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PHYSICAL COMPLAINTS IN AGEING PERSONS WITH SPINAL MUSCULAR ATROPHY

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Objective: **While life expectancy is improving for persons with spinal muscular atrophy, new physical complaints may arise. To investigate this, we studied persons with a long duration and severe course (high functional limitations) of the disease.**

Design: **Cross-sectional descriptive study.**

Subjects/Patients: **Persons with spinal muscular atrophy.**

Methods: **Questionnaires and structured interviews on prevalence of physical complaints and their duration. Of 190 questionnaires 99 were returned; of 23 persons (with the longest disease duration and high functional limitation level) selected for structured medical interviews 9 participated.**

Results: **Patterns common within and different between the different types of spinal muscular atrophy were identified. Of the 10 most common complaints, types 1–2 had a significantly higher prevalence of kyphoscoliosis, difficulty in coughing, joint contractures and voice/speech problems, while type 3 had a significantly higher prevalence of fatigue. No statistically significant correlation was found between the appearance of physical complaints and disease duration. However, sleeping and swallowing problems were in the 5 most common complaints with the shortest mean time of appearance. The structured interview revealed hypermobility in the hand, suffusion of the eyes, and itching as new complaints with high prevalence.**

Conclusion: **There are indications that the frequency of less well-known physical complaints increases with ageing.**

Key words: spinal muscular atrophy, ageing, physical problems, physical complaints.

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INTRODUCTION

Life expectancy in general is currently increasing. This also applies to persons with a progressive disease such as spinal muscular atrophy (SMA), although there is a difference between SMA type 2 (symptomatic at childhood, not able to walk) and type 3 (symptomatic at childhood or adulthood, able to walk) (typing according to Emery (1)). In large studies Zerres et al. (2, 3) describe the life expectancy of people with SMA type 2 and type 3 as being better than predicted. People with SMA type 3, in particular, seem to have a normal life expectancy, although progression of the disease varies between individuals. The rate of progression is related to the severity of impairments such as scoliosis or lung function (4, 5) and functional abilities (2, 6).

Several impairments in physical functions are described in patients with SMA: contractures and scoliosis (5, 7), nutritional problems (8, 9), restricted lung function (5, 10) and restricted cardiac function (5, 11, 12). Although these impairments are described, it is not always mentioned at which stage of the disease they appear. Nowadays several impairments can be treated effectively, for example spinal surgery can not only correct the scoliosis, but also improve lung function (4), and lung rehabilitation can increase life expectancy (10, 13). Thus, with technical and medical improvements, life expectancy for people with the more progressive types of SMA improves. The question arises as to whether new physical complaints arise related to SMA that previously were masked by life-threatening symptoms or death.

To explore the possibility of new or less well-known complaints, a descriptive cohort study was performed of the physical impairments of persons with SMA types 2 and 3 with a long duration of the disease (diagnosed at least 10 years before and diagnosed before the age of 33 years). Particular attention was focussed on the group with the most severe disease progression (most functional limitations).

Two research questions were investigated: (i) Is there a correlation between the appearance of (new) physical complaints and the duration and severity of SMA? (ii) Is there a difference in patterns of physical complaints between SMA types 2 and 3?

MATERIAL AND METHODS

Study design

A descriptive cohort study was performed. Members of the Dutch patients' association for neuromuscular disorders (Vereniging Spierziekten Nederland) known to have the diagnosis SMA (not necessarily confirmed with DNA analysis) were invited to participate. Inclusion criteria were: the diagnosis was made at least 10 years ago and the diagnosis had been established before the age of 33 years. A subgroup was selected with the longest duration of the disease (as defined by the reported time between the first symptoms and the date of the questionnaire) and the highest functional limitations (established by the sickness impact profile score, see below). Cut-off points (explained in analysis) were determined for SMA type 1–2 as a disease duration of at

