ORIGINAL RESEARCH PAPER

Radiology

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

CEREBRAL PALSY – COMPARISON OF DYNAMIC SUSCEPTIBILITY CONTRAST ENHANCED MRI PERFUSION IMAGING AND SPECT PERFUSION IMAGING

KEYWORDS: Cerebral palsy, SPECT, DSC MRI, perfusion, hypoperfusion

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ABSTRACT *Cerebral Palsy is a static encephalopathy with prenatal, perinatal and post natal hypoxic brain injury being its major causes. The morphological abnormalities in Cerebral Palsy are well documented. Fifty five patients (36 males, 19 females; age range: 1 yr – 13 yrs 8 months) with clinically diagnosed cerebral palsy were evaluated by Single Photon Emission Computed Tomography (SPECT) after giving 5-10 mCi of 99mTc –ECD intravenously and evaluated using a low energy – high resolution gamma camera and T2* Dynamic Susceptibility Contrast Enhanced MRI (DSC MRI) with SE Echo Planar Imaging sequence after injecting 0.2 mmol/kg bodyweight of Gadolinium based contrast. The clinical subtypes were spastic quadriplegia (n =28, 50.9%), spastic diplegia (n=16, 29.1%), spastic hemiplegia (n=6, 10.1%), mixed CP(n=2), hypotonic, extrapyramidal and ataxic CP (n=1). On SPECT, hypoperfusion was noted in frontal lobe in 81.5%, followed by temporal lobe (62.9%), basal ganglia (29.6%), occipital lobe (25.6%), thalamus (22.2%), cerebellum (3.7%). However, DSC MRI demonstrated hypoperfusion in frontal lobe in 78.8%, followed by parietal lobe (75%), temporal lobe (63.5%), basal ganglia (34.6%), thalamus (30.8%) and occipital (21.2%). The comparison of two modalities show good agreement with kappa values as measure of agreement varying from 0.371 to 0.805 and p values varying from 0.006 to <0.001.*

Introduction

Cerebral palsy (CP) is a static encephalopathy, manifesting as defects in posture and motion. They result from a central nervous system insult, sustained in the early period of brain development, usually in utero and in first 3 to 5 years of extra-uterine life. The etiology of cerebral palsy is diverse with hypoxic ischaemic injury being a predominant cause in large subset of patients which produce a common clinical phenotype (1, 2). The initial diagnosis of CP remains clinical with majority of diagnosis made in the first year of life. Magnetic resonance imaging is the modality of choice in evaluating morphological abnormalities in CP. It shows abnormalities in 87% of the cases with white matter damage of immaturity noted in 42.5% of the cases, followed by basal ganglia lesions, cortical/ subcortical lesions, malformations and focal infracts (3). As etiology of CP in majority of cases has been attributed to hypoxic or vascular insult, CP have been evaluated using Positron Emission Tomography (PET) and Single-photon emission computed tomography (SPECT) which show gray matter involvement even in absence of morphological abnormality(4,5). This study was planned with aim to evaluate perfusion abnormalities in patients with Cerebral Palsy using T2* Dynamic Susceptibility Contrast Enhanced MRI and compare it with Technetium-99m-Ethyl Cysteinate Diethylester (99mTc –ECD) Brain SPECT using a low energy high resolution Gamma Camera.

Materials and Methods

Methodology

This prospective study was done over a span of two years in department of radiology, paediatrics and nuclear medicine. It consisted of 55 patients (36 males, 19 females; age range 1 yr – 13 yrs 8 months; mean age 5.03 years) with cerebral palsy diagnosed clinically by consistent trained observer (KSR) using physical examinations, Denver development screening test and neurological examinations such as Electromyography (EMG), electroencephalogram (EEG), Brain stem Evoked Response Audiometry (BERA) and Visual Evoked Potential (VEP). There were classified as per Minera's description. Congenital malformations, Neurodegenerative diseases, CNS infections, leukodystrophies and neuromuscular disorders were included in the exclusion criteria. Children less than one year of age were also not included in this study. Informed consent was obtained from the guardians of the patients to be included in the study and undergoing imaging procedures. Patients were classified into major subtypes of spastic quadriplegia (n =28, 50.9%), spastic diplegia (n=16, 29.1%), spastic hemplegia (n=6, 10.1%), mixed CP (n=2), hypotonic (n=1), extrapyramidal (n=1) and ataxic CP (n=1). Antenatal risk factors were noted in 41.8% of the cases with commonest being pregnancy induced hypertension (PIH), perinatal risk factors were noted in 80% of the patients with birth asphyxia accounting for 68.2% cases. Low birth weight and prematurity was noted in 50% and 36.4% of the cases.

