7
	4 (8)	0	0	0	3	5
Total	69	2	7	20	21	19
Rolling over	1 (40)	1	19	16	0	4
	2 (15)	0	0	10	4	1
	3 (7)	0	0	2	3	2
	4 (10)	0	0	0	4	6
Total	72	1	19	28	11	13
Scoliosis	2 (3)	0	1	1	1	0
	4 (7)	0	0	0	4	3
Total	10	0	1	1	5	3
Sitting	1 (16)	0	9	6	1	0
	2 (33)	0	4	19	7	3
	3 (19)	0	0	5	12	2
	4 (11)	0	0	0	4	7
Total	79	0	13	30	24	12
Smiling	1 (26)	1	9	12	0	4
	2 (18)	0	0	14	2	2
	3 (16)	0	0	1	10	5
	4 (6)	0	0	0	0	6
Total	66	1	9	27	12	17

Conclusion

NFS is a solitary classification system for the patients of all ages with diminished complexity of the assessment system for the practitioners. Thus, we conclude that the newly developed NFS is a unique tool that can be used to gauge the betterment of patients receiving hESC therapy. Thus, this newly developed classification, functional and evaluation system can be used globally to help the patients with CP.

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Speech	1 (31)	4	15	8	4	0
	2 (36)	0	4	22	4	6
	3 (14)	0	0	2	9	3
	4 (4)	0	0	0	2	2
Total	85	4	19	32	19	11
Standing	1 (42)	2	19	15	4	2
	2 (16)	0	1	11	3	1
	3 (17)	0	0	5	11	1
	4 (8)	0	0	0	5	3
Total	83	2	20	31	23	7
Swallowing	1 (9)	0	2	4	2	1
	2 (20)	0	4	13	2	1
	3 (21)	0	0	6	11	4
	4 (12)	0	0	0	6	6
Total	62	0	6	23	21	12
Toilet training	1 (46)	4	19	14	5	4
	2 (10)	0	2	4	2	2
	3 (12)	0	0	3	5	4
	4 (10)	0	0	0	5	5
Total	78	4	21	21	17	15
Trunk control	1 (31)	1	14	9	5	2
	2 (25)	0	3	16	3	3
	3 (14)	0	0	5	6	3
	4 (10)	0	0	0	4	6
Total	80	1	17	30	18	14
Vision	1 (8)	0	4	3	1	0
	2 (15)	0	1	6	6	2
	3 (9)	0	0	3	4	2
	4 (6)	0	0	0	3	3
Total	38	0	5	12	14	7
Walking	1 (47)	6	24	10	6	1
	2 (13)	0	1	9	2	1
	3 (16)	0	0	7	8	1
	4 (11)	0	0	0	8	3
Total	87	6	25	26	24	6
Writing	1 (51)	7	23	15	5	1
	2 (12)	0	3	7	1	1
	3 (4)	0	0	2	2	0
	4 (1)	0	0	0	1	0
Total	68	7	26	24	9	2
*BL=Base line						

Table 2: Comparison between GMFCS and NFS Scores of Patients with CP

Age group	GMFCS at *BL	NFS at *BL	G M F C S at End of session	NFS at End of session
0-2 Years	5	27	1	113
	5	28	1	105
	5	26	2	90
	5	39	3	101
	5	38	2	95
	5	16	2	67
	5	29	3	95
	5	10	2	33
	5	33	2	107
	5	32	2	86
	3	32	1	118
	3	41	2	82
2-4 Years	5	31	2	124
	5	35	1	117
	4	44	1	122
	5	38	2	110
	5	31	2	110
	4	33	2	114
	5	47	1	130
	5	47	2	115
	5	40	1	128
	5	34	1	82
	3	69	3	82
	5	31	2	53
	4	51	2	120
	5	54	2	118
	5	52	3	92
4-6 Years	5	41	2	128
	5	39	3	122
	5	40	3	121
	2	46	1	84
	4	41	1	130
	5	39	1	129
	5	57	2	121
	4	50	2	126
	3	76	2	110
	2	72	1	120
	2	54	2	72
	2	65	2	97
	5	40	2	85
	4	40	2	113
	4	68	2	113
	4	44	2	74
	3	68	2	105
	5	19	3	48
	2	33	1	65
	5	36	3	92
	5	41	3	82
6-12 Years	5	35	3	87
	3	51	2	121
	5	44	2	121
	2	66	1	125
	5	41	2	130
	3	55	2	114
	5	33	2	91
	4	59	2	105
	4	43	1	103
	5	35	2	109
	4	40	2	98
	2	71	2	110
	3	34	2	82
	4	46	3	63
	1	24	1	48
	2	49	1	75
	5	27	2	81
	3	69	1	113
	4	55	2	102
	4	35	1	61
	3	26	2	86
	5	41	2	130
	3	28	2	71
	4	52	2	118
	3	47	2	71

Table 3: Slight Improvement Noticed with NFS After hESC Therapy

No. of patients	Age (Years)	GMFCS at *BL and End of session	NFS at *BL	NFS at End of session
1	2-4	3	69	82
2	4-6	2	54	72
		2	65	97
2	6-12	2	71	110
		1	24	48
*BL=Base line				

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