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Table I. *Study population*

	Responders (n=99)	Non-responders (n=91)
Men/Women (%)	45/55	57/40*
SMA-1 (%)	7	8
SMA-2 (%)	22	8
SMA-3 (%)	55	28
SMA-unknown (%)	15	43*
Mean disease duration (years)	34.4	22.2**

* Four persons missing item.
** 23 persons missing item; if the date of membership of the patients' association was taken as a date for diagnosis the mean disease duration was 23.8 years.
SMA = spinal muscular atrophy.

least 31 years and a SIP-score higher than 24; for SMA type 3+ (for grouping: see analysis) the cut-off points were a disease duration of at least 41 years and a SIP-score higher than 19. The subgroups were asked to participate in a structured medical interview. Informed consent was obtained for the structured interviews. The medical ethical committee approved the study.

Assessment instruments

Questionnaires were sent by post asking for age at the time of the study, age at first symptoms, age at diagnosis, type of SMA, inherited form of SMA, frequency of and reason for hospitalization, frequency of surgery and indication for surgery, co-morbidity (according to König-Zahn et al. (14)), complaints/physical problems (list of 51 items based on literature and an open answer question), frequency and type of medication, SIP-68 (15) for functional limitations and social demographic items. The co-morbidity list (according to König-Zahn) is a general list for public health studies, while the complaints/physical problems list was designed specially for this study. An overlap of symptoms/physical complaints is present. SIP-68 has been validated for the Dutch population including neuromuscular disorders (15). If a person was unable to complete the questionnaires they were advised to request support from a proxy.

A structured medical interview was performed by a trained physician (IdG), since it is known that patients might give false negative answers in chronic progressive disease, because they become gradually adjusted and do not experience a physical impairment as a problem. The medical interview was based on the section of functions and structure of the ICIDH-2, now called ICF (WHO 2001 (16)).

Study population

Of the 190 questionnaires posted, 99 were returned (response rate 52%). Based on the registration of the patients' association (VSN) the non-responders could be compared with the responders (Table I). The non-responders had a shorter duration of the disease than did the responders. In the non-responders slightly less SMA 1 and 2 were reported. Twenty-three persons were selected for structured interviews (cut-off points: see analysis); 4 did not give prior informed consent to an interview, and thus 19 were invited. Of the selected persons 8 were men and 11 women, mean age was 49 years (range 31–67 years), self-reported type of SMA: 1 SMA-1, 3 SMA-2, 14 SMA-3 and 1 SMA-type unknown. Ten persons agreed to a structured medical interview (response rate 53%), 9 eventually participated (1 withdrew due to travel distance): 3 men, 6 women, mean age 51.4 years (range 41–57); 2 reported to have SMA-2 and 7 SMA-3. The distribution of the SMA types in the interviews is comparable to that of the responders group. In the structured medical interviews age at first symptoms and SMA type were checked. Eight of the 9 persons could be classified as SMA type 3 and 1 as SMA type 2, although the latter had reported having type 3 and 2 of the SMA type 3 persons had said they had type 2.

Analysis

The reported type of SMA-1 is unlikely to be type 1 according to the criteria of Emery (1); it would most probably be SMA-2. For this reason we combined the results of SMA-1 and SMA-2 and named this group SMA 1–2. A some of the responders did not know their type, but based on their answers on age of first symptoms, age at diagnosis and functional abilities this group was most likely to be type 3. For this reason their results were combined with SMA-3 and this group named SMA 3+. Since the purpose of this study was to determine whether new symptoms arise with increasing age, we divided the groups into persons with a relatively short duration of the disease, a group with relatively long duration of the disease and a mid-group (by means of dividing the range of disease duration in three equal parts). For SMA 1–2 the chosen cut-off points were disease duration shorter than 23 years and longer than 31 years, for SMA 3+ these cut-off points were shorter than 31 years and longer than 42 years. These cut-off points were combined with cut-off points for high functional limitations (SIP-scores) in order to select the group with a severe disease course, since one would expect this group to have the highest frequency of physical complaints related to the disease duration.

