whereas the majority of *SMN2*-derived transcripts lack exon 7 (Δ7-*SMN*).

Phenotypic variations in SMA are inversely correlated with *SMN2* copy number, and a higher *SMN2* copy number ameliorates the clinical phenotype.[1,9,10] *SMN2* might compensate for the loss of *SMN1* by modifying disease severity through production of a small amount of full-length SMN protein. Thus, treatment strategies for SMA have focused on increased production of the SMN protein from *SMN2*.

Valproic acid (VPA) is a histone deacetylase (HDAC) inhibitor as well as an anticonvulsant used for treatment of epileptic patients, as it increases SMN levels in SMA patients through activation of *SMN2* transcription and splicing correction of *SMN2* exon 7.[11,12] Its effects as a therapeutic agent of SMA are expected.[13–20] In the present study, we evaluated the efficacy of VPA in SMA patients.

Methods

The present study was carried out from January 2012 to March 2013.Seven consecutive Japanese SMA patients were recruited, of whom six were type 2 and one was type 3. The type 2 patients were as follows: case A, 34-year-old man; case B, 33-year-old woman; case C, 23-year-old man; case D, 30-year-old woman; case E, 2 years and 10-month-old girl; and case G, 15-year-old girl, whereas the type 3 patient was a 42-year-old man denoted as case F.

None of the participants possessed the *SMN1* gene, and had three copies of *SMN2* and the neuronal apoptosis inhibitory protein. All except for cases B and E used non-invasive ventilation at night. The demographic features of the patients are summarized in Table 1. All patients underwent physiotherapy, such as range of motion exercises of the extremities and respiration, before, during and after the study. The frequency and contents of physiotherapy differed among the patients, and were dependent on their situation including hospitalization, outpatient status and other factors.

VPA was given daily for 6 months to reach trough levels of 50–100 mg/dL, a dosing level typical of that used in epilepsy patients. L-carnitine was also given. We evaluated using the Modified Hammersmith Functional Motor Scale for SMA (MHFMS),[21] and also examined respiratory function and carried out *SMN* transcript analysis using quantitative real-time polymerase chain reaction (qRT–PCR) measurements with peripheral white blood cell samples[22] obtained from the patients before and 1, 3 and 6 months after starting VPA treatment. Blood samples were obtained from all patients in the daytime after fasting.

For *SMN* transcript analysis, we measured total-*SMN*, FL-*SMN* and Δ7-*SMN* transcript levels using qRT–PCR, with the latter two quantitated from the levels of the products encompassing *SMN* exons 7 and 8, and exons 5, 6 and 8, respectively. We used glyceraldehyde-3-phosphate dehydrogenase (*GAPDH*) as an endogenous reference gene, and the levels of *SMN* are expressed relative to those of *GAPDH*.[22] The detailed methods utilized for qRT–PCR have been described.[22] We also evaluated the ratio of FL-*SMN* to Δ7-*SMN* transcript (FL/Δ7-*SMN*). For respiratory function, we assessed vital capacity (VC), maximum insufflation capacity (MIC) and cough peak flow (CPF).[23,24] In addition, we also checked subjective symptoms, side-effects and bodyweight changes in each patient.

Statistical analysis. ANOVA with Tukey's or a Games–Howell *post-hoc* test were used to evaluate the differences in *SMN* transcript levels for each evaluation time. Statistical significance was accepted at $P < 0.05$.

Ethics. Written informed consent (for adults), or parental consent and assent (for children) were obtained for all participants. The study protocol was approved by the local ethical committees of Toneyama National Hospital and the University of Kobe.

Results

VPA and L-carnitine administration. Table 2 shows the dose of VPA administered and VPA concentration in each patient. Case A was eliminated before the 1-month evaluation because of sleepiness induced by VPA and discomfort caused by L-carnitine. Cases B–E and G completed

Table 1 Demographic features of patients with spinal muscular atrophy

Case	Sex	Age (years)	Type	*SMN1* exon7	*SMN1* exon8	*SMN2* copy number	NAIP	Respiratory status	Scoliosis	Motor function
A	Male	34	2	Delete	Delete	3	(+)	Night NPPV	(+++)	Assisted sitting
B	Female	33	2	Delete	Delete	3	(+)	Voluntary	(+)	Assisted sitting
C	Male	23	2	Delete	Delete	3	(+)	Night NPPV	(+++)	Assisted sitting
D	Female	30	2	Delete	Delete	3	(+)	Night NPPV + O2 inhalation in daytime	(+++)	Assisted sitting
E	Female	2 years 10 months	2	Delete	Delete	3	(+)	Voluntary	(+)	Assisted sitting
F	Male	42	3	Delete	Delete	3	(+)	Night NPPV	(+/-)	Sitting
G	Female	15	2	Delete	Delete	3	(+)	Night NPPV	(+)Spinal surgery	Assisted sitting

NAIP, neuronal apoptosis inhibitory protein; NPPV, non-invasive positive pressure ventilation.

Table 2 Results obtained from each patient. Dose of valproic acid, valproic acid concentration, score for Modified Hammersmith Functional Motor Scale for SMA, respiratory function, transcription amount of *SMN* and change in body weight.

Case	Time period (months)	VPA administration (mg)	VPA concentration (μg/mL)	MHFMS	VC (mL)	MIC (mL)	CPF (L/min)	FL-*SMN*	Δ7-*SMN*	FL/Δ7-*SMN*	Total -*SMN*	Body weight (kg)
A	Pre			0	965	–	115	0.51 (±0.06)	1.77 (±0.13)	0.28 (±0.02)	1.19 (±0.37)	
B	Pre			4	840	960	140	0.56 (±0.02)	1.12 (±0.19)	0.50 (±0.07)*	1.02 (±0.03)	31.4
	1	400	50	4	1000	810	95	0.80 (±0.05)	0.68 (±0.03)	1.17 (±0.03)*	5.47 (±2.11)	
	3	400	45	5	850	1000	165	0.86 (±0.35)	0.92 (±0.39)	0.95 (±0.14)	3.27 (±1.33)	
	6	400	42	5	810	1060	130	1.08 (±0.13)	0.58 (±0.26)	2.05 (±0.57)	1.61 (±0.13)	33.4
C	Pre			0	380	630	85	0.39 (±0.03)	2.02 (±0.47)	0.20 (±0.04)	2.82 (±0.67)	16
	1	200	39	0	400	600	90	0.49 (±0.09)	1.37 (±0.24)	0.36 (±0.07)	4.78 (±0.09)*,**	
	3	400	62	0	430	580	95	0.51 (±0.17)	1.16 (±0.76)	0.78 (±0.80)	2.96 (±0.34)*	
	6	400	75	0	500	710	100	0.45 (±0.24)	1.26 (±0.25)	0.39 (±0.27)	3.09 (±0.15)**	17.5
D	Pre			0	380	440	75	0.60 (±0.40)	0.83 (±0.13)	0.73 (±0.14)	3.61 (±0.19)*,**	19
	1	200	35	0	350	550	80	0.67 (±0.24)	1.13 (±0.13)	0.60 (±0.24)	2.96 (±1.27)	
	3	200	34	0	350	610	85	0.61 (±0.004)	1.14 (±0.69)	0.77 (±0.61)	2.51 (±0.10)*	
	6	400	70	0	370	750	90	1.07 (±0.35)	1.09 (±0.18)	0.98 (±0.33)	2.25 (±0.11)**	20
E	Pre			11	410	–	–	0.83 (±0.02)*,**	1.25 (±0.05)*	0.67 (±0.03)*	2.59 (±0.21)*	10
	1	25	13	11	400	–	–	1.04 (±0.004) *	1.12 (±0.17)	0.95 (±0.16)	3.18 (±0.18)**	
	3	75	25	11	250	–	–	1.16 (±0.08)**	1.31 (±0.05)**	0.88 (±0.03)*	4.27 (±1.00)***	
	6	100	34	18	410	–	–	0.57 (±0.13)	0.99 (±0.06)*,**	0.58 (±0.15)	0.68 (±0.35) *,**,***	11
F	Pre			10	3950	–	400	0.31 (±0.06)	0.25 (±0.08)*	1.29 (±0.19)	1.01 (±0.03)	76
	1	200	18	10	4200	–	400	1.02 (±0.07)	1.18 (±0.21)*	0.88 (±0.10)	1.37 (±0.39)	
	3	400	26	9	4290	–	420	1.64 (±0.91)	1.37 (±0.55)	1.15 (±0.25)	1.24 (±0.43)	79
G	Pre			1	400	1570	95	0.62 (±0.16)	1.13 (±0.16)	0,55 (±0.02)	1.12 (±0.11)*	19
	1	200	47	1	410	1440	95	0.66 (±0.15)	1.09 (±0.17)	0.60 (±0.08)	1.31 (±0.32)	
	3	400	50	1	410	1350	105	0.57 (±0.13)	1.44 (± 0.10)	0.40 (± 0.10)	0.73 (±0.01)*	
	6	400	43	1	420	1200	95	0.76 (±0.01)	1.65 (±0.78)	0.53 (±0.21)	1.77 (±0.02)*,**	18

All data for *SMN* transcription are expressed as the mean (±SD).

*,**,*** $P < 0.05$. Tukey's or a Games–Howell *post-hoc* test was used to evaluate the differences in each level of *SMN* transcript or ratio of FL/Δ7-*SMN*in each patient.