Imaging Procedures

The SPECT and DSC perfusion MRI were performed within 1 month of each other with 54.5 % of patients undergoing MRI scan prior to SPECT evaluation. The investigators were blinded to the results achieved in the other modality.

After adequate sedation was given to the patients, 0.2 to 0.3 mCi/Kg (minimum dose of 03 mCi) of 99mTc –ECD was injected intravenously and SPECT images obtained 30 to 60 minutes post injection with a SIEMENS SYMBIA TRUE POINT SPECT- CT dual head gamma camera equipped with low energy, high resolution gamma camera with 360 degree arc of rotation. One-hundred twenty projections were acquired using a 128 X 128 matrices for 20 min. Scatter correction and back projection with a Butterworth filter (cutoff frequency 1.1 cycle/cm, order 0.10) was performed. Attenuation correction of the trans-axial images (slice thickness = 1.67 mm) were performed by Chang's method, and coronal and sagittal slices were calculated from the original trans-axial images. The SPECT images were qualitatively evaluated by two experienced nuclear medicine physicians (MJJ) for the evaluation of perfusion abnormality within cerebral cortices, basal ganglia, thalami and cerebellum.

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After adequate sedation, MRI was performed on 3.0 Tesla super conducting MR system (TRIO – SEIMENS, Erlanger, Germany). T2* DSC MRI with SE Echo Planar Imaging sequence with 0.2 mmol/kg of body weight contrast (Gadolinium based contrast) was performed. Cerebral Blood Volume (CBV) and Cerebral Blood Flow (CBF) were evaluated from thalamus, basal ganglia, frontal, parietal, temporal and occipital cortex. Total scan time was approximately 20 – 30 minutes. The images were separately evaluated by two experienced radiologists blinded to the result of SPECT and observations of the other observer(GSM,GS).

Results

On DSC MRI Perfusion study, all patients except three patients showed perfusion impairment. Those patients who did not show perfusion impairment consisted of one patient with non lissencephalic malformation and one each with diplegic and extrapyramidal CP (Table 1). The most common site of hypo-perfusion was frontal lobe (n=41), and followed by parietal lobe (n=39), temporal lobe (n=33), basal ganglia(n=18) ,thalamus (n=16), occipital lobe (n= 11). The only case of extrapyramidal CP did not show any perfusion defect as mentioned above. Hypo-perfusion within basal ganglia was seen not only in mixed type but also in 48% of spastic quadriplegic, 18.8% of spastic diplegic and 16.7% of hemiplegic patients. Frontal hypo-perfusion was seen in 80% in quadriplegic, 75% in diplegic, 83.3% in hemiplegic, 100% in mixed hypotonic and ataxic CP patients. Temporal lobe hypo-perfusion was seen in 68% of quadriplegics, 50% of diplegic, 83.3% of hemiplegics, 50% of mixed CP and 100% of hypotonic and ataxic CP patients. Parietal lobe hypo-perfusion in 80% quadriplegic, 66.2% in diplegic, 100% in hemiplegic, hypotonic and ataxic CP patients. Cerebellar hypo-perfusion was not seen in any of the patients.

On SPECT study, all patients except two patients with spastic diplegia, showed perfusion impairments (Table 2). The most common site of hypo-perfusion was frontal lobe (n=44), and followed by temporal lobe (n=39), parietal lobe (n=33), basal ganglia (n=15), occipital lobe (n= 14), thalamus (n=12) and cerebellum (n=2). Temporal lobe hypo-perfusion was seen in all types of CP. Hypo-perfusion within basal ganglia was seen in 29.6% of spastic quadriplegic, 18.75% of spastic diplegic, 16.7% of hemiplegic, 100% of hypotonic patients. Temporal lobe hypo-perfusion was seen in 77.8% of quadriplegic, 56.25% of diplegic, 66.7% of hemiplegic and 100% of other types of CP patients. Frontal hypo-perfusion was seen in 92.7% in quadriplegic, 62.5% in diplegic, 83.3% in hemiplegic, 100% in mixed, ataxic and hypotonic CP patients. Parietal lobe hypo-perfusion in two thirds of quadriplegic, half of diplegic, all hemiplegic, hypotonic and extrapyramidal CP patients. Cerebellar hypo-perfusion was seen only in one patient each of quadriplegic and diplegic type of CP.

