JAPANESE GREEN TEA DIET ATTENUATES MOTOR DYSFUNCTION AND NEUROPATHOLOGICAL LESIONS IN WOBLER MOUSE MOTOR NEURON DISEASE

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Abstract
Background: Japanese green tea (JGT) contains catechins, serine and multi-vitamins A, B1, B2, B3, C, E, β-carotene, forale. These substances are reported to have antioxidative and neuroprotective effects on motoneurons.

Objective: The purpose of this study is to evaluate whether JGT diet can retard progression of motor symptoms and spinal cord lesions in wobbler mouse motoneuron degeneration.

Methods: Wobbler mice fed regular food or five kinds of food mixed with 2.0% JGT (2.0 g/kg/day), 0.36% catechins, 0.028% theanin, 0.054% caffeine or combination of catechins, theanin, caffeine. The concentration of catechins, theanin and caffeine corresponds to 2.0% JGT. Diet therapy (n=15/group) started from disease onset at 3-4 weeks of age, and continued for 4 weeks. Motor function of the forelimbs was assessed weekly for 4 weeks (n=10/group). Neuropathologic changes of spinal motoneurons and astrocytes were compared statistically among six groups (n=5/group) after 4 weeks treatment.

Results: JGT-feeding mice maintained forelimb motor function more than 4 weeks (p< 0.01). In other 5 groups, deformity and muscle weakness of the forelimbs were abolished at 3-5 weeks post-treatment. Body weight was increased significantly in the JGT group compared to other five groups. JGT diet suppressed denervation muscle atrophy in the biceps muscle (p< 0.01) and inhibited motoneuron degeneration and astrocytic proliferation in the 5th and 6th cervical cord (p< 0.01).

Conclusion: The data indicated that 2.0% JGT diet delayed motor deficits and neuropathological changes in wobbler mice. JGT diet may assist to keep motor function in amyotrophic lateral sclerosis patients.
Japanese green tea (JGT) containing components

Catechins (polyphenol): 10%
EC, ECg, EGC,
EGCG (Epigallocatecatechin gallate)
Free amino acids: 2.5%
theanin, arginine, aspartate, glutamate, serine
Vitamins: A, B1, B2, Nicotinate, C, E
Mineral: Ca, P, Mg, Mn, Fe, Al, Cu, Zn
Caffeine: 2.2%
Tannin: 13.3%
Treatment: 6 groups

1. Oral chaw in 2.0% JGT = 2.0 g/kg/day, (n=15)
2. Oral chaw in 0.36% catechins (n=15)
3. Oral chaw in 0.028% theanin (n=15)
4. Oral chaw in 0.054% caffeine (n=15)
5. Oral chaw mixed with catechins, theanin and caffeine (n=15)
6. Regular food: vehicle (n=15)

Each dose of catechins, theanin and caffeine corresponds to 2.0% JGT

Study duration: 4 weeks

4 weeks after disease onset at age 3-4 weeks
Therapeutic evaluation

1. Symptomatic evaluation weekly (n=10/group)
   - Forelimb deformity
   - Pull strength of forelimbs

2. Neuropathologic evaluation (n=5/group)
   - Biceps muscle weight
   - Biceps muscle morphometry
   - Motoneuron counting in the C5-6 cord
   - Astrocyte density in the C5-6 cord
Forelimb Deformity Scale

Grade 1: paw atrophy
Grade 2: curled digits
Grade 3: curled wrists
Grade 4: J-shaped forelimb flexion to chest

JGT-feeding mice delayed muscle contracture in the forelimbs.

p < 0.01
Pull strength of forelimbs

Vehicle
Green Tea (2.0 %)
Catechin (0.36 %)
Theanin (0.028 %)
Caffein (0.054 %)
3 Mixture

JGT-feeding mice kept pull-strength of forelimbs.

\( p < 0.01 \)
Biceps Muscle Weight & Histology

JGT-feeding mice suppressed denervation muscle atrophy in the biceps muscle.
Number of spinal motoneurons

JGT-feeding mice attenuated degeneration of spinal motoneurons compared to vehicle.
Proliferation of astrocytes

JGT-feeding mice suppressed astrocyte proliferation.

GFAP staining

JGT-feeding mice suppressed astrocyte proliferation.
Experimental summary

- JGT-feeding wobbler mice maintained motor function and suppressed denervation muscle atrophy in the forelimb muscle.
- 2% JGT diet inhibited motoneuron degeneration and astrocytic proliferation in the cervical cord.
Protective effects of green tea in neurodegenerative diseases

1. Motoneuron disease model
Epigallocatechin gallate prevents oxidative-stress-induced death of Mutant Cu/Zn-superoxide dismutase (G93A) motoneuron cells by alteration of cell survival and death.

2. Parkinson's disease model
Green tea polyphenol (-)-epigallocatechin-3-gallate prevents N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced dopaminergic neurodegeneration.
Conclusion

1. The present study indicated that 2.0 % JGT diet protected skeletal muscles and spinal motoneurons in wobbler mouse neuromuscular disease.

2. Food administration of catechins, theanin, caffeine or three mixture does not have beneficial effects.

3. JGT includes various anti-oxidant and neuroprotective components.

4. Those combined effects could contribute to a therapeutic potential for human motoneuron disease.