CPF, cough peak flow; MIC, maximum insufflation capacity; VC, vital capacity.

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the 6-month study, whereas case F was eliminated after 3 months because of chronic cholecystitis (no evident relationship to VPA trial).

VPA was started at 25–200 mg/day and gradually increased, with a final dosage in cases B, C, D and G of 400 mg/day, and 100 mg/day in case E, while the dose in case F at 3 months was 400 mg/day. VPA concentration reached an optimal range after 3 months in case C, and 6 months in case D. In cases B and G, the transient moderate VPA concentration was decreased under the optimal range at 6 months. In cases E and F, VPA concentration was at less than the optimal range during the study. Serum levels of VPA concentration in each patient are summarized in Table 2.

In cases A and B, L-carnitine was administered at 300 mg throughout the study. In case C, after starting L-carnitine at 300 mg, the dosage was decreased to 100 mg from the second week because of abdominal discomfort, and then increased to 200 mg from week 6. In case D, L-carnitine was started at100 mg and increased to 200 mg in week 5, then decreased to 100 mg in week 6 because of discomfort. In cases E and G, L-carnitine was administered at 100 mg throughout the study. In case F, L-carnitine was started at 100 mg and increased to 200 mg in week 5.

MHFMS, respiratory function and SMN transcript. Table 2 shows sequential changes in scores for MHFMS, respiratory function and transcription amount of *SMN* for each patient. Furthermore, Table 3 presents a summary of changes in MHFMS score, and rates of change in respiratory function and FL-*SMN* transcription from pretreatment to 6 months after beginning VPA administration in each case (3 months in case F).

MHFMS for cases C, D and G did not change during the dosage period (cases C and D: 0 points, case G: 1 point). MHFMS in case B was 4 points in a pretreatment evaluation and 5 points at 6 months later, while that in case F was 10 points at pretreatment and 9 points at 3 months. MHFMS in case E was 11 points at the pretreatment evaluation and increased to 18 points at 6 months. Case E gained motor function to turn from side to side.

There was a great number of improved respiratory function items even in cases with a VPA blood level lower than optimal, all of which were cases with progression. VC increased in cases C, F and G, while MIC increased in cases B, C and D, but decreased in case G, and CPF increased in cases C, D and F.

The transcription amount of FL-*SMN* generally showed an increasing tendency, whereas that of Δ7-*SMN* and total-*SMN*, and the ratio of FL/Δ7-*SMN* showed no consistent tendency in accordance with VPA administration in the patients. In some cases, the difference in level of *SMN* transcript or ratio of FL/Δ7-*SMN* was significant.

VPA concentration, MHFMS, respiratory function and transcription amount of FL-SMN in each case. Case B: VPA blood level after 6 months administration was lower than an optimal level. However, MIC increased and the FL-*SMN* transcription product quantity showed an increasing tendency.

Case C: VPA blood level was within an optimal level, whereas VC, MIC and CPF increased, and the quantity of the FL-*SMN* transcription product showed an increasing tendency.

Case D: VPA blood level was within an optimal level, whereas MIC and CPF increased. The quantity of the FL-*SMN* transcription product showed an increasing tendency.

Case E: MHFMS score was dramatically improved, as described earlier. However, VPA blood level at 6 months after administration was lower than optimal, and the quantity of the FL-*SMN* transcription product showed a decreasing tendency.

Case F: Although VPA blood level was lower than an optimal level and MHFMS worsened, VC and CPF increased, and the quantity of the FL-*SMN* transcription product showed an increasing tendency.

Case G: VPA blood level was lower than an optimal level and MIC decreased. There was no change in MHFMS, However, VC increased and the quantity of the FL-*SMN* transcription product showed an increasing tendency.

Subjective symptoms, side-effects and changes in bodyweight. Case A: Malaise, sleepiness and a precordial sense of incongruity.

Case B: Condition immutability and sleepiness.

Case C: Condition immutability and a precordial sense of incongruity.

Case D: Difficulty with fatigue and a precordial sense of incongruity.

Case E: Parents think that tremors have decreased.

Table 3 Summary of data obtained for each patient at end of administration of Valproic acid (6 months, 3 months for Case F). Valproic acid concentration, changes in Modified Hammersmith Functional Motor Scale for SMA, respiratory function and transcription amount of FL-*SMN*.

Case	VPA concentration	MHFMS	VC	MIC	CPF	FL-*SMN*
B	Below	1	−3.6	10.4	−7.1	Increasing tendency
C	Optimal	0	31.6	12.7	17.6	Increasing tendency
D	Optimal	0	−2.6	70.5	20	Increasing tendency
E	Below	7	0	-	-	Decreasing tendency
F	Below	−1	8.6	-	5	Increasing tendency
G	Below	0	5	−23.6	0	Increasing tendency

Data shown represent changes in score of Modified Hammersmith Functional Motor Scale for SMA (MHFMS), rate of change (%) in respiratory function from pretreatment to 6 months after administration of valproic acid (VPA) (3 months in case F).
CPF, cough peak flow; MIC, maximum insufflation capacity; VC, vital capacity.

Case F: Condition immutability.
Case G: Condition immutability and sleepiness.

Many of the patients reported no subjective symptoms. Three complained of sleepiness including a dropout case (case A), while a precordial sense of incongruity was noted by three patients, including case A. There was also a complaint of belching, which was thought to be an effect of carnitine administration. There was no liver function abnormality reported and carnitine fractionation was normal. Table 2 shows changes in bodyweight for each patient. In five of the six patients, bodyweight increased by 1–3 kg from pretreatment, whereas that decreased by 1 kg in case G.

Discussion

After a 6-month administration of VPA, many items related to respiratory function were improved in the participants of the present study. Our items used to evaluate respiratory function, such as MIC and CPF, were not utilized in previous reports. Increasing MIC and CPF is important for patients with neuromuscular diseases to maintain good respiratory condition.[23] Our results showed that those improved values indicate the effectiveness of VPA administration to maintain a good respiratory condition even in adult SMA patients who show progression. Although Swobota reported improvements in maximum inspiratory pressures, forced vital capacity and forced expiratory volume in 1 s in patients aged over 5 years in an open label study,[15] there were no changes in any results of pulmonary function testing carried out in a double-blind trial thereafter.[17] Furthermore, no previous studies have reported that respiratory function was clearly improved with VPA administration, except for one that speculated that improved respiratory function might have been a result of growth and development.[18]

As a next step, our evaluation items of respiratory function, such as MIC and CPF, which have not been used in previous studies, should be evaluated as part of a placebo-controlled randomized trial to confirm the effects of VPA on respiratory condition in SMA patients.

In contrast, there was no relationship between VPA blood level and change in FL-*SMN* transcription products. Also, the level of VPA in blood in cases with improved MHFMS was less than an optimal level. Thus, improvement at the study end-point was not necessarily associated with VPA blood level or FL-*SMN* transcription product.

Past reports of VPA administration in SMA patients are summarized in Table 4, with most of those cases being SMA type 2 and 3.[13–20] The VPA dose in each of those reports is assumed to have been in accordance with the dose or blood level when used as an anticonvulsant. In four reports, carnitine administration was combined.[15,17–19] Two of those were designed as a double-blind study, whereas the others were open label.[17,20] In six reports, either *SMN* transcription level or SMN protein level was evaluated.[14–18,20] As an evaluation of motor function, the original Hammersmith Functional Motor Scale (HFMS) or MHFMS was used in four reports,[15,17–19] whereas a muscle strength test was also used in five reports.[13,17–20] One study found increased levels of *SMN* mRNA in association with VPA administration,[14] and another noted increased levels of SMN protein with VPA administration.[16] However, in three reports, there was no evident change in *SMN* transcription level with VPA administration[15,17,18] In the report by Weihl, motor function efficacy was noted in SMA type 3 and 4 patients,[13] whereas Darbar reported that HFMS improvement in SMA type 3 was not observed.[19] Kissel reported no statistically significant differences regarding changes in maximum voluntary isometric contraction in ambulatory SMA adults.[20] Also, Swoboda reported that children aged under 5 years,[15] furthermore, those aged 2–3 years with SMA type 2 showed MHFMS improvement with VPA administration.[17]

So the effects of VPA on SMA patients are controversial. Based on the present results, we expect that respiratory function in adult patients with progression, as well as motor function in younger children, has a possibility to improve after VPA administration. However, our open study was limited by the number of cases analyzed, and establishment of a control was difficult. We cannot conclude that the change in end-point after VPA administration is exclusively related to VPA administration. In particular, in the MHFMS of case E, growth development could have influenced our evaluation of clinical manifestations. The effects of growth development on motor functional evaluation should be evaluated in a placebo-controlled randomized trial.

As for the effects of VPA on SMN, promotion of *SMN2* gene transcription by activation of the *SMN2* gene promoter (production increase of full length type *SMN2* mRNA and Δ7-*SMN2* mRNA), splice progress of the *SMN2* gene exon 7 by gene activation to encode a splicing related protein and a combination of these two mechanisms have been considered.[11,12] An increase in FL- and Δ7-*SMN* transcription product quantity is expected to occur with VPA administration. Furthermore, VPA is a multifunctional drug that is expected to have a neuroprotective effect.[25] Therefore, it is also speculated that VPA blood level, FL-*SMN* transcription product quantity and improvement in outcome are not necessarily linked.