The SPECT and DSC MRI Perfusion was evaluated for hypoperfusion and the different anatomical segments were evaluated as unilateral, bilateral or no hypoperfusion. The comparison between two modalities show good agreement when evaluating all types of cerebral palsy with agreements varying from the lowest of 39 cases among total of 52 cases in parietal lobe (Table 3) to best agreement of 48 cases out of 52 cases evaluating occipital lobe. The kappa values as measure of agreement vary from 0.371 to 0.805 and p values vary from a high of 0.006 (which is also statistically significant) to <0.001 (which is highly significant) (Table3). Cerebellum was not included in the comparative analysis as no positive case was noted in DSC MRI perfusion.

Discussion

CP is not a single pathophysiological entity but refers to a group of disorders whose common clinical determinants are posture and gait abnormalities, early onset and static course. Hence, CP has been divided in various clinically determined subgroups of spastic quadriplegia, spastic diplegia, spastic hemiplegia, choreo-athetoid CP, hypotonic CP, ataxic CP and mixed CP (1,2,6,7). Its subtypes differs with regard to parts of the body involved, specific difficulties experienced; and other associated disabilities (8,9).

In developed countries because of improved perinatal care, antenatal risk factors are responsible for CP in almost 85-90% of cases. Even birth asphyxia and other perinatal complications are seen more in children with existing antenatal risk factors (10). In India on the other hand, birth asphyxia still remains one of the important risk factors of CP because of poor perinatal care. In our study, we found antenatal risk factors present in 41.8% and perinatal risk factors in 80% of the patients.

Neuroimaging, especially magnetic resonance imaging (MRI), plays an increasing role in the diagnosis of CP (11). It has the potential to visualize physiological and pathological morphological changes during brain development. During the early 3rd trimester, and in the preterm-born infant, periventricular white matter (PWM) is especially affected. Towards the end of the 3rd trimester, and in the term – born infant, grey matter, either cortical or deep grey matter (e.g. basal ganglia and thalamus) appear to be more vulnerable (12,13,14). Infarcts of the middle cerebral artery (MCA) are reported mainly in term or near-term born infants, although they may occur in the very preterm infant (15).

In our study, 52 patients were evaluated by MRI and SPECT both. Two patients were morphologically normal (Case no. 29 and 47) Both the cases which were morphologically normal on MRI had Spastic diplegia and showed perfusion abnormalities on both SPECT perfusion and DSC perfusion imaging.

Hence, morphological abnormalities are not seen in all patient of cerebral palsy and in some cases the clinical features cannot be explained by the structural findings of the MRI scan. Hence, advanced MR imaging like Diffusion tensor tractography and perfusion imaging not only increase the sensitivity of the diagnostic modality but also helps in understanding of the disease pathogenesis (5,16).

In 1997, JD Lee et al (5), compared MR morphology and SPECT Perfusion in 51 patients. In their series the clinical subtypes of cerebral palsy were spastic diplegia (n = 35), spastic quadriplegia (n = 11), spastic hemiparesis (n = 2), choreoathetoid (n = 2) and mixed (n = 1). They found thalamic hypoperfusion in all patients except one (98%), followed by hypoperfusion in the temporal lobe (52.9%), basal ganglia (41.2%), cerebellum (39.2%) and extra temporal cortices (21.6%). As compared to our series, their series had spastic diplegia constituting the majority of the study load, whereas, spastic quadriplegia constitute the majority of our patients. Also comparatively, number of patients with spastic hemiplegia are also more in our series. Hence, the different pattern of perfusion abnormalities is noted in the two series.

