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Case Report

A Case Study on the Use of Megestrol Acetate and Korean Medical Treatment for the Loss of Appetite and Weight Loss in Patients with Amyotrophic Lateral Sclerosis(ALS)※

Ho Hyun Jeong[1], Sang Mi Lee[1], Jong Chul Lee[1], Man Yong Park[1], Dong Woung Kim[2], Bong Keun Song[2] and Sung Chul Kim[1,*]

[1]Department of Acupuncture & Moxibustion Medicine, Gwang-Ju Oriental Medical Hospital, Wonkwang University

[2]Department of Internal Medicine, Gwang-Ju Oriental Medical Hospital, Wonkwang University

[Abstract]

Objectives : Weight loss and loss of appetite in amyotrophic lateral sclerosis patients are common symptoms, these are associated with survival as well as nutritional condition. The changes in weight and appetite were reported after treatment using Megestrol acetate and Korean medical treatments.

Methods : Amyotrophic lateral sclerosis patient with weight loss and loss of appetite were treated by administering megestrol acetate a known anti-malignant tumor agent and Korean medical treatments such as acupuncture, pharmacopuncture and herbal medicine. The changes in weight and appetite were checked using body mass index(BMI) and simplified nutritional appetite questionnaire(SNAQ).

Results : There was a more than 17 kg increase in weight. BMI increased from 15.94 kg/㎡ to 21.97 kg/㎡ and SNAQ score increased from 7 to 16. Owing to several side effects, Megestrol acetate was stopped after which only Korean medical treatments were provided. After which the lasting effects in BMI and appetite could be seen.

Conclusion : There are few studies on weight loss and loss of appetite in ALS patients. Using only megestrol acetate can cause several considerable side effects. Which respect to this, the findings in this study could open up new clinical guideline possibilities.

Key words :
Amyotrophic lateral sclerosis(ALS);
Weight loss;
Anorexia;
Oriental medical treatment;
Megestrol acetate

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* Corresponding author : Department of Acupuncture & Moxibustion Medicine, Gwang-Ju Oriental Medical Hospital, Wonkwang University, 1140-23, Hoejae-ro, Nam-gu, Gwangju, 503-832, Republic of Korea
Tel : +82-62-670-6441 E-mail : kkscndl@hanmail.net

Ⅰ. Introduction

Amyotrophic Lateral Sclerosis (ALS) is a progressive and fatal neurodegenerative disorder involving primarily the motor neurons in the cerebral cortex, brainstem and spinal cord. Within 2~4 years, it causes progressive and severe muscle weakness, eventually causing death due to respiratory muscle palsy[1]. During the course of the disease prevalence of malnutrition varies between 16 and 55 % in ALS patients. These patients suffer from clinically severe weight loss[2]. Nutritional status is known as a prognostic factor for survival in ALS patients. A body mass index(BMI) below 18.5 kg/㎡ caused by weight loss results in a 7.7 times higher mortality rate, compared to patients with normal weight[3]. The causes of weight loss in ALS patients are various but are likely to include hypermetabolism, malnutrition, cachexia and loss of appetite[4,5]. Loss of appetite is a multifactorial syndrome resulting from a lot of symptoms such as depression, psychological distress, constipation and changes in controlling eating behavior etc[6,7].

Until now, treatment for ALS has been actively discussed and studied, but a certain cure has not presented as yet. Current treatment is primarily supportive. Drug therapy with Riluzole known as a glutamate release inhibitor extends survival by two-to-three months[8]. Several treatments such as BTx therapy, radiotherapy and anti-cholinergic drug therapy have effects on sialorrhea in ALS patients[9] also Non invasive positive pressure ventilation(NIPPV) helps ALS patients with dyspnea[10]. However most of the existing treatments have not focused on weight loss in ALS patients.