Regarding the change in quantity of the *SMN* transcription product after VPA administration, we considered the effects of fluctuations in the system of measurement. Whether an increase in SMN protein in peripheral blood leukocytes reflects an increase in that in ventral horn cells remains unknown. It is also not clear if an increase in SMN protein in the ventral horn cells is directly associated with clinical manifestation improvement. In addition, if an imperceptible change in motor function occurs, it might not be possible to detect the difference using the method of evaluation utilized in the present study. Thus, subtle changes in clinical signs and symptoms might not be detected by the present evaluation method.

It was also difficult to evaluate the effects of physiotherapy on motor and respiratory functions in a comprehensive manner because of variations in each patient. In the present cases, uniform physiotherapy was not possible because of functional differences among our patients, the therapeutic

Table 4 Summary of reports related to administration of valproic acid in patients with spinal muscular atrophy

Author	Clinical trial phase	VPA	Carnitine	SMA type	*n*	Age	Duration	Evaluation				Results	Conclusion	Year	Ref
								Motor function	PFT	SMN	Others				
Weihl *et al.*	Open	Administration 500–1000 mg/day Mean serum level 87 μg/mL	–	3,4	7	17–45 years (mean 17 years)	1–15 months (mean 8 months)	Muscle strength	–	–	–	Improvement of motor strength and subjective benefit	VPA treatment is efficacious in adult SMA type 3/4	2006	13
Brichta *et al.*	Open	Administration 1200–1800 mg/day Serum level 70–100 mg/L	–	Carrier	10	50.0 ± 10.9 years	>5 weeks	–	–	SMN protein analysis SMN2 messenger RNA (blood)	–	Increased SMN messenger RNA and protein levels in seven carriers Elevated SMN2 messenger RNA levels in seven patients Unchanged or decreased in 13 patients	Long-term clinical trials in SMA patients that correlate SMN expression in blood with individual motor function tests are required	2006	14
		Serum level 38–99 mg/L		1	5	1.6 ± 0.9 years	>4 weeks			SMN2 messenger RNA (blood)					
		Serum level 47.9–98.3 mg/L		2	11	10.3 ± 7.1 years									
		Serum level 58.5–99.0 mg/L		3	4	20.8 ± 6.9 years									
Swoboda *et al.*	Open	Serum level 50–100 mg/dL	Administration 50 mg/kg/day	1	2	2–3 years	6 months	MHFMS	FVC, FEV1, MEP, MIP (over 5 years)	Quantitative assessment of SMN mRNA	CMAP, MUNE, DEXA	Increased mean score on the MHFMS scale in SMA 2 However, significant improvement restricted to SMA 2 participants under 5 years of age Some items improved in PFT Unchanged Full length SMN levels Significantly reduced Δ7-SMN levels	The study provides good evidence that VPA can be used safely in SMA subjects over 2 years of age in the setting of close monitoring of carnitine status	2009	15
				2	29	2–14 years									
				3	11	2–31 years									
Piepers *et al.*	Open	Serum level 70–100 mg/mL	–	2,3	6	1.6–16.5 years	4 months	–	–	SMN protein concentration of l ymphocyte	–	Significantly increased SMN protein levels: five of six	SMN protein quantification by ELISA is a useful tool for evaluating the effects of treatment in SMA	2010	16

Table 4. Continued

Author	Clinical trial phase	VPA	Carnitine	SMA type	*n*	Age	Duration	Evaluation				Results	Conclusion	Year	Ref
								Motor function	PFT	SMN	Others				
Swoboda *et al.*	Double blind	Serum level 50–100 mg/dL	Administration 50 mg/kg/day (maximum of 1000 mg)	2,3	30	1.8–8.7 years (mean 4.3 years)	6+6 months	MHFMS, Myometry measurement	FVC, FEV1, MEP, MIP (over 5 years)	Quantitative assessment of SMN mRNA	CMAP, DEXA, PedsQL	Children ages 2–3 years that received 12 months treatment had significantly improved MHFMS scores No change of QOL, CMAP, myometry measurements, and SMN Treatment not associated with changes in the PFT outcomes (over 5 years) Excessive weight gain was the most frequent drug-related adverse event	No benefit of treatment with VPA and L-carnitine in young non-ambulatory SMA	2010	17
		Placebo	Placebo	2,3	31	2.1–7.9 years (mean 4.4 years)	Placebo 6 months + VPA 6 months								
Kissel *et al.*	Open	Serum level 50–100 mg/dL	Administration 50 mg/kg/day (maximum of 1000 mg)	2,3 standers and walkers	33	2.8–16.3 years (median 6.9 years)	12 months	MHFMS-Extend, TTF, FMM, Myometry measurement (over 5 years)	FVC, FEV1, MEP, MIP (over 5 years)	Quantitative assessment of SMN mRNA	CMAP, DEXA, PedsQL	Weight gain of 20% above body weight occurred in 17%. No significant change of MHFMS-Extend, TTF, FMM, PedsQL and SMN transcript level FVC, FEV1 showed improvement at one year as expected with normal growth	VPA is not effective in improving strength or function in SMA children	2011	18
Darbar *et al.*	Open	Administration 20 mg/kg/day	Administration 100 mg/kg/day	2,3	22	2–18 years (mean 5.5 years)	1 year	MRC method, HFMS	–	–	Barthel Index	Gained no muscle strength SMA 2 presented significant gain in HFMS, but not type 3 Improvement of Barthel Index	VPA may be a potential alternative to ameliorate the progression of SMA	2011	19
Kissel *et al.*	Double blind, cross over	Administration 10–20 mg/kg/day Trough levels of 50–100 mg/dL	–	Ambulant adults with SMA	33	19.9–55.3 years (mean 37.2 years)	Placebo 6 months + VPA 6 months (cross over)	MVICT, SMAFRS, hand-held dynamometer, distance in 6-min walk, time to climb 4 standard stairs	FVC, FEV1, MIP	SMN2 copy number, mRNA levels, and SMN protein levels	CMAP, MUNE, DEXA, QOL	There was no change in outcomes at 6 or 12 months	VPA did not improve strength or function in SMA adults	2014	20

CMAP, maximum ulnar compound muscle action potential; DEXA, dual-energy X-ray absorptiometry; ELISA, enzyme-linked immunosorbent assay; FEV1, forced expiratory volume in 1 s; FMM, fine motor modules; FVC, forced vital capacity; HFMS, Hammersmith Functional Motor Scale; MEP, maximum expiratory pressure; MIP, maximum inspiratory pressure; MHFMS, Modified Hammersmith Functional Motor Scale for SMA; MHFMS-Extend, Modified Hammersmith Functional Motor Scale-Extend; MRC method, Medical Research Council method; MUNE, motor unit number estimation; MVICT, maximum voluntary isometric contraction testing; PedsQL, Pediatric Quality of Life Inventory; PFT, pulmonary function testing; QOL, quality of life; SMAFRS, modified SMA Functional Rating Scale; TTF, timed tests of function.

environment (hospitalization, outpatient status and so on) and ethical reasons. Thus, variations in physiotherapy should be minimized to better evaluate the effectiveness of VPA in future studies.

We found no serious side-effects caused by VPA administration. However, many of our patients gained bodyweight as compared with pretreatment, which was induced by VPA. Excessive weight gain has negative effects on motor and respiratory conditions in such patients, thus careful administration of VPA is required. As for carnitine administration, we should recognize side-effects including a precordial sense of incongruity and a complaint of belching, which have not been reported in previous reports.

VPA is expected to show good effects as a therapeutic drug for SMA in younger patients for motor functional improvement and even in adult patients for respiratory improvement. To fully elucidate its effectiveness and efficacy in SMA patients, development of an evaluation method to better determine minimal changes in clinical manifestations including respiratory function items, such as MIC and CPF, which were not used in previous reports, as well as introduction of a new biomarker that can be easily evaluated and is able to differentiate responders to VPA treatment from non-responders are required. Although improvements in MHFMS in the young girl and respiratory function improvements in the older subjects were observed in the present study, our results are difficult to interpret because of the open label nature and small scale. The effects of growth development on motor functional evaluation in child cases, respiratory function using MIC and CPF, and efficacy of VPA for SMA should be evaluated using a placebo-controlled randomized trial protocol.