In our series, 52 patients were subjected to MRI DSC perfusion imaging and showed perfusion impairments in all except for three patients. These patients consisted of a single patient with non lissencephalic malformation, one patient each with spastic diplegia and extrapyramidal CP. Rest of the patients showed hypoperfusion in frontal lobe (78.8%), followed by parietal (75%) and temporal lobes (63.5%). Occipital, Basal ganglia and thalamus were involved 21.2%, 34.6% and 30.8% patients respectively. No hypoperfusion was noted in the cerebellum. To our knowledge, no previous study assesses MR perfusion in cerebral palsy.

On comparing MR perfusion and SPECT perfusion, good agreement was noted between the two modalities with high kappa values and statistically significant p values. In 1998, Harris GJ et al demonstrated comparable result in DSC MR imaging and SPECT in Alzheimer's disease and commented that sensitivity with DSC MR imaging was considerably better than with visual clinical readings of SPECT scans (74% in moderate and 50% in mild Alzheimer disease cases) (17).

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Also SPECT regional Cerebral Blood Flow (rCBF) agents like hexamethylpropyleneamine oxime (HMPAO) and Ethyl Cysteinate Diethylester (ECD) were designed for use with rotating Gamma Cameras, which have low sensitivity. Consequently, relatively stable in vivo rCBF tracers (at least 60 min) should be used in such systems. These radiotracers are extracted by the brain on first arterial pass after intravenous injection and subsequently retained for several hours. Retention by brain (or protracted diffusion from the brain) is due to various trapping mechanisms, such as metabolic degradation or conformational alteration. Stable distribution allows prolonged imaging times, so that relatively high resolution images can be produced by specialized collimators. Although count ratios among the brain regions correctly represent relative CBF, most retention mechanism do not lend themselves to simple mathematical models to provide absolute quantification.

The original tracer microsphere model works reasonably well form IMP (iodine labelled N-isopropyl-p-iodoamphetamine) and HIPDM (N,N,N'-trimethyl-N'-(2-hydroxy-3-methyl-5-iodobenzyl)-1,3,propanediamine) but not for ECD or HMPAO. More sophisticated models have been proposed. Unfortunately, these models depend on knowing the input function, which requires arterial blood sampling (not a routine practice in most nuclear medicine laboratories).

The principal disadvantage of the static tracer is a consequence of one of its advantage – long in vivo residence time. In addition to the multi-hour biochemical half life, the 6 hours physical half life of ^{99m}Tc means that one must wait for 4 to 6 half lives before radioactive background of an initial scan is below detectable limits. Hence one must wait for at least 1 day and preferably 2 days, before repeating the imaging sequence.

Additionally, neither ^{99m}Tc – HMPAO nor ^{99m}Tc –ECD are perfect chemical microspheres, consequently they underestimate rCBF values above about 60ml/min/100g, with the error increasing in proportion to rCBF.

However, DSC MRI is a robust brain perfusion imaging technique. Due to inherent lack of radiation, MRI scan can be repeated to monitor the progress of the disease. However, SAR guidelines should be kept in mind especially in high field strength.

However, the new MR systems designs are more SAR- efficient due to parallel imaging with multichannel receiver coil arrays, which is becoming an integral part of high field MR neuroimaging. This technique reduces the effect of SAR by means of a decreased RF exposure achieved by reducing the number of pulses required to obtain a given image with set resolution. Hence SAR is of a major concern only in fetal imaging (18,19).

As both the perfusion modalities are either qualitative or semi-quantitative in nature and the maps generated are relative perfusion maps. Hence, global hypoperfusion / bilateral hypoperfusion can be overlooked by the modalities, compromising the sensitivity of the modalities to identify bilateral / global abnormalities.

As there is a linear correlation between the perfusion and the metabolism of the brain tissue, it can be extrapolated that the hypoperfused regions of the brain, identified in our study are also the hypometabolic and hence partially explain the pathogenesis of different physiological type of CP, which cannot be explained by morphological brain imaging.

Conclusion

Use of perfusion imaging techniques helps in making the imaging in CP more sensitive and helps in describing the pathogenesis of certain disabilities which are not explained by morphological findings alone. Though SPECT and DSC MRI perfusion are equally sensitive in showing hypoperfusion, DSC MRI due to its inherent radiation safety can be performed routinely in patients with Cerebral Palsy. More so, as DSC MRI can be coupled with morphological brain imaging for which MRI is the investigation of choice. Hence, making MRI and DSC MRI as one stop shop for diagnosis and evaluation of CP.

