Intraarterial heparin flushing effect on motor evoked potentials in chronic ischemic stroke patients

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ABSTRACT

Background: Stroke has always been a complicated disease which affects not only the patient quality of life but also the patient family. In ischemic stroke patients, one of the most complicated outcomes was the disruption of motor function. Increased motor function is a visible positive outcome of stroke patients.

Aim: This study aims to measure the motor evoked potentials values which the results might give us more insights into how this disease affects the motor neuron pathway.

Methods: This study was an experimental pre-posttest study involved 75 patients diagnosed with chronic ischemic stroke (onset of more than 30 days). The MEPs value was measured by adjusting the IAHF procedure in 2015.

Results: There was no significant difference between motor evoked potential value (amplitude, latency, central motor conduction time) pre and post intraarterial heparin procedure (IAHF) (p>0.05). Occasionally, there was a significant difference in latency value in lacunar, subcortical, and cortical-subcortical area after IAHF (p<0.05).

Conclusion: This study shows that the size and localization of the affected area might determine the results of IAHF.

Keywords: IAHF, MEPs, amplitude, latency, CMCT, ischemic stroke


INTRODUCTION

Stroke is one of the leading cause of death and disability in adults. Unfortunately, until now the treatment for stroke is still limited to the narrow time window, distance factor between medical facilities and required tools and skills that even limited to particular medical centers. The limitation leads to affect much quality of life. The narrow time window and another problem that prevent the patient from getting the appropriate treatment makes a new method of therapy is needed.

IAHF (intraarterial heparin flushing) therapy is a modified DSA procedure where continuous heparin flushing is maintained via the directed catheter into the patient brain vasculature. The usage of heparin either as a bolus or diluted with saline has been well-known in interventional radiology procedure. The safety of heparin usage has been proven which make it recommended as primary therapy in cerebral venous thrombosis case. There is a method to measure the accomplishment by MEPs (motor evoked potentials) values as well as using TMS (transcranial magnetic stimulation) technique.

In the first time, an electrical stimulation used on muscles and nerve fibers in the late 18th century by Galvani. The first practical electromagnetic stimulation device for human use was designed and built by Barker. TMS basic principles was to modulates brain electrical environment using magnetic fields, that will pass through the patient skull and scalp. These magnetic fields are produced by crossing a rapid alternating electrical current through a coil with a ferromagnetic core. TMS can be administrated in single pulses or as a brief series of pulses either for research, diagnostic, or therapeutic purposes. When it used clinically, several thousand pulses are usually applied for minutes to hours. TMS has been used as an investigation tool to investigate possible mechanisms underlying both spontaneous and therapy-induced post-stroke motor recovery. Besides, TMS basic principle was also to operate on the electrical current which directed through a hand-held copper-stimulating coil as the consequent production of a transient magnetic field. When held over the scalp, the rapidly changing magnetic field induces a small electrical current in underlying brain tissue which will produce depolarization processes of nerve cells which resulted in the stimulation or disruption of brain activity.

Central motor conduction time (CMCT) describes the conduction time from motor cortex to the spinal cord alpha-motoneurons. These include
the difference between conduction time from cortex to muscle and peripheral motor conduction time. Pathological CMCT & latency lengthening are caused by demyelination of the corticospinal fibers and degenerative or ischemic changes. CMCT measurements are worth in cerebral ischemic stroke, neurodegenerative diseases which affecting the corticospinal tract. In these disorders, CMCT may be useful in disclosing changes before clinical manifestation occurs. In term of amplitude, it describes the integrity of the corticospinal tract and normal excitability of motor cortex. It might indicate damage in motor neuron, inhibition in the corticospinal tract, and decreased corticospinal excitability.

Observed MEPs value changing during stroke incident reduced amplitude and increased CMCT. The clinical application of TMS mainly concerns testing of the functional integrity of the corticospinal tract in central nervous systems- affecting disorders. MEP results which obtained by TMS methods represents a useful early prognostic marker of motor function recovery in patients with ischemic stroke disease. TMS also can be used as a technique to evaluates the corticospinal motor pathway, thus estimates motor function. Those who have hemiparesis after acute ischemic stroke was proved to be useful as an early prognostic indicator of the motor and functional recovery.

METHODS

This study was an experimental pre and post-test study that involved 75 patients diagnosed with chronic ischemic stroke (onset more than 30 days) with motor deficit symptoms such as hemiparesis (not from another disease). They had no history of kidney failure, cardiac decompensation, malignancy, mental disorder, and seizure. In addition, they were able to understand given instruction as well as consent to become the subject of this study. The data included them who conducted the IAHF procedure in 2015. For more information, this study excluded them who allergic to contrast or heparin, had a blood coagulation disorder, kidney failure, cardiac decompensation, malignancy, not able to undergo MRI, seizure, uncooperative, and also had a motor deficit caused by another disease.