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References

1 Kolb SJ, Kissel JT. Spinal muscular atrophy: a timely review. *Arch. Neurol.* 2011; **68**: 979–84.
2 Zerres K, Davies KE. 59th ENMC InternationalWorkshop: Spinal Muscular Atrophies: recent progress and revised diagnostic criteria 17–19 April 1998, Soestduinen, The Netherlands. *Neuromuscul. Disord.* 1999; **9**: 272–8.
3 Wang CH, Finkel RS, Bertini ES *et al.* Consensus statement for standard of care in spinal muscular atrophy. *J. Child Neurol.* 2007; **22**: 1027–49.
4 Lefebvre S, Bürglen L, Reboullet S *et al.* Identification and characterization of a spinal muscular atrophy-determining gene. *Cell* 1995; **80**: 155–65.
5 Lefebvre S, Burlet P, Liu Q *et al.* Correlation between severity and SMN protein level in spinal muscular atrophy. *Nat. Genet.* 1997; **16**: 265–9.
6 Wirth B. An update of the mutation spectrum of the survival motor neuron gene (SMN1) in autosomal recessive spinal muscular atrophy (SMA). *Hum. Mutat.* 2000; **15**: 228–37.
7 Monani UR, Lorson CL, Parsons DW *et al.* A single nucleotide difference that alters splicing patterns distinguishes the SMA gene *SMN1* from the copy gene *SMN2*. *Hum. Mol. Genet.* 1999; **8**: 1177–83.
8 Lorson CL, Hahnen E, Androphy EJ, Wirth B. A single nucleotide in the*SMN* gene regulates splicing and is responsible for spinal muscular atrophy. *Proc. Natl Acad. Sci. USA* 1999; **96**: 6307–11.
9 Mailman MD, Heinz JW, Papp AC *et al.* Molecular analysis of spinal muscular atrophy and modification of the phenotype by SMN2. *Genet. Med.* 2002; **4**: 20–6.
10 Harada Y, Sutomo R, Sadewa AH *et al.* Correlation between *SMN2* copy number and clinical phenotype of spinal muscular atrophy: three *SMN2* copies fail to rescue some patients from the disease severity. *J. Neurol.* 2002; **249**: 1211–9.
11 Brichta L, Hofmann Y, Hahnen E *et al.* Valproic acid increases the SMN2 protein level: a well-known drug as a potential therapy for spinal muscular atrophy. *Hum. Mol. Genet.* 2003; **12**: 2481–9.
12 Sumner CJ, Huynh TN, Markowitz JA *et al.* Valproic acid increases SMN levels in spinal muscular atrophy patient cells. *Ann. Neurol.* 2003; **54**: 647–54.
13 Weihl CC, Connolly AM, Pestronk A. Valproate may improve strength and function in patients with type III/IV spinal muscle atrophy. *Neurology* 2006; **67**: 500–1.
14 Brichta L, Holker I, Haug K, Klockgether T, Wirth B. In vivo activation of SMN in spinal muscular atrophy carriers and patients treated with valproate. *Ann. Neurol.* 2006; **59**: 970–5.
15 Swoboda KJ, Scott CB, Reyna SP *et al.* Phase II open label study of valproic acid in spinal muscular atrophy. *PLoS ONE* 2009; **4**: e5268.
16 Piepers S, Cobben JM, Sodaar P *et al.* Quantification of SMN protein in leucocytes from spinal muscular atrophy patients: effects of treatment with valproic acid. *J. Neurol. Neurosurg. Psychiatry* 2011; **82**: 850–2.
17 Swoboda KJ, Scott CB, Crawford TO *et al.* SMA CARNI-VAL trial part I: double-blind, randomized, placebo-controlled trial of L-carnitine and valproic acid in spinal muscular atrophy. *PLoS ONE* 2010; **5**: e12140.
18 Kissel JT, Scott CB, Reyna SP *et al.* SMA CARNIVAL TRIAL PART II: a prospective, single-armed trial of L-carnitine and valproic acid in ambulatory children with spinal muscular atrophy. *PLoS ONE* 2011; **6**: e21296.
19 Darbar IA, Plaggert PG, Resende MB, Zanoteli E, Reed UC. Evaluation of muscle strength and motor abilities in children with type II and III spinal muscle atrophy treated with valproic acid. *BMC Neurol.* 2011; **11**: 36.
20 Kissel JT, Elsheikh B, King WM *et al.* SMA valiant trial: a prospective, double-blind, placebo-controlled trial of valproic acid in ambulatory adults with spinal muscular atrophy. *Muscle Nerve* 2014; **49**: 187–92.
21 Krosschell KJ, Maczulski JA, Crawford TO, Scott C, Swoboda KJ. A modified Hammersmith functional motor scale for use in multi-center research on spinal muscular atrophy. *Neuromuscul. Disord.* 2006; **16**: 417–26.
22 Harahap IS, Saito T, San LP *et al.* Valproic acid increases SMN2 expression and modulates SF2/ASF and hnRNPA1

expression in SMA fibroblast cell lines. *Brain Dev.* 2012; **34**: 213–22.
23 Kang SW, Bach JR. Maximum insufflation capacity: vital capacity and cough flows in neuromuscular disease. *Am. J. Phys. Med. Rehabil.* 2000; **79**: 222–7.
24 Finder JD, Birnkrant D, Carl J *et al.* Respiratory care of the patient with Duchenne muscular dystrophy: ATS consensus statement. *Am. J. Respir. Crit. Care Med.* 2004; **170**: 456–65.
25 Sugai F, Yamamoto Y, Miyaguchi K *et al.* Benefit of valproic acid in suppressing disease progression of ALS model mice. *Eur. J. Neurosci.* 2004; **20**: 3179–83.

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How Physicians Support Mothers of Children with Duchenne Muscular Dystrophy

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Abstract

Communicating about Duchenne muscular dystrophy and its prognosis can be difficult for affected children and their family. We focused on how physicians provide support to the mothers of children with Duchenne muscular dystrophy who have difficulty communicating about the condition with their child. The eligible participants were certified child neurologists of the Japanese Society of Child Neurology. Participants responded to questionnaires consisting of free descriptions of a vignette of a child with Duchenne muscular dystrophy and a mother. We analyzed 263 responses of the participants. We found 4 themes on advising mothers, involving encouraging communication, family autonomy, supporting family, and considering the child's concerns. These results provide a better understanding of the communication between physicians and family members who need help sharing information with a child with Duchenne muscular dystrophy. These findings will assist clinical practitioners in supporting families and the affected children throughout the course of their illness.

Keywords

Duchenne muscular dystrophy, physicians, mothers, communication, qualitative study

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In recent years, the circumstances of patients with Duchenne muscular dystrophy have undoubtedly improved. Despite this progress, Duchenne muscular dystrophy is still a severe disease causing a significant burden to patients as well as their families. The lives of parents with a child with Duchenne muscular dystrophy are profoundly affected, and they generally suffer from high levels of stress.[1]

Duchenne muscular dystrophy is a recessive X-linked progressive muscular disease, which is caused by a mutation in the gene responsible for dystrophin production.[2] Duchenne muscular dystrophy occurs primarily in boys. Boys with Duchenne muscular dystrophy have progressive loss of muscle function and weakness, resulting in a loss of ambulation and deterioration of respiratory and cardiac functions. Clinical management and care for Duchenne muscular dystrophy has improved in the past few decades because of corticosteroid treatment, noninvasive mechanical ventilation, and cardioprotective medications, resulting in prolonged life expectancies.[3-6]

It is a difficult process for the affected child and its family to receive the diagnosis of Duchenne muscular dystrophy and communicate about the child's prognosis. Although pharmacologic interventions and corticosteroid therapy have been reported as effective in slowing the decline of muscle strength and function in Duchenne muscular dystrophy,[2,7,8] there are no curative treatments in existence. Informing a family of the life-limiting condition of their child can be one of the most difficult and stressful events for a physician to experience.[9] Emotional responses of physicians could have consequences on how the diagnosis process progresses. In addition, the manner in which the condition is explained and communicated by medical professionals has an impact on the parents and child. Generally, one of the recommended communication styles is explaining the condition and providing information on the course of the disease at a level that is comprehensible to both the child and family.

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Although there is a great deal of research on disease communication for major pediatric diseases such as childhood cancer,[10,11] Duchenne muscular dystrophy differs in both prognosis and therapeutic potential. There are few studies focusing on communication between physicians and the families of children with Duchenne muscular dystrophy.[12]

This study aimed to explore how physicians explain the diagnosis and support families with a child with Duchenne muscular dystrophy. The original study was designed to reveal physicians' attitudes and examine how they dealt with the difficulties inherent in explaining the condition to affected children. This article focuses on how physicians deal with and support mothers who ask for advice on explaining the condition to their children.

Methods

Participants

We obtained permission to mail survey questionnaires to board-certified child neurologists of the Japanese Society of Child Neurology. The eligible members of certified child neurologists were 1,022 physicians, the same number of participants as in our previous study.[12]

Thirteen participants were not eligible because their addresses were unknown. The final sample consisted of 1,009 pediatric neurologists in the Japanese Society. This survey was conducted between August 2010 and February 2011.

Procedure

We developed the questionnaires based on a review of the literature and an exchange of opinions among clinical psychologists (HF, OI) and experienced physicians (TS, TM, HF, SS) with experience in pediatric neurology and muscular dystrophy. The main part of the questionnaire consisted of free descriptions regarding a case vignette, which addressed how physicians deal with and support mothers who ask for advice on explaining Duchenne muscular dystrophy to their children. Additionally, it included domain items of physician's views about important factors in explaining the condition and their attitudes towards doing so. Details of the study methodology were reported elsewhere.[12]

This study was approved by the research ethics committee of the National Hospital Organization Toneyama National Hospital.

Case Vignette

A hypothetical case depicting a mother who needs help in dealing with her child's needs was constructed for this qualitative study. A detailed description of the case is as follows:

An 11-year-old boy who was diagnosed with Duchenne muscular dystrophy at the age of 18 months is now in the fifth grade at elementary school. The boy started using a wheelchair in fourth grade because he had begun to experience difficulty in standing and walking at that time. For several years, the boy has gone to the physician about twice per year. No signs of mental retardation have been observed. According to his mother, the boy had a class at school in which pupils thought about "living." This class prompted him to vaguely think of the future and learn more about his disease. Although he had already been informed about his needs in daily life, and he knew his disease was a muscular disorder, the future or his prognosis had not been discussed at home. The mother did not know how to explain this to him and had come to the physician for a consultation.

