《Original Article》

Factors related ultrasonic bone density in subacute myelo-optico neuropathy (SMON) patients

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Abstract

Objective: To clarify the bone mineral density (BMD) in female sub-acute-myelo optico neuropathy (SMON) patients, and the relationship between BMD and their life style. Design: The study population consisted of 65 female SMON patients aged 28-89 years old living in Aichi Prefecture. BMD was measured as stiffness (St) by using an ultra sonic bone densimeter (A-1000 Achilles of Lunar Corp). Height, weight, BMI, history of childbirth and delivery, onset age of menopause, intake of milk, intake of small fish, Barthel Index, the number of retaining teeth, and a history of bone fracture were used as factors of life style. Results: Average percent age-adjusted St (Adjusted St) and standard deviation (SD) was 88.4±13.2. The rate of patients with low Adjusted St (less than 89) was higher in patients with low height, light weight and low BMI, with history of childbirth and delivery, with early onset of menopause, and with low intake of milk. There were not seen to be large differences between two groups in SMON severity (severe and moderate, and slight and none), in Barthel Index (less than 99 and 100), in the number of retaining teeth (less than 19 and 20 or more). Conclusion: Factors related St were height, weight, history of childbirth and delivery, onset of menopause and intake of milk. Average St in female SMON patients was lower than the average St of Japanese healthy females within the same age group.

Introduction

There were reports from many patients who were prescribed a drug (5-chloro-7-iodo-8-hydroxyl-quinolin, which are also called clioquinol or chinoform) in Japan in the years around 1950-1960. This drug was used widely as an anti-amaebicidal and anti-bacterial drug in Japan. The total number of patients reached over 9,000 according to a national survey in 1970. This drug-adverse disease was called sub-acute myelo-optico neuropathy (SMON) [1]. SMON typically started with sub-acute or sometimes acutely abdominal pain, diarrhea followed by dysesthesia (impairment of the senses) in the lower half body, paralysis and visual disturbances. The Ministry of Health and Welfare recognized SMON as a drug-adverse disease in 1960. Since 1960, the Ministry has formed SMON research committees, and has supported SMON patients by examining their health condition. In Aichi Prefecture, there were around 400 patients in 1960. Since 1960, the Aichi-prefecture SMON research committee has examined SMON patients in cooperation with The Aichi Prefecture SMON patient group. An examination of ultrasonic bone density was conducted in 1994-1997. We would like to report some

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results of this examination.

Method

1, Participants

Participants were female SMON patients who lived in Aichi prefecture, and took the general SMON examination including ultrasonic bone density measurements from 1994 to 1997.

2, Body indices

Height and weight were measured, and the body mass index (BMI) was calculated.

3, History of menstruation and delivery

The onset age of menopause and history of childbirth and delivery were noted.

4, Nutrition

Frequency of intake of milk and intake of small fish were noted.

5, SMON severity

SMON patients had sensory disturbances, motor dysfunction and visual disturbances. These disturbances and dysfunction were integrated into a comprehensive severity scale according to 5 levels: extremely severe, severe, moderate, slight and none. This level of severity was called SMON severity, and this definition of severity adopted by the Japan SMON research committee has been used since 1960.

These levels of severity were diagnosed by neurologists of SMON research committee in the SMON examination.

6, Barthel Index

Measurements for assessing daily life activities and disability used the Barthel Index (BI). BI shows a sum score value range from 0 (dependence) to 100 (independence) according to 10 personal activities [2].

7, History of bone fracture

History of bone fracture in the past was noted.

8, Ultrasonic bone density measurements

We evaluated the index stiffness (St) which was calculated from the speed of sound (SOS) and broadband ultrasonic attenuation (BUA) on the os calcis using an ultra sonic bone densitometer (A-1000 Achilles of Lunar Corp) [3]. From the St, percentage- adjusted St (Adjusted St) was calculated [4]. Adjusted St shows the percentage of the average St of the Japanese healthy female of the same age group. As the average Adjusted St of healthy female in age, we used output data from A-100 Achilles.

9, Data analysis

Bivariate analysis was carried out by chi-square test to determine the statistical difference between the two groups. The level of significance was set at $p<0.05$.

Results

1, Participants

The number of patients who participated in this research was 65 females. The average and standard deviation of age was 67.5 ± 9.9 and it's range was between 28 to 89.

2, SMON severity

The number of patients in each rank of severity were one (1.5%) in extremely severe, 4 (6.2%) in severe, 36 (55.4%) in moderate, 22 (33.8%) in slight and 2 (3.1%) in none.