Domestic studies on ALS patients have been conducted by Park et al[11], Ryu et al[12], Kwon[13] etc, but studies on ALS patients with weight loss or loss of appetite are inadequate. Especially, since there have been no studies so far using Korean medical treatments such as acupuncture, pharmacopuncture, herbal medicine treatments.

We administered *Apetrol Oral Suspension* a known anti-malignant tumor agent with Korean medical treatments to an ALS patient who has weight loss and loss of appetite from 18th September 2011 to 17th August 2012. The changes that appeared in weight and appetite during this period were reported.

Ⅱ. Case study

1. Patient

Kim ○○, Man, 53 years
(Height : 168 cm, Weight : 65 kg)

2. Symptoms

Both limb weakness, dyspnea, anorexia, fasciculation(both limb)

3. Onset

2009. 7

4. Past medical history

Lt 2nd finger skin graft operation

5. Family history

N/S

6. Present medication

Xanax Tab. 0.25 mg 3 T #3, Rilutek Tab. 50 mg 1 T #1, Zolpidem Tartrate 6.25 mg 1 T #1, Beecom Tab. 2 T #2, Oropherol soft Cap. 100 mg 2 T #2, Decaquinon Cap. 2 T #2, Mago Cap. 500 mg 2 T #2, Lexapro Tab. 10 mg 1 T #2, Pranol Tab. 40 mg 1 T #2, Legalon Cap. 140 2 T #2

7. Present history

ⓐ 2009. 7 : Rt foot weakness onset. Seoul University Hospital. EMG etc. 'Motor neuron disease' diagnosed. Received medication treatment (for 1 year)

ⓑ 2010. 8 : Hanyang University Hospital. Several test. 'ALS' diagnosed.

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ⓒ 2010. 12 : Jeil Hanbang Hospital. Admission treatment(for 1M).
ⓓ 2011. 4 : Hanyang University Hospital. Received medication, injection treatment(1 time/month)
ⓔ 2011. 9. 18 : Gwang-Ju Oriental Medical Hospital, Wonkwang University admission(by wheel chair).

8. Examination views

ⓐ EKG : normal
ⓑ LAB : PLT 113.0 L, Lym % 23.2 L, PCT 0.1 L, Glucose 189.0 H, TIBC 237.0 L, UA Glucose 500, Transferrin 199 L
ⓒ Motor grade : shoulder 5-/5-, elbow 5-/5-, wrist 5-/5-, finger 5-/5-, hip 4/4, knee 5-/5-, ankle 3-/3-, 1st toe 3-/3-
ⓓ Neurological examination
Mental state : alert
Pupil reflex : 2+/2+
Knee jerk reflex : →→
Biceps reflex : →→
Babinksi sign : -/-

9. Korean medical diagnosis

Wei symptom(痿證)

10. Treatment method

1) Apetrol oral suspension

Apetrol oral zuspension manufactured by LG life science Ltd. was used from 2011. 10. 20 to 2012. 8. 17 except 2011. 12. 23~2013. 1. 16, 2012. 2. 20~2012. 3. 14, when *Apetrol oral suspension* (10 mg) was administered to the patient 30 minutes after eating breakfast.

2) Acupuncture & pharmacopuncture

① Monday, Wednesday, Friday

ⓐ 2011. 9. 18~2012. 1. 15

Sa-am acupuncture liver tonification(陰谷KI_1 · 谷泉LR_8 · 經渠LU_8 · 中封LR_4) was conducted on both sides by single-use 0.25×40 mm needles(DongBang acupuncture Inc, Korea). The KI_1 and LR_8 acupoint needles were electrically charged at 2 Hz and also stimulated using infra red rays for 15 minutes.

0.1 cc of Scolopendrid pharmacopuncture(Korean pharmacopuncture institute) was injected equally at acupoints of *Hagwan*(ST_7) · *Jichang*(ST_6) · *Cheondol* (CV_{22}) · *Daechu*GV_{14}) · *Amun*(GV_{15}) · *Pungbu*(GV_{16}) · *Gyeonjeong*(GB_{21}).