We asked for an open-ended question about how to deal with the mother in this situation.

Analysis

Qualitative data were analyzed using the thematic analysis approach. Thematic analysis is a method of identifying and analyzing the themes within qualitative data.

The responses of the free descriptions were carefully read several times to identify themes and subthemes from the physicians' viewpoints on how to deal with and support the mothers. These processes resulted in the categorization of specific subthemes. Two researchers (HF, OI)—male, certified clinical psychologists—with experience of psychological research in the field of muscular dystrophy extracted the themes, and disagreements were discussed until consensus was reached. Once the themes were identified, the responses were reviewed again, and the frequencies of the themes were calculated. A qualitative research software package was not used for the collating and coding. Consolidated criteria for reporting qualitative studies (COREQ) checklist was used as a reporting framework.[13]

Additionally, we performed χ^2 test, using SPSS Statistics 21.0 software (SPSS Japan Inc., Tokyo, Japan), to assess the difference in the approach by age.

Results

We received 311 replies (30.9%). Within the 311 replies, 263 were included for the analysis of the free description of the case vignette. Twenty-two were excluded because of no experience in the specialty field of muscular dystrophy. Twenty-six were excluded because answers for free description were missing. The majority of the participants were men (70.7%), with a mean age of 50.6 years. They had been working in pediatric neurology for a mean of 20.4 years and in the specialty field of muscular dystrophy for a mean of 13.4 years. Table 1 describes the demographic information of participants.

Four key themes were identified through thematic analysis and each theme contained several subthemes. There are no significant differences in frequencies of the themes and subthemes by age of the physicians. Themes and subthemes are summarized in Table 2 and the details are described below.

Help With Communication

Explanation from the physician. The most common response was telling the mother that the primary physician would or could explain the nature of the condition to the child. In the case vignette, the mother asked the physician for advice because of her difficulty in explaining the condition. Telling the mother that the physician is able to explain the condition would provide support in such cases.

> It is about time to directly tell the child about the disease in detail and how to handle it in life. However, since telling

Table 1. Demographic Information of Participants

	n		
Gender			
Male	186		
Female	77		
Age group			
35-39	37		
40-49	80		
50-59	109		
≥60	37		
Workplace[a]			
Public hospital	82		
University hospital	77		
Private hospital	59		
Clinic	45		
National Hospital Organization	24		
	Mean	SD	Range
Age	50.6	9.1	35–86
Years working in pediatric neurology	20.4	8.9	1–55
Years working in muscular dystrophy	13.4	10.4	1–55

Abbreviation: SD, standard deviation.
[a]Some of the participants' responses included 2 or more locations.

> everything at once would confuse the child, the physician should talk to the child directly on several occasions. (P55)
>
> This child is 11 years old with no mental disability. So, if the child wants to know about the disease, the truth should be given accurately. I would tell the mother that the child's doctor could explain it to the child directly. Although the child might be bewildered at the time, the child would understand it better in the future. (P56)

Physicians take an active role in facilitating communication among family members and physicians. They thought it was better to have the primary care physician properly tell the child about the disease.

Suggests talking to the child because of his growth. According to the developmental stage of the child, how he views himself, and what he wishes to know about himself, the physicians encouraged the mother to provide an explanation and talk with her child.

> The child has reached the age of getting interested in his own things and of needing to prepare for positively confronting the disease. After telling the child the name of the disease, we should provide support so that the child can cope with what needs to be done from now on, particularly respiratory rehabilitation and cardiac management, on the child's own initiative. (P17)
>
> I would tell them that considering both the child's age and psychological state, it was the right time to start giving an objective explanation about the disease. As the child's doctor, I would help the child learn about the disease, while taking into account the parents' wishes. (P66)
>
> This must be properly discussed sooner or later, and if the child wants to know about the disease now, then it may be a good time. (P22)

Physicians referred to the growth of the child and the child's desire to know, and decided it was appropriate to talk about the disease with the child at that time. In addition, their perspective was that the child's desire to know was related to his growth.

No need for an explanation. A small number of the physicians thought it was not necessary to tell the prognosis and the future given the age and the developmental level of the child.

> I do not think it is necessary for the mother to explain about respiratory failure or heart failure, which could occur in the near future. Isn't it better to talk to the child after the child becomes more aware? (P35)
>
> I would not tell the [child of his] prognosis until the condition becomes more advanced. We are not supposed to let him lose hope at this point." (P242)

The intention of the physicians in withholding the prognosis from the child was to allow them to maintain hope for the future. It is believed that being aware of the life-limiting nature of the disease could have a negative impact on the child's adjustment.

Do not hide the facts. Parents of a child with an intractable disease often have trouble disclosing the facts of the disease, which could lead them to hide the nature of the disease from the child. Despite the difficulties in disclosing the facts, a small number of physicians emphasized the need to explain the facts.

> I would suggest honestly talking to the child about the disease and the mother's views of life and death. In so doing, it is not necessary to choose words so that the child can understand, but rather, to be honest. (P34)
>
> The disease is gradually progressing, and the child shows no mental retardation. Since the child wants to know more about the disease, hiding it would jeopardize the relationship between the child and his parents as well as the medical staff. (P53)

Concealing the facts from affected children might give them an unrealistic image of the disease and set them up to have difficulties in accepting the facts of the disease and the natural course of the disease progression. Therefore, physicians thought they should not conceal the facts from the child, even though they did not tell the child "everything."

Family's Autonomy

Confirm the family's intentions. The family's intentions affect the process of disclosure and communication about the condition. Parents might have different ideas about conveying the details of the condition. Physicians affirmed their attitudes and encouraged them to discuss the decision within the family.

Table 2. Key Themes of the Physicians' Responses

Theme	*n*	Content
Help with communication		
Explanation from the physician	94	The doctor takes on the role of disclosing the information to the affected child or tells the mother that he/she can talk to the child.
Suggests talking to the child because of his growth	81	The physician suggests talking to the affected child since he is growing and wishes to learn more about the disease.
No need for an explanation	21	The physician says to the mother that she should not explain what does not need to be explained at that time.
Do not hide the facts	11	Even though you do not need to tell everything, you should not hide the facts about the disease or lie to the child.
Family's autonomy		
Confirm the family's intentions	57	Have a discussion with the family of the affected child and determine what to do.
Help the parents understand the disease better	25	The physician provides an explanation to the parents to enhance their understanding of Duchenne muscular dystrophy.
Talk about what the mother understands	24	Suggest that the mother should tell the affected child what she knows about the disease.
The family cares about and supports the affected child	11	Tell the child that his family cares about and supports him.
Support for the family		
Support resources and patients' associations	32	Refer the family to patients' associations, family associations, and counseling.
Support for the mother's emotional responses	16	Support the mother as she experiences confusion and emotional responses.
Consideration of the child's concerns		
Talk to the affected child according to his level of understanding	26	Think about the child patient's current age, understanding, and emotional state.
Listen to the child's concerns	23	Talk to the child while asking about his concerns and what he wants to know.

> I would tell the patient's family to discuss and decide whether or not to talk about the disease including the prognosis and whether or not the doctor should be the one to do it. (P70)

> As I would like to explain about the disease and follow-up plans for the child, please set up a counseling (genetic) opportunity, or have a discussion about it between the parents. (P15)

To help parents be more autonomous in explaining the disease to the child, physicians encouraged parents to think about how they would explain the disease and they provided encouragement to them while they made their decision. Physicians also expressed a desire to respect the parents' decision.

Help the parents understand the disease better. Physicians offered to provide information about the disease so the parents could obtain a better understanding of the condition.

> The doctor should talk specifically about the symptoms, general prognosis, and treatments (steroid, respiratory, cardiovascular) so that the parents can first understand the medical condition. (P90)

> Discuss with the mother, check her level of understanding, and answer her questions to enhance her understanding. (P174)

The mother's comprehension has an impact when she talks with the family about the child's condition. Some parents do not completely understand the nature and prognosis of the disease so physicians try to teach them so they are knowledgeable about the disease.

Talk about what the mother understands. Physicians also suggested that the mother should tell the affected child what she knows about the disease when her child has reached a certain age.

> Since the child has reached the age of being able to understand about "living" and "life," I'd like to suggest telling the child the information deemed necessary in a straightforward manner. (P211)

Moreover, some physicians thought the child should be able to understand his disease by that time and suggested the mother try to talk to the child little by little about what she understood.

The family cares for and supports the affected child. Some physicians emphasized that the parents should tell the child that the parents would always provide care and support for the child. When informing the child of the nature of the disease, parents should make sure to let the child know that his family will always be there for him and care about him. When the child is given information about the challenges of the disease, the family should understand the child's response, provide support to him, and anticipate that he will react with shock.

Support for the Family

Support resources and patients' associations. Another recommendation was that mothers be provided information about patients' associations and psychological counseling as support resources for the child and mother.