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3, ultrasonic bone density

SOS, BUA, St and Adjusted St on the os calcis were shown in Table 1. Average Adjusted St and SD was 88.4±13.2. The number of patients according to Adjusted St is shown in Table 2. Then number of patients in Adjusted St 80-89 was the largest. Average Adjusted St in SMON patients was 11.6% lower than the average St of Japanese females in the same age group.

4, The relationship between Adjusted St and the factors

We analyzed the relationship between Adjusted St and the factors which were considered to be related to bone density. We defined Adjusted St 90 or more as normal BMD. Height, weight, BMI, history of childbirth and delivery, the age of menopause, intake of milk, intake of small fish, SMON severity, Barthel Index, and the number of retaining teeth were used as the factors to determine this. The relationship between the factors and the rate of patients with normal Adjusted St is shown in Table 3.

The rate of patients with normal Adjusted St was significantly higher in patients with weight being 50 kg or more, height 150 cm or more, BMI 22 or more than in patients with weight less than 49 kg, height less than 149 cm and BMI less than 21. The rate of patients with normal Adjusted St was significantly higher in patients without a history of childbirth and delivery, 50 years or more of according to the onset age of menopause than in patients with history of delivery and less than 49 years of the onset of age of menopause. Concerning food,

Table 1. Speed of sound (SUS), Broadband ultrasonic attenuation (BUA), stiffness (St) and percent age-adjusted St (Adjusted St) in SMON patients

N=65

	Mean S.D.
SUS (m/sec)	1494.3 ±22.0
BUA (dB/MHz)	93.6 ±11.3
St	61.0 ±11.3
Adjusted St	88.4 ±13.2

Table 2. Number of patients according to Adjusted St

N=65

Adjusted St	number of patients (%)
Less than 79	15
89-89	23
99-99	19
100 or more	8

Table 3. Number of patients with normal Adjusted St (90 or more) according to factors

Factors		total number	with normal Adjusted St		
			Number	%	significance
weight (kg)	less than 49	39	13	33.3	
	50 or more	26	15	57.7	*
height (cm)	less than 149	37	14	37.8	
	150 or more	28	13	40.4	*
BMI	less than 21	41	15	36.6	
	22 or more	23	12	52.2	*
history of childbirth and delivery	yes	27	14	36.8	
delivery	no	38	13	48.1	
onset age of menopause	less than 49	29	8	27.6	
	50 or more	28	16	57.1	*
number of retaining teeth	less than 19	12	8	66.7	
	20 or more	18	11	61.1	n.s.
milk	take often	21	6	28.5	
	not take often	44	20	45.5	*
small fish	take often	21	10	47.6	*
	not take often	44	16	35.4	
severity	severe or moderate	40	17	42.5	n.s.
	slight or none	24	10	41.7	
Barthel Index	less than 99	23	10	43.5	n.s.
	100	42	17	40.5	
history of bone fracture	yes	22	7	31.8	
	no	43	27	62.8	*

* $p<0.05$ (x^2 test)
n.s. : not significant

the rate of patients with normal Adjusted St was significantly higher in patients who consumed milk more often than those who didn't. However, the rate of patients with normal Adjusted St was lower in patients who ate small fish more often than those who did not eat small fish so often. The rate of patients with normal Adjusted St was significantly lower in patients with history of bone fractures than without a history of bone fractures. There were not seen to be large differences between two groups in the SMON severity groups (severe and moderate, and slight and none), in Barthel Index (less than 99 and 100), in the number of retaining teeth (less than 19 and 20 or more).

There were 22 (33.8%) patients with a history of bone fractures out of 65. There were a dose-response relationship between the rate of patients with a history of bone fractures and Adjusted St as shown in Figure 1.