Table 1: Correlation of spectrum of intracranial lesions seen on DSC MRI Perfusion and subtype of cerebral palsy

Type of CP Lesion	Quadriplegic n=25	Diplegic n=16	Hemiplegic n=6	Mixed n=2	Ataxic n=1	Hypotonic n=1	Extrapyramidal n=1	Total n= 52
Hypo-perfusion	24(96%)	15(93.8%)	6(100%)	2(100%)	1(100%)	1(100%)	0(0%)	49 (94.2%)
Frontal	20(80%)	12(75%)	5(83.3%)	2(100%)	1(100%)	1(100%)	0(0%)	41 (78.8%)
Parietal	20(80%)	9(66.2%)	6(100%)	2(100%)	1(100%)	1(100%)	0(0%)	39 (75%)
Temporal	17(68%)	8(50%)	5(83.3%)	1(50%)	1(100%)	1(100%)	0(0%)	33(63.5%)
Occipital	7(28%)	1(6.2%)	2(33.3%)	0(0%)	0(0%)	1(100%)	0(0%)	11 (21.2%)
Basal Ganglia	12(48%)	3(18.8%)	1(16.7%)	2(100%)	0(0%)	0(0%)	0(0%)	18 (34.6%)
Thalamus	07(28.0%)	07(43.8%)	1(16.7%)	1(50%)	0(0%)	0 (0%)	0(0%)	16 (30.8%)
Cerebellum	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0 (0%)	0(0%)	0 (0%)

Abbreviations: CP, cerebral palsy; DSC MRI : T2* Dynamic Susceptibility Contrast Enhanced MRI

Table 2: Correlation of spectrum of intracranial lesions seen on SPECT and subtype of cerebral palsy

Type of CP Lesion	Quadriplegic n=27	Diplegic n=16	Hemiplegic n=6	Mixed n=2	Ataxic n=1	Hypotonic n=1	Extrapyramidal n=1	Total n= 54
Hypo-perfusion	27(100%)	14(87.5%)	6(100%)	2(100%)	1(100%)	1(100%)	1(100%)	52 (96.3%)
Frontal	25(92.7%)	10(62.5%)	5(83.3%)	2(100%)	1(100%)	1(100%)	0(0%)	44 (81.5%)
Parietal	18(66.7%)	8(50%)	6(100%)	0(0%)	0(0%)	1(100%)	1(100%)	34 (62.9%)
Temporal	21(77.8%)	9(56.3%)	4(66.7%)	2(100%)	1(100%)	1(100%)	1(100%)	39(72.2%)
Occipital	8(18.2%)	3(18.75%)	2(33.3%)	0(0%)	0(0%)	1(100%)	0(0%)	14 (25.9%)
Basal Ganglia	10(29.6%)	3(18.75%)	1(16.7%)	1(50%)	0(0%)	1(100%)	0(0%)	16 (29.6%)
Thalamus	7(25.9%)	4(25%)	1(16.7%)	0(0%)	0(0%)	0 (0%)	0(0%)	12 (22.2%)
Cerebellum	1(3.7%)	1(6.25%)	0(0%)	0(0%)	0(0%)	0 (0%)	0(0%)	02 (3.7%)

Abbreviations: CP, cerebral palsy; SPECT : Single-photon emission computed tomography

Table 3 : Correlation between SPECT and DSC MRI Perfusion findings in all CP patients

	Hypoperfusion	Agreement	Kappa Value	P value
1	Total	49/52	0.371	0.006
2	Frontal	45/52	0.698	<0.001

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3	Parietal	39/52	0.618	<0.001
4	Temporal	44/52	0.755	<0.001
5	Occipital	48/52	0.805	<0.001
6	Basal Ganglia	43/52	0.702	<0.001
7	Thalamus	44/52	0.612	<0.001
8	Cerebellum	50/52	NA	NA

Abbreviations: CP, cerebral palsy; SPECT : Single-photon emission computed tomography; DSC MRI : T2* Dynamic Susceptibility Contrast Enhanced MRI

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