> "Please try to provide accurate information about the disease, incorporating its positive aspects and helpful stories of other patients with the same disorder. In addition, how about hearing stories of families who have actually talked to their child patients?" (P40)

> I would suggest that the mother referred to support resources such as patients' associations and genetic counseling, and providing an opportunity for the patient, the patient's mother, and doctor to discuss the disease. (P112)

Parents with considerable experience of having a child with Duchenne muscular dystrophy could perhaps serve as role models for parents with less experience. Physicians related that sharing information among families of different ages could provide support to younger families.

Support the mother's emotional responses. Physicians also focused on the emotional responses of the mother, including worry, anxiety, and confusion.

> Check on the mother's concerns first and learn what she is most worried about. (P138)

> Ask the mother what she understands and how she is feeling. Provide support for the mother and ask her wishes. (P139)

As the disease progresses, parents often repeatedly experience feelings of sorrow, loss, and guilt. Looking at the mother's emotional responses can help the physician encourage her to express her emotional distress, which might lead to her being able to construct a supportive relationship with the physician.

Consideration for the Child's Concerns

Talk to the affected child according to his level of understanding. When telling the child about his condition, physicians and the family should consider his age, understanding, and psychological state.

> It is important to give information to the child gradually, based on his level of understanding. (P79)

> When answering the child's questions, devise ways of explaining the disease according to his comprehension of the words being used and with the use of good judgment. (P151)

Physicians believed the child's cognitive development and psychological state should be considered in deciding how and what to tell.

Listen to the child's concerns. One of the recommendations was to listen to the child's concerns to figure out their needs and ease their anxiety.

> Go on with the discussion slowly after fully understanding the child's knowledge and concerns, and also giving careful consideration to his personality. (P210)

> Start by asking the affected child what he wants to know and is concerned about. Then, discuss that with him, explain whenever possible, and respond to him with affection if there is anything unknown. (P291)

Physicians also stated that supporting resources are needed to assist in providing support for the emotional response of the child. They recommended confirming whether the child is able to get support from family members, schoolteachers, and friends.

Discussion

This study focused on how physicians dealt with and supported mothers of patients with Duchenne muscular dystrophy who asked for advice on explaining the disease to their children. For physicians, tailoring the explanation of the diagnosis and prognosis for the level of comprehension for the child and the family can be a challenging task.[14]

Because of the progressive nature of the disease, there should be a gradual approach to the process of disclosure and the explanation of Duchenne muscular dystrophy. Each time the disease progresses (eg, use of wheelchair, loss of ambulation, or decline of respiratory function), physicians provide the child and the family with relevant information for that level of functional impairment. In case the child has not been informed about the fundamental nature of the disease, sessions where the child knows about severe prognosis can be a difficult moment for parents. In this study, physicians' attitudes towards parents' needs were found to consist of 4 themes. They were not affected by age of the physicians, suggesting that other factors determine the approaches to those kinds of families.

Help With Communication

The first was "help with communication." Having the responsibility to tell their child with Duchenne muscular dystrophy about the disease and its genetic nature could be a burden for mothers. As the child grows, mothers have more opportunities to talk about the child's future and the nature of the child's illness. However, mothers of children with Duchenne muscular dystrophy are often reluctant to talk about the condition.[15] The physician told the mothers that he or she is willing to tell the child about the disease, which might ease the mother's distress and facilitate communication about the disease. Additionally, talking about the growth of the child can work supportively, alleviating her pain and difficulties. These experiences could facilitate open conversation about the difficult condition between the child and family. Parents of children with severe chronic genetic diseases, like Duchenne muscular dystrophy, tend to think that because the children experience the effects of the condition in their everyday life, they know what is going on.[16] Usually, there are difficulties in communicating a genetic condition with an affected child; however, communications between parents and affected children cultivate shared understanding and knowledge. Six fact sheet could a useful tool to

encourage the autonomy of young patients, managing their care and making decisions about their health interventions.[17] This is particularly important in transition process.

Family's Autonomy

The second theme identified was "family's autonomy." Autonomy in parents and patients is an essential part in advancing the process of sharing information about the disease. Physicians recommended that the mother obtain more information and tell the affected child what she understands. They also emphasized the role of the family in supporting and caring for the affected child. These attitudes support the parents' capacity to manage difficult conditions. In our previous study, pediatric neurologists agreed that parents' understanding and acceptance of the condition were critical for explaining the condition.[12]

In a previous study conducted in the United Kingdom, about a half of the parents of children with Duchenne muscular dystrophy did not tell the diagnosis to the child because of the life-limiting nature of the disease.[18] It can be a very difficult problem when the parents are not prepared to communicate about the disease to the child. Therefore, medical professionals or counselors could help prepare them and provide support while they decide on how to talk with the child. Medical staff are considered to have an important role in facilitating such communication and thus improving family adjustment.[14] However, some children prefer that the parents discuss the condition in a less formal way, and this may reduce anxiety in the children.[19]

Although parents think it is critical that they talk about their child's condition with him, many desire to delay such a talk until the progression of the disease seems more imminent. In other words, there is a tendency for parents to avoid reality to limit their distress.[15,16] The family history of Duchenne muscular dystrophy also affects the process.[20]

Support for the Family

"Support for the family" was the third theme identified. Caring for a child with Duchenne muscular dystrophy is emotionally difficult for parents. As the disease progresses, parents often feel strong emotions, such as feelings of sorrow, loss, guilt, anxiety, depression, and frustration,[1,18,21,22,] whereas parents of patients with muscular dystrophy could have positive consequences from caregiving, despite practical difficulties.[23] Support resources from outside of the family have been found to be important in parents' adjustment and coping with Duchenne muscular dystrophy.[24] As such, physicians should refer the parents to support groups and recommend that they participate with the child. Peer groups can be a vital source of support for families and children[25]; however, parents and affected children can have ambivalent feelings toward support groups.[26] By going to a group and meeting older children and families, they have to confront the progressive nature of the disease; thus, some parents experience strong negative feelings about attending these groups. This is a very difficult problem, as feeling connected to other people is a very important contributor to psychological adjustment.[27]

Consideration for the Child's Concerns

Patients with Duchenne muscular dystrophy experience repeated losses during adolescence as they develop and establish their own self-concepts. The disease influences their psychological adjustment and personality development; therefore, some of them may seek psychological support, whether consciously or unconsciously, during a difficult time. Although parents and physicians sometimes have difficulties in facing the emotional responses of the child when informing him of the disease and its life-limiting nature, communicating about the condition with medical professionals could help patients and their families hope for more out of life.[28]

Limitations

Several limitations should be noted in the present study. Response rate was low in this study. Because all certified child neurologists do not engage in the specialty field of muscular dystrophy, the proportion of responders of our research seemed reasonable. All the responders included in current study had experience of practice in the field of muscular dystrophy. This study was a questionnaire survey, which employed a case vignette to investigate how physicians would deal with and support mothers who ask for advice on explaining the diagnosis of Duchenne muscular dystrophy to their children affected by it. Generally, the process of supporting families of children with Duchenne muscular dystrophy begins at the child's diagnosis and continues as the disease progresses, with continuous interactions between the physician and family. Further research is needed to investigate the actual roles of physicians and the interactions with the families during the disease progression. Participants of this study were Japanese physicians with experience of practice in the field of muscular dystrophy; therefore, their responses were naturally affected by the conditions of medical care in their specific region and cultural background.[29] Experience of practice in the field of other pediatric and neurologic disorders may also contribute to their approaches. However, several themes were similar to those found in a previous study examining the experience of genetic counselors in another setting and region[30]; thus, it suggested that the important themes of the current study could apply in other countries and cultures. Novel treatments, such as exon skipping therapy, are being developed, and these will lead to more effective interventions for improving muscle strength and functioning in Duchenne muscular dystrophy patients.[31,32] The perception of Duchenne muscular dystrophy could change with the development of efficacious treatment, which may affect the disclosure process between parents and affected children.

Conclusion

Despite these limitations, to our knowledge, this is the first study that has examined physicians' recommendations to mothers of children with Duchenne muscular dystrophy regarding the disclosure of information about the condition to their child. Although there is no single or best way to deal with the difficulties the parents of children with Duchenne muscular dystrophy face, keeping these key themes in mind could aid physicians in their clinical practice. Further studies are required to establish helpful guidance for physicians on suitable ways to disclose information about the diagnosis and prognosis of Duchenne muscular dystrophy to parents and their children.

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Author Contributions

HFujin, TS, TM, HFujim, SShin, and OI designed the study and wrote the protocol. SShib and YI contributed to data collection and interpretation of data. HFujin and OI conducted qualitative analysis. HF wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Declaration of Conflicting Interests

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Ethical Approval

This study had ethical approval from the research ethics committee of the National Hospital Organization Toneyama National Hospital.