After checking for allergic reactions using a skin test, 0.1 cc of bee-venom pharmacopuncture(Korean pharmacopuncture institute) was administered equally on the acupoints of *Joksamni*(ST_{36}) · *Susamni*(LI_{10}) · *Hapgok*(LI_4) · *Guheo*(GB_{40}) · *Pungsi*(GB_{31}).

ⓑ 2012. 1 . 16~8. 17

In existing acupuncture and pahrmacopuncture treatment, scolopendrid and bee-venom pharmaco-puncture were changed to hominis placenta pharm-acopuncture. 0.2 cc of Hominis placenta pharmaco-puncture(Korean pharmacopuncture institute) was injected equally at acupoints of *Sinsu*(BL_{23}) · *Jangmun*(LR_{13}) · *Amun*(GV_{15}).

② Tuesday, Thursday, Saturday

Scalp acupuncture in the motor area was conducted by single-use 0.3×40 mm needles(DongBang acu-puncture Inc, Korea) for 15 minutes.

0.2 cc of hominis placenta pharmacopuncture(Korean pharmacopuncture institute) was injected equally at acupoints of *Sinsu*(BL_{23}) · *Jangmun*(LR_{13}) · *Amun*(GV_{15}).

Additionally, every Tuesday or Thursday, 5~10 cc of Hominis placenta pharmacopuncture was injected at several acupoints of *Dongmaek* meridian.

3) Herbal medicine

ⓐ 2011. 9. 23~2011. 10. 3 : *Jihwangeumja* decoction (地黃陰子) was administered 30 minutes after eating meals three times a day.
ⓑ 2011. 12. 14~2011. 12. 22 : *Okong* decoction(蜈蚣湯) was administered 30 minutes after eating meals three times a day.
ⓒ 2011. 12. 23~2012. 6. 10 : *Okonggami* decoction (蜈蚣湯加味) was administered 30 minutes after eating meals three times a day.
ⓓ 2012. 6. 11~6. 22 : *Ogapi* decoction(五加皮湯) was administered in the same way.

Table 1. Herbal Medicine Treatment

Date	Herbal medicine
2011. 9. 23~10.3	*Jihwangumja Decoction*(based on *Donguibogam*)
2011.12. 14~22	*Scolopendra* 8 g, *Radix ginseng* 4 g, *Fructus schisandrae* 6 g, *Chaenomeles sinensis Koebhne* 8 g, *Fructus crataegi* 4 g, *Fructus amomi rotundus* 4 g, *Fructus amomi xanthioidis* 4 g, *Radix platycodi 8* g, *Radix glycyrrhizae* 8 g, *Broiled Radix aconiti lateralis preparata 2* g(3 times/d)
2011. 12. 23~ 2012. 1. 24	*Scolopendra 10* g, *Radix ginseng* 4 g, *Fructus crataegi* 4 g, *Fructus amomi rotundus* 4 g, *Fructus amomi xanthioidis* 4 g, *Radix platycodi* 6 g, *Radix glycyrrhizae 10* g, *Broiled Radix aconiti lateralis preparata 6* g, *Cortex magnoliae officinalis* 4 g, *Radix puerariae* 10 g, *Semen glycine* 10 g, *Fructus schisandrae* 6 g(3 times/d)
2012. 1. 25~6. 10	*Scolopendra* 8 g, *Radix ginseng* 4 g, *Fructus crataegi* 4 g, *Fructus amomi rotundus* 4 g, *Fructus amomi xanthioidis* 4 g, *Radix platycodi* 6 g, *Radix glycyrrhizae* 8 g, *Broiled Radix aconiti lateralis preparata 2* g, *Cortex magnoliae officinalis* 4 g, *Radix puerariae* 10 g, *Semen glycine* 10 g, *Fructus schisandrae* 6 g, *Batryticatus bombycis* 2 g, *Holotrichia* 2 g, *Herba cirsii* 4 g, *Arillus longan* 4 g, *Semen raphani* 4 g(3 times/d)
2012. 6. 11~22	*Cortex acanthopanacis* 12 g, *Semen raphani* 8 g, *Herba cirsii* 10 g, *Cortex cinnamomi* 6 g, *Fructus hordei germinatus* 6 g, *Fructus amomi rotundus* 10 g, *Semen benincasae* 6 g, *Radix ginseng* 4 g, *Fructus chaenomelis* 10 g, *Thallus laminariae* 4 g, *Fructus ziziphi jujubae* 4 g, *Rhizoma zingiberis recens* 4 g(3 times/d)
Whenever patient complains of costipation	*Mazain Powder, Lubirax*(*Plantago ovata* 2,168 mg, *Senna alexandrina* 496 mg)(2 times/d)