The MEPs value was measured both pre-IAHF and 4.5 hours post-IAHF procedure. MEP size measurement was performed by using TMS Neurosoft Variant 4 (Neurosoft, Ivanovo, Russia). Big ring coil was placed on vertex as well as single pulse stimulation take the time. Side B of the coil (anticlockwise) was used to stimulate left hemisphere as against side A (clockwise) to the right one. As to measure latency (ms), amplitude (mV), CMCT (ms) and RMT (% intensity) of MEP were recorded with stimulation of submaximal threshold 80% MEP at each side. The patients here was classified by infarct size and lesion area. Then, the data were analyzed using a paired T-test, or it’s alternative Wilcoxon test.

RESULTS

In general subject population, the obtained amplitude value pre and post-IAHF procedure were 0.91±1.48 and 0.83±1.31, respectively. There was no significant difference to be found (p>0.05) although the amplitude means differences was -0.07±1.00. The obtained latency value pre and post-IAHF procedure were 25.27±6.23 and 24.40±6.67, respectively. There was no significant difference to be found (p>0.05 although the latency means differences was -0.87±8.90. The obtained CMCT value pre and post-IAHF procedure were 11.61±5.59 and 11.89±6.44, respectively. There was no significant difference to be found (p>0.05) although CMCT means differences was 0.28±8.43.

As shown in Table 4, the results were categorized into three different lesion area. In the cortex area, the amplitude value pre and post-IAHF procedure were 0.70±1.60 and 0.52, respectively (p>0.05). In the subcortex area, its value pre and post-IAHF procedure were 1.04±1.53 and 0.95, respectively (p>0.05). In the cortex-subcortex area, its value was 0.18±0.13 and 0.41, respectively (p>0.05).

The Latency value in the cortical area pre and post-IAHF procedure was 27.12±10.19 and 24.18±5.78, respectively (p>0.05). In the subcortical and cortical-subcortical area, there was a significant difference (p<0.05) where the latency value in the subcortical area pre and post-IAHF procedure was 25.62±5.08 and 24.20±6.99, respectively as well as in the cortical-subcortical area was 19.50±4.23 and 26.34±5.69, respectively.

CMCT value of MEPs in the cortical area pre and post-IAHF procedure was 25.62±5.08 and 24.20±6.99, respectively as well as in the cortical-subcortical area was 19.50±4.23 and 26.34±5.69, respectively.

As shown in Table 5, the results were categorized into lesion size as lacunar and non-lacunar. The amplitude in lacunar size lesion pre and post-IAHF
was 1.07±1.62 and 1.00±1.47, respectively (p>0.05) as against in non-lacunar size lesion was 0.60±1.14 and 0.54±0.89, respectively (p>0.05). There was a significant difference found in latency value in the lacunar area as about 25.85±5.45 and 23.26±6.36, respectively, but not in the non-lacunar area as about 24.21±7.40 and 26.41±6.83, respectively (p>0.05). In CMCT value, there is also neither significant difference (p>0.05) between pre-IAHF (11.61±5.11) and post-IAHF (11.02±6.27) in the lacunar nor the non-lacunar area (11.59±6.46 and 13.43±6.54, respectively).

### Table 1 General MEPs value pre and post-IAHF procedure

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-IAHF</th>
<th>Post-IAHF</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEPs</td>
<td>Mean±SD</td>
<td>Median (Min-Max)</td>
<td>Mean±SD</td>
</tr>
<tr>
<td>Amp</td>
<td>0.91±1.48</td>
<td>0.26 (0.02-6.61)</td>
<td>0.83±1.31</td>
</tr>
<tr>
<td>Lat</td>
<td>25.27±6.23</td>
<td>23.50 (8.68-48.17)</td>
<td>24.40±6.67</td>
</tr>
<tr>
<td>CMCT</td>
<td>11.61±5.59</td>
<td>10.00 (-1.20-36.30)</td>
<td>11.89±6.44</td>
</tr>
</tbody>
</table>

* T test or Wilcoxon test p<0.05; Amp= amplitude; Lat=Latency; CMCT= Central motor conduction time

### Table 2 MEPs mean differences

<table>
<thead>
<tr>
<th>Variable</th>
<th>MEPS</th>
<th>Mean±SD</th>
<th>Median (Min-Max)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔAmp</td>
<td>-0.07±1.00</td>
<td>-0.14 (-4.76-3.95)</td>
<td>0.534</td>
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</tr>
<tr>
<td>ΔLat</td>
<td>-0.87±8.90</td>
<td>-0.7 (-28.27-28.82)</td>
<td>0.402</td>
<td></td>
</tr>
<tr>
<td>ΔCMCT</td>
<td>0.28±8.43</td>
<td>-0.18 (-26.95-26.50)</td>
<td>0.771</td>
<td></td>
</tr>
</tbody>
</table>

