INTRODUCTION

Stroke is in the 2nd position as a non-communicable disease that causes death. Based on RISKESDAS 2018, national prevalence of stroke in Indonesia was 10.9 per milli(2). Standardized therapy is thrombolytic therapy(5). Study showed that first generation thrombolytic drugs are not effective to treat patients with ischemic stroke(6). Necroptosis is programmed necrosis, caspase-independent cell death in stroke characterized by organel swelling and rupture of cell membrane mediated by death signal pathway (7). Oxidative stress plays an important role in the pathology of neuronal cell death after ischemic stroke. Green tea is one of the most consumed beverages in the world with its major component EGCG (14)(15). EGCG used as antioxidant will target reduction of ROS and increasing antioxidant enzyme during necroptosis (16). Early therapy of 0.5% green tea extract in 3 weeks will produce inhibition effects towards brain ischemia processes such as peroxidation lipid, level of DNA oxidative damage, neuronal cell death, and infarct in the brain (17). This study aims to prove that Green tea with its active compound EGCG can decrease neuronal cell death morphology.

METHODS

ANIMAL: This study used Rattus norvegicus middle cerebral artery occlusion (MCAO) model treated with green tea and. The sample of this study was healthy male Rattus norvegicus MCAO model (200-275 g) that met the criteria. Before made to MCAO model, male rat adjusted to the new environment for 7 days. MCAO model made by modification method using bulldog clamp to occlude cerebral media artery for 180 minutes.

INTERVENTION: The sample divided into 3 group (control groups, EGCG 30 mg/kgBW/day, and green tea extract “Meditea” 30 mg/kgBW/day). In one group contained 11 rat. Green tea treatment done once a day for 7 days. After being made to the brain tissue was taken from the motoric cortex and made for histopathological examination stained by Hematoxylin eosin. Proportion of necroptosis morphology examined and classified based on D.C Allred M.D guideline of scoring, proportion classified in score 0-5(18).

ANALYSIS: Analysis done by descriptive analysis and normality test for each group. If distribution is abnormal, Kruskal Wallis followed by Mann Whitney test to distinguish EGCG effect towards neuronal cell necroptosis morphology. Lastly, we perform Spearman correlation test, to find out correlation between variables.

RESULT

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ± SEM</th>
<th>n</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sham</td>
<td>0.44 ± 0.527</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1.80 ± 0.422</td>
<td>10</td>
<td>0.00*</td>
</tr>
<tr>
<td>EGCG 30 mg/kgBW</td>
<td>1.10 ± 0.316</td>
<td>12</td>
<td>0.010**</td>
</tr>
<tr>
<td>Green tea extract</td>
<td>1.30 ± 0.483</td>
<td>11</td>
<td>0.018**</td>
</tr>
<tr>
<td>“Meditea” 30 mg/kgBW</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

There is no significant difference in EGCG group compared to Green tea extract group (p>0,05). There is significant correlation between neuron cell necroptosis morphology and both EGCG and Green tea extract (p<0.05). Correlation is negative which mean, an EGCG/ Green tea extract will decrease neuron cell necrosis morphology.

DISCUSSION

EGCG will inhibit ROS produced by this mechanism below during necroptosis pathway:
1. Prevent mitochondrial damage furthermore stimulates RIP1 and RIP3 oxidation and autophosphorylation towards necroptosis pathway(113).
2. Inhibit positive feedback of ROS that will increase production of necrosome in necroptosis(25)
3. Activate caspase 3 and 8 after 8 hours of green tea therapy(26)(27)
4. EGCG inhibit synthesis of some inflammatory mediators : TNF-α, IL-6 and IL-8(28)(29)
5. EGCG able to decrease expression of TNFR1 and RIP3(30)

Our study match with the theory above, because the result shows that there is reduction in neuronal cell death necroptosis morphology during histopathological examination. Both administration of EGCG 30mg/kgBW and “Meditea” green tea extract 30 mg/kgBW shows reduction in neuronal cell necroptosis morphology. If we compared between control group and both EGCG and green tea extract group, there is significant difference between control-EGCG and control-green tea extract.

CONCLUSION

In conclusion, Camellia sinensis (green tea) with its active compound EGCG significantly correlated with decrease of neuronal Necroptosis morphology in Rattus norvegicus MCAO models.

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