Whenever the patient complained of constipation, '*Mazain* powder(麻子仁散)' or '*Lubirax*' were administered three times a day(Table 1).

11. Assessment & Result

The primary outcome was change of weight and BMI. Weight and BMI were checked on the 1st at every month(Table 2, Fig. 1).

Secondary outcome was a change of appetite assessed by Simplified nutritional appetite questionnaire(SNAQ). The patient was asked to complete the SNAQ, which is a 4-item single-domain questionnaire. The responses are scored by using a 5-point(A to E), verbally labeled, Likert-type scale. The total SNAQ score is the sum of scores on the 4 items, with lower scores indicating deterioration in appetite. Possible scores range from 4(worst) to 20(best)(Fig. 2).

Table 2. Weight and BMI Change

Date	Weight(kg)	BMI(kg/㎡)
2011. 5	45	15.94
2011. 6	45	15.94
2011. 7	44	15.59
2011. 8	45	15.94
2011. 9	45	15.94
2011. 10	48.5	17.18
2011. 11	53.1	18.81
2011. 12	53.5	18.96
2012. 1	56.1	19.88
2012. 2	56.4	19.88
2012. 3	56.8	20.12
2012. 4	56.6	20.05
2012. 5	57.5	20.37
2012. 6	60.0	21.26
2012. 7	60.0	21.26
2012. 8	62.0	21.97