References

1. Nereo NE, Fee RJ, Hinton VJ. Parental stress in mothers of boys with Duchenne muscular dystrophy. *J Pediatr Psychol*. 2003;28:473-484.
2. Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. *Lancet Neurol*. 2010;9:77-93.
3. Eagle M, Baudouin SV, Chandler C, et al. Survival in Duchenne muscular dystrophy: improvements in life expectancy since 1967 and the impact of home nocturnal ventilation. *Neuromuscul Disord*. 2002;12:926-929.
4. Ishikawa Y, Miura T, Aoyagi T, et al. Duchenne muscular dystrophy: survival by cardio-respiratory interventions. *Neuromuscul Disord*. 2011;21:47-51.
5. Mizuno T, Komaki H, Sasaki M, et al. Efficacy and tolerance of gastrostomy feeding in Japanese muscular dystrophy patients. *Brain Dev*. 2012;34:756-762.
6. Sato Y, Yamauchi A, Urano M, et al. Corticosteroid therapy for Duchenne muscular dystrophy: improvement of psychomotor function. *Pediatr Neurol*. 2014;50:31-37.
7. Manzur AY, Kuntzer T, Pike M, et al. Glucocorticoid corticosteroids for Duchenne muscular dystrophy. *Cochrane Database Syst Rev*. 2008;:CD003725.
8. Moxley RT, 3rd, Ashwal S, Pandya S, et al. Practice parameter: corticosteroid treatment of Duchenne dystrophy: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology*. 2005;64:13-20.
9. Fallowfield L, Ford S, Lewis S. No news is not good news: information preferences of patients with cancer. *Psychooncology*. 1995;4:197-202.
10. Murray SA, Kendall M, Boyd K, et al. Archetypal trajectories of social, psychological, and spiritual wellbeing and distress in family care givers of patients with lung cancer: secondary analysis of serial qualitative interviews. *BMJ*. 2010;340:c2581.
11. Patterson JM, Holm KE, Gurney JG. The impact of childhood cancer on the family: a qualitative analysis of strains, resources, and coping behaviors. *Psychooncology*. 2004;13:390-407.
12. Fujino H, Saito T, Imura O, et al. Survey for assessing how Duchenne muscular dystrophy is explained to children with the disorder [in Japanese]. *No To Hattatsu*. 2013;45:11-16.
13. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *Int J Qual Health Care*. 2007;19:349-357.
14. Poysky J, Kinnett K. Facilitating family adjustment to a diagnosis of Duchenne muscular dystrophy: April 24-25, 2008, Miami, Florida. *Neuromuscul Disord*. 2009;19:733-738.
15. Erby LH, Rushton C, Geller G. "My son is still walking": stages of receptivity to discussions of advance care planning among parents of sons with Duchenne muscular dystrophy. *Semin Pediatr Neurol*. 2006;13:132-140.
16. Metcalfe A, Plumridge G, Coad J, et al. Parents' and children's communication about genetic risk: a qualitative study, learning from families' experiences. *Eur J Hum Genet*. 2011;19:640-646.
17. Schrans DG, Abbott D, Peay HL, et al. Transition in Duchenne muscular dystrophy: an expert meeting report and description of transition needs in an emergent patient population: (Parent Project Muscular Dystrophy Transition Expert Meeting 17-18 June 2011, Amsterdam, the Netherlands). *Neuromuscul Disord*. 2013;23:283-286.
18. Plumridge G, Metcalfe A, Coad J, et al. Family communication about genetic risk information: particular issues for Duchenne muscular dystrophy. *Am J Med Genet A*. 2010;152A:1225-1232.
19. Metcalfe A, Coad J, Plumridge GM, et al. Family communication between children and their parents about inherited genetic conditions: a meta-synthesis of the research. *Eur J Hum Genet*. 2008;16:1193-1200.

20. Daack-Hirsch S, Holtzer C, Cunniff C. Parental perspectives on the diagnostic process for Duchenne and Becker muscular dystrophy. *Am J Med Genet A*. 2013;161A:687-695.
21. Read J, Kinali M, Muntoni F, et al. Siblings of young people with Duchenne muscular dystrophy—a qualitative study of impact and coping. *Eur J Paediatr Neurol*. 2011;15:21-28.
22. Webb CL. Parents' perspectives on coping with Duchenne muscular dystrophy. *Child Care Health Dev*. 2005;31:385-396.
23. Magliano L, Patalano M, Sagliocchi A, et al. "I have got something positive out of this situation": psychological benefits of caregiving in relatives of young people with muscular dystrophy. *J Neurol*. 2014;261:188-195.
24. Fee RJ, Hinton VJ. Resilience in children diagnosed with a chronic neuromuscular disorder. *J Dev Behav Pediatr*. 2011;32: 644-650.
25. Hodges L, Dibb B. Social comparison within self-help groups: views of parents of children with Duchenne muscular dystrophy. *J Health Psychol*. 2010;15: 483-492.
26. Firth MA. Diagnosis of Duchenne muscular dystrophy: experiences of parents of sufferers. *BMJ*. 1983;286:700-701.
27. Miller JR. Family response to Duchenne muscular dystrophy. *Loss Grief Care*. 1991;4:31-42.
28. Mack JW, Joffe S. Communicating about prognosis: ethical responsibilities of pediatricians and parents. *Pediatrics*. 2014; 133:S24-S30.
29. Parsons SK, Saiki-Craighill S, Mayer DK, et al. Telling children and adolescents about their cancer diagnosis: cross-cultural comparisons between pediatric oncologists in the US and Japan. *Psychooncology*. 2007;16:60-68.
30. Ulph F, Leong J, Glazebrook C, et al. A qualitative study exploring genetic counsellors' experiences of counselling children. *Eur J Hum Genet*. 2010;18: 1090-1094.
31. Cirak S, Arechavala-Gomeza V, Guglieri M, et al. Exon skipping and dystrophin restoration in patients with Duchenne muscular dystrophy after systemic phosphorodiamidate morpholino oligomer treatment: an open-label, phase 2, dose-escalation study. *Lancet*. 2011;378:595-605.
32. Fairclough RJ, Wood MJ, Davies KE. Therapy for Duchenne muscular dystrophy: renewed optimism from genetic approaches. *Nat Rev Genet*. 2013;14:373-378.

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原 著

Original Article

神経筋疾患による脊柱変形に対する脊椎外科治療アンケート調査

A Questionnaire Study on Surgical Treatment for Scoliosis in Neuromuscular Disorders

齊藤利雄

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要 旨

神経筋疾患脊柱変形に対する，国内での脊椎外科治療アンケート調査を行った．日本側弯症学会88施設からの回答中，脊柱変形矯正固定術施行は14施設，脊髄性筋萎縮症やDuchenne型筋ジストロフィーなど合計70例の手術報告があり，呼吸不全などの手術合併症や術後ADL悪化などの報告もあるものの，おおむね良好な結果が得られていた．本手術は患者のQOL向上のための治療選択肢として非常に重要であると考えられた．

Abstract

Purpose：Spinal fusion is recommended for patients with neuromuscular disorders such as spinal muscular atrophy (SMA) and Duchenne muscular dystrophy (DMD). However, the actual condition in Japan is not clear. A questionnaire study on spine surgery in Japan was performed.

Subjects and methods：Questionnaire mails on spinal surgery were sent to institutes appeared on Homepage of Japanese Scoliosis Society. The questionnaire included experience of spine surgery of neuromuscular disorders, summary of operated cases, and adaptation standard for surgery, and so on.

Results：Eighty eight institutes answered the questionnaire (38%). Spine surgery operation was done in 14 institutes (15% of answer). Seventy operation cases were reported, including 14 patients with SMA, 22 with muscular dystrophy, 16 with cerebral palsy, 5 with spina-bifida, 3 with Chiari-malformation, and so on. Distributions of the numbers and varieties of operation cases were different among institutes. Complications of operation were respiratory failure, infection, heart failure, and so on. Fourteen SMA cases included 6 males and 8 females aged 11～23 years old (mean 13.6). Values of Cobb angle of pre-operation were 55～143 degree (mean 106.7), and those of post-ope were 17～83 (mean 43,6). While, 19 with DMD were males aged 12～22 years old (mean 13.9). Values of Cobb angle of pre-operation were 35.7～115 degree (mean 65.3), and those of post-ope were 5～50 (mean 23.7). Postoperative remarks of patients and families were almost satisfactory for sitting balance, however also included deteriorated difficulties of care. For adaptation standard for spine surgery, lower limit of age ranged from 3 to 15 years old, and upper limit from 10 to 75 years old. Lower limit of Cobb angle ranged from 25 to 90 degrees, and upper limit from 60 to 150 degrees. Unstable sitting balance was stated as indication for surgery.

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Conclusions：Among pediatricians and neurologists, information of spine surgery is not fully known. Sharing information of spine surgery between pediatricians, neurologists and orthopedic surgeons will be desired for further expansion of surgical treatment to neuromuscular scoliosis.

