Dynamic Contrast Enhanced (DCE) Perfusion Indices as a Measure of Blood Brain Barrier (BBB) Disruption in Different Stages of Neurocysticercosis

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Introduction

Neurocysticercosis (NCC) is a parasitic infection, caused by establishment of cysticercus larva of Taenia solium in the central nervous system of its host (man or pig). Single cyst is found in 20-53% of cases, while when multiple, few cisticerci are usually found. The signs and symptoms depend upon the number, topology and stage of the cyst as well as the host immune response, and include seizures, signs of elevated intracranial pressure, movement disorders and hydrocephalus. In most cases symptoms appear years after the initial invasion, either by inflammation around the parasite, mass effect, or residual perilesional scarring. Morphologically 3 stages of the NCC are recognized: 1) viable, or vesicular stage 2) colloid, or granular stage 3) fibrocalkified nodule stage. Different stages of NCC show a heterogeneous pattern on conventional MR imaging, making these difficult to be precisely classified. Earlier studies have shown contrast enhancement with or without perifocal edema in degenerating cysts. We performed dynamic contrast enhanced (DCE)-MRI in patients with different stages of the cysts to see the relationship between the perfusion indices and the degree of perifocal oedema. This is the first preliminary study describing the perfusion indices in different stages of NCC.

Materials and methods

Subjects: A total of thirty cysts from 15 patients with a definitive diagnosis of NCC on conventional MRI (scolex demonstration) were included in the study. All these were classified into group1: Cysts without post contrast enhancement and without oedema, (n=10); group2: Cysts with post contrast enhancement but without oedema (n=10); group3: Cysts with post contrast enhancement and surrounding oedema, (n=10). Informed consent was obtained before DCE-MRI.

Data acquisition: All patients underwent both conventional and DCE-MRI on a 1.5 Tesla scanner (Echo-speed plus, General Electric, Milwaukee, USA) using quadrature transmit–receive head coil. The institutional ethical as well as the research committee approved the study protocol.

MRI data processing and quantitative analysis: Voxel wise tissue $T_2^*$ was calculated from FSE $T_2$, $T_1$ and PD weighted images. Quantitative analysis of concentration time was performed for calculation of cerebral blood volume (CBV) and cerebel blood flow (CBF). Pharmacokinetic model was implemented for permeability ($K_{trans}$) and lumped constant ($K_{ep}$) calculation. Corrected CBV map was generated by removing the leakage effect of the disrupted BBB. For the calculation of perfusion indices ROIs (10mm$^3$) were drawn on the region with the highest value as defined by the CBV color-coded map on each slice. Relative quantification of CBV ($C_{CBV}$) and CBF ($rCBF$) were quantified by placing the ROI on normal contra-lateral portion of the brain.

Statistical analysis: One way analysis of variance (ANOVA), using Bonferroni multiple comparisons was performed to compare various perfusion indices among the three groups of cysts. Pearson’s correlation was performed to see the correlation between perilesional oedema volume and perfusion indices.

Results: The various perfusion indices obtained by putting regions of interest over the cysts are summarized in table1. Bonferroni multiple comparisons showed that the value of $K_{trans}$, $K_{ep}$, ve and vp was found to be higher in group2 cysts as compared to group1 and group3. Though not significant, the value of $K_{trans}$, $K_{ep}$, Ve, and vp was found to be higher in group2 cysts as compared to group1.$C_{CBV}$ and $rCBF$ was not significantly different among the three groups. A positive significant Pearson’s correlation was observed between volume and $K_{trans}$ ($r=0.98$, $p=0.001$), volume and $K_{ep}$ ($r=0.89$, $p=0.01$), volume and ve ($r=0.81$, $p=0.03$), and volume and vp ($r=0.93$, $p=0.01$).

Table 1: showing the values of perfusion indices for the three groups.

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>GROUP 1</th>
<th>GROUP 2</th>
<th>GROUP 3</th>
<th>ANOVA (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K_{trans}$</td>
<td>0.02±0.0</td>
<td>0.04±0.03</td>
<td>0.43±0.06</td>
<td>0.0</td>
</tr>
<tr>
<td>$K_{ep}$</td>
<td>0.02±0.0</td>
<td>0.14±0.01</td>
<td>0.95±0.28</td>
<td>0.0</td>
</tr>
<tr>
<td>$rCBF$</td>
<td>1.82±0.64</td>
<td>1.88±0.53</td>
<td>1.19±0.75</td>
<td>0.2</td>
</tr>
<tr>
<td>$C_{CBV}$</td>
<td>1.85±0.77</td>
<td>1.25±0.18</td>
<td>1.14±0.94</td>
<td>0.3</td>
</tr>
<tr>
<td>ve</td>
<td>0.04±0.08</td>
<td>0.46±0.13</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>vp</td>
<td>0.04±0.00</td>
<td>0.13±0.00</td>
<td>0.0</td>
<td></td>
</tr>
</tbody>
</table>

Discussion: In this study we have found significantly high value of $K_{trans}$, $K_{ep}$, ve and vp in cysts with both post contrast enhancement and perilesional oedema (group3), suggesting that these cysts pose maximum inflammatory response as compared to other groups. The positive value of $K_{trans}$, $K_{ep}$, and vp in group2 cysts indicate the opening of BBB but to a lesser extent than group3 cysts. Nil value of $K_{trans}$, $K_{ep}$, ve and vp in group1 cysts which appears to be innocuous on MRI advocates an intact BBB. We also found significant correlation between oedema volume and with $K_{trans}$, $K_{ep}$, ve and vp. Matrix metalloproteinase-9 (MMP-9) plays a key role in the disruption of the BBB and the blood–CSF barrier, which may cause brain edema and tissue damage. Vascular endothelial growth factor (VEGF) has also been implicated in the increased BBB permeability in initial phase of acute stroke while in tumors and infection it primarily governs angiogenesis. In a recent study the expression of MMP-9 is proposed as marker of BBB disruption and disease activity in BT, correlated with $K_{trans}$