* T-test. Significant if p<0.05; Amp= amplitude; Lat=Latency; CMCT= Central motor conduction time

### Table 3 MEPs value based on lesion area

<table>
<thead>
<tr>
<th>MEPs</th>
<th>Lesion Area</th>
<th>Pre-IAHF</th>
<th>Post-IAHF</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Median (Min-Max)</td>
<td>Mean±SD</td>
<td>Median (Min-Max)</td>
</tr>
<tr>
<td>Amp</td>
<td>Cortex (n=11)</td>
<td>0.70±1.60</td>
<td>0.12 (0.05-5.43)</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td>Sub (n=57)</td>
<td>1.04±1.53</td>
<td>0.34 (0.02-6.61)</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>Cortex-Sub (n=7)</td>
<td>0.18±0.13</td>
<td>0.14 (0.4-0.36)</td>
<td>0.41</td>
</tr>
<tr>
<td>Lat</td>
<td>Cortex (n=11)</td>
<td>27.12±10.19</td>
<td>23.60 (8.68-48.17)</td>
<td>24.18±5.78</td>
</tr>
<tr>
<td></td>
<td>Sub (n=57)</td>
<td>25.62±5.08</td>
<td>24.20 (16.50-41.30)</td>
<td>24.20±6.99</td>
</tr>
<tr>
<td></td>
<td>Cortex-Sub (n=7)</td>
<td>19.50±4.23</td>
<td>20.50 (12.00-23.50)</td>
<td>26.34±5.69</td>
</tr>
<tr>
<td>CMCT</td>
<td>Cortex (n=11)</td>
<td>14.19±9.92</td>
<td>11.90 (1.20-36.30)</td>
<td>11.92±4.99</td>
</tr>
<tr>
<td></td>
<td>Sub (n=57)</td>
<td>11.41±4.39</td>
<td>10.00 (5.02-25.00)</td>
<td>11.81±6.61</td>
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<tr>
<td></td>
<td>Cortex-Sub (n=7)</td>
<td>9.15±4.66</td>
<td>8.90 (7.2-16.40)</td>
<td>12.52±7.83</td>
</tr>
</tbody>
</table>

*Wilcoxon test p<0.05; Amp= amplitude; Lat=Latency; CMCT= Central motor conduction time.
DISCUSSION

Using MEP values in patients who suffered from a stroke to obtain prognostic value in motor recovery is not a new approach. Several studies have shown this method as a measurement to predict the functional status of extremities in a patient who suffered from stroke. In the general population, there was no significant difference in MEP values post-IAHF procedure, but there were some significant differences in latency when the results were categorized into both lesion area and lesion size. There was a decreased value of CMCT in the cortical and lacunar area which possibly showed a restoration process in neuron fibers. The amplitude measurement in this study entirely differed from the previous research in 2015. The previous one used an amplitude ratio (amplitude of affected side and amplitude of unaffected site) rather than an amplitude value only (on the affected side). An increase of amplitude ratio coincided with increased MRC scale grade. On the other hand, in this study, a decreased but not significant value of amplitude was recorded in almost category except in cortex-subcortex area. This difference can be input to future research to prefer using amplitude ratio rather than the amplitude value only. The amplitude ratio is stronger to the difference in cortical excitability in the bilateral hemispheres which represents the degree of corticospinal connectivity.

MEP variability even a motor improvement was achieved post-IAHF which might show another alternative mechanism that has a role in the progression of corticospinal tract conduction post-IAHF procedure. Normalized corticospinal conduction in a stroke patient with motor recovery might have been mediated via improved conduction pathway through the lesion. These findings of conduction impairment in the corticospinal pathway in patients which gained normal motor function suggest that alternative mechanism such as cortical reorganization and increased activity of secondary motor areas and nonpyramidal tracts might contribute to the motor recovery. Other theories like plastic reorganization can be described into these three major mechanisms: “unmasking of existing but functionally inactive pathways, sprouting of fibers from surviving neurons and formation of new synapses, and redundancy of CNS circuitry allowing alternative paths to take over functions.”

CONCLUSION

In general population, there is no significant difference in MEP values post-IAHF procedure on chronic ischemic stroke patients, but it shows significant changes especially in latency value which found in the lacunar area and also in the subcortical and cortical-subcortical area of stroke lesions.

LIMITATIONS

There is only a short period of measurement (4.5 hours) after the procedure, and the possibility of ratio measurement is better than a single value alone. In the future, the author expects that there will be more study performed with more prolonged measurement time.

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