Key words：側弯症(scoliosis)，神経筋疾患(neuromuscular disorder)，脊柱固定術(spine surgery)

緒　言

脊髄性筋萎縮症(SMA)やDuchenne型筋ジストロフィー(DMD)など小児期発症の進行性神経筋疾患では，成長につれ脊柱変形が進行し臨床上もしばしば問題になる．国外では，これらの神経筋疾患による側弯に対し脊柱変形矯正固定術は広く行われている治療法であり[1,2,3,4,6,10]，国内でも，神経筋疾患による脊柱変形の経過やその手術療法など，脊椎外科領域では多くの報告がある[7,8,9]．しかしながら，SMAやDMDなどの小児期発症神経筋疾患の診察に当たってきた国内の小児科・神経内科を主とする医師の間では，神経筋疾患の脊柱変形に対しては保存的治療にとどめることも多く，脊椎変形に対する外科治療は，小児科・神経内科医師には一般的治療とは言い難い治療法であった[5]．その理由の一つには，小児科・神経内科の医師が脊柱変形矯正固定術に関する情報を得る機会が決して多くなかったことが挙げられる．

本検討は，神経筋疾患による脊柱変形の国内の脊柱変形矯正固定術の治療状況を調査し，小児科・神経内科医師が神経筋疾患脊柱変形の治療方針決定のための一助とすることを目的とした．

対象と方法

日本側弯症学会ホームページに掲載されている学会員施設に，アンケート用紙を郵送し書面での回答を求めた．主なアンケート内容は，1)2005年以降の神経筋疾患の側弯に対する脊柱変形矯正固定術手術経験の有無，2)手術症例の情報，3)脊柱変形矯正固定術の適応症例・不適応症例に関する意見，4)コルセット使用に関する意見である．アンケート送付は，2010年9月に行い10月20日までの回収とした．

調査施行にあたっては，日本側弯症学会に施行の旨の確認を行い，国立病院機構刀根山病院臨床研究審査委員会の承認を得た．

結　果

日本側弯症学会掲載施設248施設に郵送し，宛先不明返送14施設を除く，88施設から回答を得た(回収率38%)．内訳は大学病院28施設，公立総合病院15施設，国立病院機構5施設，医療法人など40施設であった．

1）2005年以降の神経筋疾患の側弯手術経験の有無

手術を施行していると回答したのは14施設(回答施設の15%)で，内訳は大学病院9施設，公立総合病院2施設，国立病院機構2施設，医療法人1施設であった．

2）手術症例の情報

手術症例は11施設から70例の報告があった．疾患内訳は，SMA 14例，筋ジストロフィー22例，脳性麻痺(CP)16例，二分脊椎5例，キアリ奇形3例(脊髄空洞症非合併)，脊髄空洞症2例，脊髄損傷2例，その他6例であった(表1)．手術症例数，疾患内訳は施設によって大きく異なっていた(表2)．

2-1．術前側弯の情報が得られたのは40例で，その内訳は，SMA 14例，DMD 19例，ほかキアリ奇形3例，CP 2例，Ullrich型筋ジストロフィー(UCMD) 1例，重症筋無力症(MG) 1例であった．

2-1.A．SMA 14例の内訳は，男6例，女8例，手術年齢11～23歳(平均13.6歳)で，術前の患者の状態は，自発呼吸12例，心不全かつnon-invasive positive pressure ventilation使用例1例，酸素投与1例であった．側弯は，術前は55～143度(平均106.7度)で左凸5例，右凸9例，術後は17～83度(平均43.6度)で，矯正率39.7～69.6%(平均60.9%)であった．後弯は，術前は41～156度(平均104.2

表1　手術症例

疾患内訳
脊髄性筋萎縮症14例
筋ジストロフィー22例
Duchenne 型筋ジストロフィー19例
Ullrich 型筋ジストロフィー1例
病型不明2例
脳性麻痺16例
二分脊椎5例
キアリ奇形3例(脊髄空洞症非合併)
脊髄空洞症2例
脊髄損傷2例
神経芽細胞腫術後麻痺1例
重症筋無力症1例
脊髄梗塞1例
横断性脊髄炎1例
先天性ミオパチー1例
脳炎後遺症1例

合計70例　11施設から症例情報の提供があった．合計70例　11施設から症例情報の提供があった．

表2　施設毎の手術症例数，疾患内訳

施設	全症例数	SMA	DMD	他神経筋疾患
A	1	1		
B	7	1	6	
C	1	1		
D	1		1	
E	38	8		30
F	5	2	3	
G	1			1
H	1			1
I	11		9	2
J	3			3
K	1	1		
合計	70	14	19	37

SMA：脊髄性筋萎縮症，DMD：Duchenne 型筋ジストロフィー

表3　手術時間

手術時間(時間)	例数
～5	3
5～6	12
6～7	11
7～8	11
8～9	9
9～10	6
10～	6

表4　術後合併症内訳

術後合併症	例数	疾患
呼吸不全	4	SMA，DMD，UCMD
感染	2	SMA，DMD
心不全	2	DMD
4本抜釘	1	DMD
食欲低下	1	DMD
脳梗塞	1	DMD
無気肺	1	SMA

SMA：脊髄性筋萎縮症，DMD：Duchenne 型筋ジストロフィー，UCMD：Ullrich 型筋ジストロフィー

度)，術後24～72度(平均43.8度)であった．

2-1.B．DMD 19例は，全例男性，手術年齢12～22歳(平均13.9歳)であった．術前の患者の状態では，ほとんどの患者では自発呼吸が保たれていたが，心不全かつ気管切開1例，心不全1例が含まれていた．側弯は，術前は35.7～115度(平均65.3度)で左凸10例，右凸8例，不明1例，術後は5～50度(平均23.7度)で，矯正率40.4～93.2%(平均64.4%)であった．

2-1.C．また．その他7例は，男1例，女6例，手術年齢8～53歳(平均18.9歳)で，術前の患者の呼吸状態は，自発呼吸5例，気管切開2例であった．側弯は，術前は14～125度(平均86.9度)，術後は5～75度(平均39.3度)で，矯正率40.0～67.3%(平均55.2%)であった．

2-2．手術時間は返送70例中58例に記載されていた．その内訳を表3に示す．手術時間は，4～16.7時間と幅広く，5～8時間が最も多かった．

2-3．術後合併症の記載はのべ12件数で，疾患はSMA 3例，DMD 6例，UCMD 1例であった．表4に内訳を示すが，呼吸不全が最も多く，4件であった．

2-4．術後の感想が得られたSMA 10例，DMD 3例，UCMD 1例の合計14例のまとめを表5に示す．多くの例で座位保持良好をはじめとして日常生活の改善が挙げられる一方，食事しにくくなった，介助しにくくなったなどの感想もあっ

た.

2-5．予後の情報が得られた11例は，SMAで「無気肺」1例の報告がある以外は，SMA 3例，DMD 2例，UCMD 1例，キアリ奇形3例，MG 1例で，「良好」9例，「問題なし」1例，であった.

2-3～5は，記載例数が少なく，未記入症例の合併症，術後の感想，予後に関する把握は不可能であった.

3）脊柱変形矯正固定術の適応症例・不適応症例に関する意見

神経筋疾患側弯の手術の適応年齢幅を問うた設問では，下限3～15歳(n＝34)，上限10～75歳未満(n＝23)と回答範囲は幅広く，適応症例の脊椎変形の程度を問うた設問でも，下限25～90度(n＝45)，上限60～150度(n＝21)と幅広かった(図1).

手術の積極的適応を自由記述で求めたまとめを表6に示す．内訳は，変形，合併症状，現症・術後の状態などに分類されたが，「座位バランス不良・座位保持困難」を挙げた回答が11例と最も多かった.

心肺機能に関する手術の不適状態の回答は表7の通りであった．88回答中54回答で心不全が，55

表5　14症例の術後の感想

	例数(延べ数)
座位保持が良好になった	8
気道感染症になりにくくなった	3
食事がとれるようになった	2
呼吸しやすくなった	1
気管切開を閉鎖しADLがアップした	1
便秘が治った	1
体重が増えた	1
視界が良くなった	1
寝返りしやすくなった	1
体調を崩さなくなった	1
満足	1
食事介助が難しくなった	1
着替えしにくくなった	1
手が口に届かなくなった	1
介助しにくくなった	1

回答は延べ数である.

表6　積極的適応症例

座位バランス不良・座位保持困難　11回答
(以下は1回答ずつ)
変形に関するもの
- 変形が大きな症例
- 胸郭変形矯正可能例
- 進行性の脊柱変形
- 前弯，側弯が強い症例
- 補助具で代償できない側弯
- 頚胸移行部で前弯の強いもの
- 車いすで20～30度の変形は適応
- 角度では考えない

合併症状に関するもの
- 疼痛
- 呼吸器症状，神経症状出現

現症・術後の状態に関するもの
- 運動機能，座位保持能力のある例
- ADL改善が期待できる
- 呼吸機能・心機能が～1000mlの出血に耐えられる

その他
- 画一的に決めがたい
- 保護者の希望
- 医療者・患者が信頼感で結ばれた環境

自由記述で回答を求めたものを分類した．返送88回答中38回答あった.

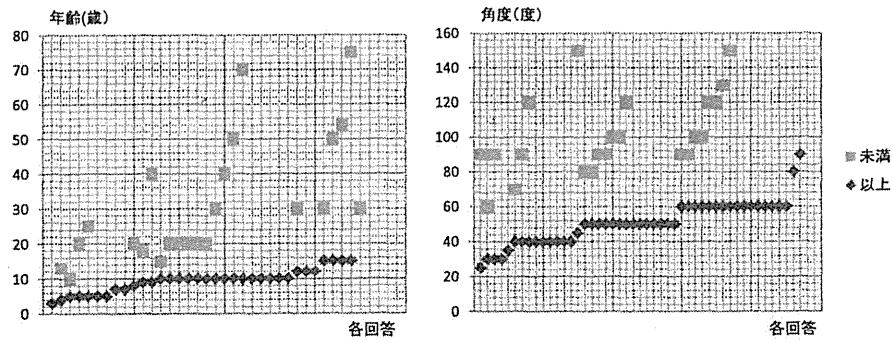

図1　神経筋疾患側弯の脊柱固定術適応症例の年齢幅と脊椎変形の程度
左：年齢幅，右：脊椎変形の程度