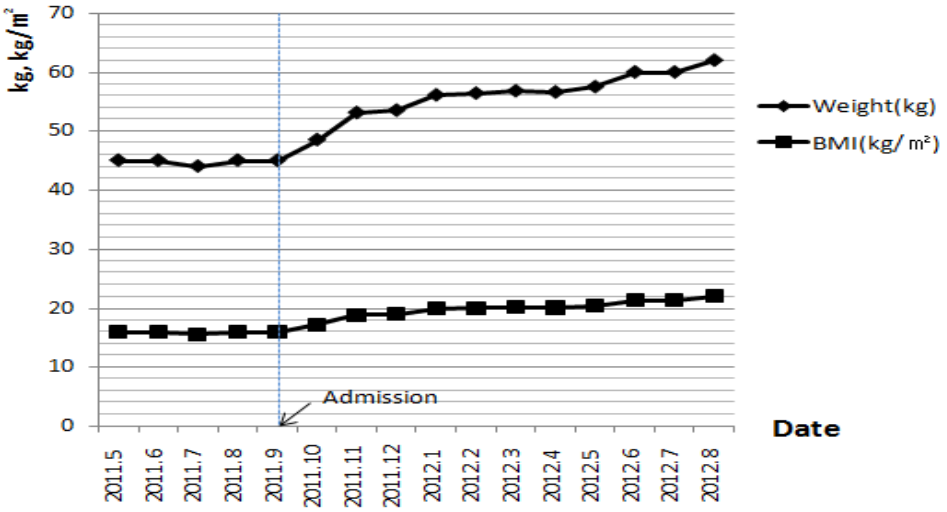

Fig. 1. Change of weight and BMI

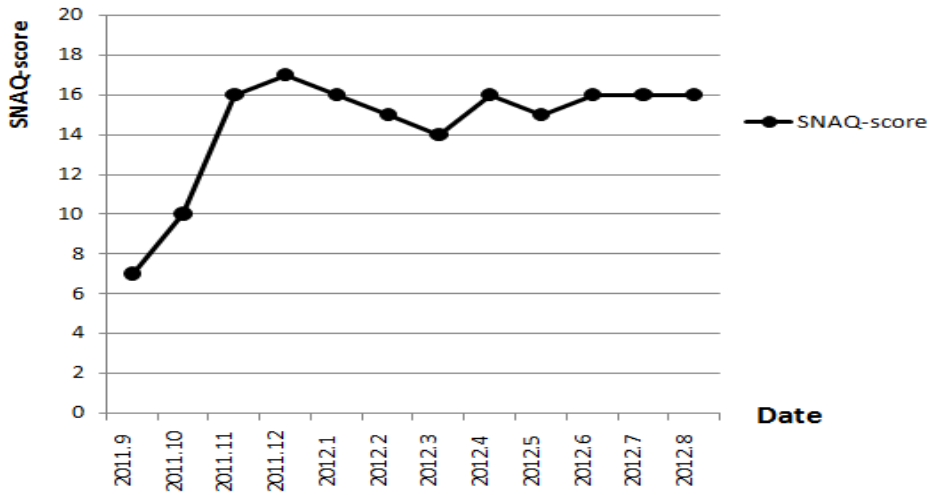

Fig. 2. Change of SNAQ score

Ⅲ. Discussion

ALS is classified as either bulbar-onset, characterized by progressive dysphagia and dysarthria or spinal-onset, characterized by peripheral neurologic features (muscle atrophy, cramps, and fasciculations) and a pyramidal syndrome(spasticity)[14]. The common disease course is characterized by progressive irreversible muscle wasting of the limbs, torso, abdomen, oro-pharyngeal and respiratory muscle regions[15]. The worldwide prevalence of ALS is reported to range between 0.4 and 2.6 / 100,000 individuals per year[16]. There is no difference between race, geography and socioeconomics[17].

During the course of ALS there is often a decline in weight that is frequently inadequately addressed in clinical practice, even though it is a significant and independent prognostic factor in survival[3]. So far, most studies on ALS have not focused on weight loss or loss of appetite in patients, but have focused on other symptoms such as muscle atrophy and spasticity, dysarthria, dysphagia, respiratory problems and sialorrhea etc. Weight loss occurs due to not yet fully understood disease-specific reasons. Several hypotheses suggest that causes of weight loss in ALS include not only dysphagia, but also higher waste of energy because of muscle fasciculations, increasing

respiratory efforts, hypermetabolism1[8], and constipation that results from the weakness of abdominal and pelvic muscles, compounded by limited physical exercise, certain medical treatments, and a diet lacking in fiber also contribute to appetite loss. Psychological distress cause also development of anorexia [7,19]. Weight loss and a lower body-mass-index (BMI) have a bad effect on survival in ALS[4].

Megestrol acetate is used for the anorexia of malignant tumor, AIDS or cachexia in mono and combination therapy. Several investigators have reported on the appetite enhancing property of *Megestrol acetate* and its possible use in cachexia. However the precise mechanism by which *Megestrol acetate* produces effects in anorexia and cachexia is unknown at the present time[20]. Taking advantage of these facts, it is used for treating weight loss in ALS patient, but on the other hand, it cannot be used consistently and in quantity because of its side effects. It is known that the side effects of *Megestrol acetate* include digestive system disorder, impotence, insomnia and urinary frequency. Actually, during the admission period *Megestrol acetate* was stopped because the patient complained of insomnia, urinary frequency and abdominal distention. Thus, *Megestrol acetate* should be used carefully and other alternative treatments should be found.