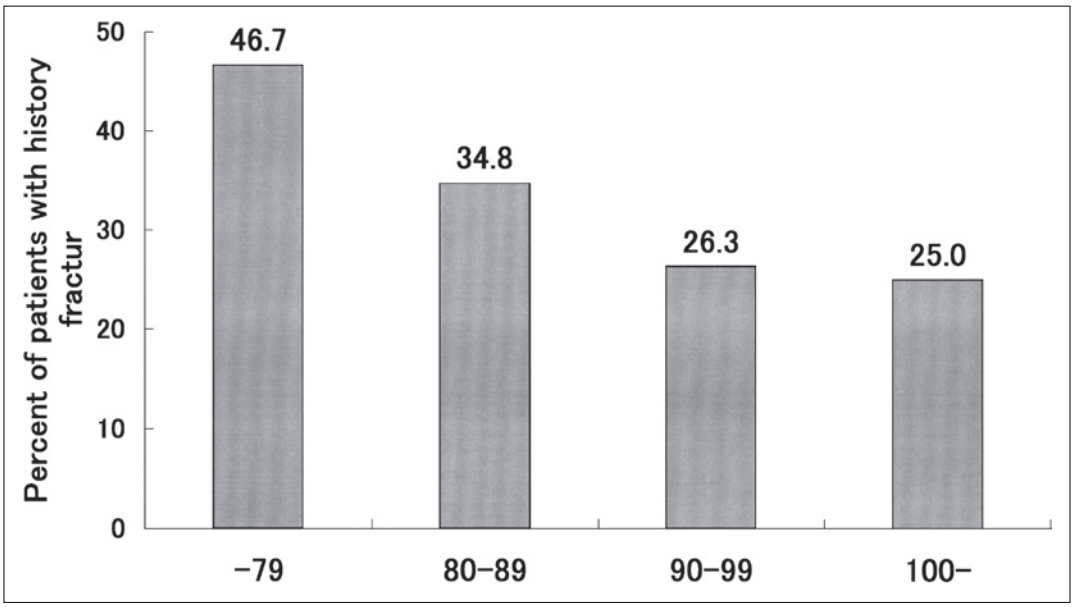

Figure 1 Percent of patients with history of bone fracture according to Adjusted St

Discussion

A history of bone fractures was seen in 129 (12.4%) out of 1042 SMON patients according to the national SMON examination in 1996 [5]. The cause of fractures in SMON patients is thought to be that they tend to fall easily due to disturbances when standing or walking due to spasms of the legs and the decrease in muscle strength. Another cause is thought to be that the fragility of bone increased, because of motor disturbances. For predicting fracture risk or prophylactic strategy against osteoporosis, bone density assessment is indispensable. There is a lot of evidence to support the use of ultrasound bone density for the assessment of fracture risk in elderly women [6]. The Ultra sound bone densitometer is helpful equipment for assessing the risk of fractures over a large population, because of its low cost, good portability, relatively short examination time, and a protection space against radiation is deemed not necessary. Calcaneal ultrasound bone density correlated well with calcaneal bone mineral density assessed by single X-ray absorptiometry and dual energy X-ray absorptiometry which has been widely used in hospitals [3,4].

In this study, the average Adjusted St in female SMON patients was lower than 100. The number of patients which showed more than 100 in Adjusted St was 8 out of 65. The research in Okayama Prefecture using the same ultrasonic densimetry reported that stiffness in SMON patients tended to be lower that of non-SMON people [7]. Ando reported that he diagnosed osteoporosis in 38 SMON patients out of 64 using DPX, and lumbar roentgenogram with osteoporotic changes [6]. Knowledge of low bone St by SMON patients is important as this will motivate them in preventing bone fractures by avoiding falls, improving their nutrition and increasing their exercise.

In this study, the rate of patients with low Adjusted St was higher in SMON patients with history of childbirth and delivery than those with no history. The rate of patients with low Adjusted St was higher in SMON patients with the onset age of menopause less than 49 years than 50 years or over. This was not contradiction against the previous papers which showed a late menopause was a decreased risk for low BMD [9,10].

Milk or small fish are rich in calcium The rate of patients with normal Adjusted St was higher in patients who drink milk more frequently [11-14]. However, the rate of normal Adjusted St was lower in patients who eat small fish more often. The cause of this contrary result is not clear. Confronting factors may exist. Concerning

ADL, there was not a large difference in Adjusted St between patients with severe or moderate and slight or none. There was also not a large difference in Adjusted St between patients with Barthel Index 100 and less than 99. This result is different from previous papers [12-14] which showed that mobile handicapped people had low bone density. Whether this result relates with the character of SMON or not is unclear.

In this study, there is a relationship between history of bone fractures and Adjusted St. One of the causes of bone fractures is considered to be due to decreased bone density.

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和文抄録

スモン患者の骨密度とその関連する要因について

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女性スモン患者の骨密度の状況とその骨密度と関連する要因について検討した。愛知県に在住する28－89歳の65人の女性スモン患者を対象に検診をおこなった。骨密度の測定はLunar Corp社のアキレスA1000を使用し、stiffnessを用いた。要因は身長、体重、BMI、出産歴、閉経年齢、ミルク、小魚の摂取状況、スモン障害度、Barthel Index、歯数、骨折の既往歴をとった。年齢補正Stのパーセント値の平均は88.4±13.2であった。要因を2群に分けて分析すると、低骨密度（年齢補正stiffnessが89以下）は低身長、低体重、低BMI、出産歴あり、低閉経年齢、ミルクの摂取の多い患者に多かった。女性スモン患者のstiffnessは同年齢の健康女性のstiffnessより低かった。

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