ALS belongs to the category of *Wei* symptom(痿證) in korean medicine. The five types of *Wei* symptom were described as "Wei symptoms include five types (痿證有五色). Heat in the lung dries lung parenchyma and leads to *Wei Pi*(肺熱葉焦者爲痿躄). Heat in the heart dries heart qi and leads to *Mai Wei*(心熱氣燥者爲脈痿). Heat in the liver leads to *Jin Wei*(肝氣熱者爲筋痿). Heat in the spleen leads to *Rou Wei*(脾氣熱者爲肉痿). Heat in the kidney leads to *Gu Wei*(腎氣熱者爲骨痿)." in ≪圖解校勘舍岩道人鍼法 · 痿證門≫[21]. We judged that the above ALS patient with weight loss was similar to type of 筋痿. Based on this, the *Sa-am* acupuncture liver tonification treatment(陰谷 · 谷泉 補, 經渠 · 中封 瀉) was selected to treat 筋痿.

Pharmacopuncture such as scolopendrid, bee-venom, hominis placenta pharmacopuncture were used for enhancing immunity, strength and treating muscle weakness and pain caused by joint contracture. It is known that treatment with bee-venom may be helpful in reducing glutamatergic cell toxicity in neurodegenerative diseases[22]. Also, it is known that hominis placenta could be a potential therapeutic agent of neurodegenerative diseases which accompanied with microglial activation[23].

In the early stages of this study, *Jihwangeumja* decoction was administered. It is known that it has high suppressive effect of weight loss in diabetic mice[24]. Scolopendrid has the effect of enhancing immunity, which could help stamina of patient[25]. Taking advantage of the nature of Scolopendrid, we make use of Okong decoction for treating ALS patient.

SNAQ, the first appetite-monitoring instrument, specifically validated for use amongst older adults in the United States, has been shown to identify persons at risk of significant weight loss. It is known that SNAQ scores 〈14 may identify people with anorexia at risk of significant weight loss[26].

In this case study, there appeared to be an increase in weight and appetite after using *Megestrol acetate* and Korean medical treatment. There was a more than 17 kg increase in weight and twice more than increase in appetite in this case.

Before admission, the weight of the patient had not considerably changed for 3 months. It had been maintained between 44 kg(BMI 15.59 kg/㎡) and 45 kg (BMI 15.94 kg/㎡). In the early stages of the study, although the patient received only Korean medical treatment, both weight and appetite increased. Weight had increased from 45 kg to 48.5 kg, and the SNAQ score had increased from 7 to 10. However BMI was still below 18.5 kg/㎡, which means a 7.7 times higher mortality rate, compared to patients with normal weight[4]. Also, SNAQ score was still below 14 which means anorexia[26]. When the patient received both *Megestrol acetate* and Korean medical treatment, there was a considerable increase in both weight and appetite. BMI increased over 18.81 kg/㎡ and SNAQ score increased over 16. However owing to the abdominal distention, insomnia and urinary frequency, *Megestrol acetate* was stopped and only Korean

medical treatments were administered for about two months. In this period, although SNAQ score slightly decrease, the score was over 14, which means no anorexia and was two times higher than the first score, also the increased weight was maintained.

Long-term or high dose use of *Megestrol acetate* causes many side effets[20]. Even though this study cannot definitively confirm that the Korean medical treatment might directly affect weight gain and improvement of appetite, it shows partly effect on increase in weight, improvement of appetite and maintenance of increased weight and appetite. It is important to show that the Korean medical treatment could be a complementary treatment to existing treatments which have many side effects and limits.

The limitations of this study include there was only one patient, uncontrolled design, and a lack of blinding. As it judges a change of weight and appetite only with two methods, there is insufficient data to make an objective and a subjective evaluation. Also, intakes and outputs should have been checked.

Although many studies emphasize the importance of managing weight and appetite in ALS patients, existing treatment for weight loss and loss of appetite is very insufficient. In this respect, despite some limitations, the findings of this study could open up new clinical guideline possibilities.

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