SPSS-7.5 was used for statistical analysis. Descriptive analysis and chi-square tests were performed.

Table II. *Co-morbidity reported by the 99 persons who responded*

Co-morbidity	n (%)
Asthmatic/bronchitis	18 (18.2)
Cardiac diseases	2 (2.0)
High blood pressure	11 (11.1)
Stroke	0 (0)
Gastrointestinal	0 (0)
Liver	1 (1.0)
Renal	0 (0)
Diabetes mellitus	7 (7.1)
Back problems	7 (7.1)
Arthrosis	5 (5.1)
Rheumatoid diseases	0 (0)
Epilepsy	0 (0)
Cancer	2 (2.0)
Tuberculosis	0 (0)
Traumatic co-morbidity	5 (5.1)
Other	10 (10.1)

RESULTS

Co-morbidity

Co-morbidity as reported on the general list of physical problems (according to König-Zahn et al. (14)) lung problems and high blood pressure were the most prevalent co-morbidities (Table II). The prevalence of chronic specific lung disease is much higher than in the normal population (18% vs 6%). In the SMA 1–2 group the prevalence is higher than in the type 3+ group: 34% vs 12%. In group SMA 1–2 the mean rate of co-morbidity is higher than in group type 3+: 0.8 vs 0.7. The rate of co-morbidity tends to increase with ageing: if one divides the duration of the disease into 3, the persons with the shortest duration have mean co-morbidity rates of 0.4, compared with 0.9 for persons with the longest duration.

Physical complaints

Muscle weakness and cold hands and feet were most frequently reported for both groups (Table III). Group SMA 1–2 shows a significantly higher prevalence for kyphoscoliosis, difficulty in coughing, joint contractures and voice/speech problems

Table III. *Top 10 complaints among the persons in the groups SMA 1–2 and SMA 3+*

	Group SMA 1–2		Group SMA 3+	
Complaints	%	Rank	%	Rank
Muscle weakness	97	1	89	1
Cold hands/feet	93	2	83	2
Kyphoscoliosis	90	3	36***	9
Difficult coughing	76	4	41**	7
Joint contractures	62	5	37*	8
Muscle trembling	55	6	47	6
Cold knees/calves	48	7	49	5
Swollen feet/legs	45	8	57	4
Choking	45	9	31%	
Voice/ speech problems	45	10	17*	
Fatigue	34		61*	3
Neck pain	38		34	10

Statistical significance between group SMA 1–2 and SMA 3+: * $p<0.05$; ** $p<0.05$; *** $p<0.001$.

compared with group SMA 3+, while in the latter group fatigue is significantly more prevalent.

All physical complaints that were asked about are shown in Table IV in order of duration of the complaint (from shortest to longest based on SMA 1–2). There is a difference in pattern between SMA 1–2 and SMA 3+. No significant correlation could be found between symptoms and disease duration. In the Dutch population the prevalence of physical complaints are all below 9%, except for headache (mean 14%; Statistical Yearbook 2003). In this study problems with a prevalence of more than 10% (headaches were omitted) and a mean appearance of less than 10 years previously in group SMA 1–2 and a mean appearance of less than 15 years previously for group SMA 3+ were: concentration, sleepy during day, neck pain, intestinal complaints, swallowing, joint pain and speech/voice (Table V). The range of duration of these problems is wide, except for concentration problems of both groups and sleepiness during the day and neck pain for group SMA 1–2.

From the structured medical interviews only new or more specified complaints with a high prevalence are reported here. All 9 persons had sleep problems, especially sleeping without a break: they woke up early in the night with (profuse) sweating. Their partners also mentioned snoring and irregular breathing during their sleep. All 9 persons had complaints of the throat while swallowing: they had the idea that food was sticking there, and 8 complained of retarded passage of the food in their stomach and intestines. Seven persons mentioned palpitations. Six had hypermobility in the joints of their upper extremities, especially in their hands. Five persons mentioned suffusion of the eyes and 1 had burning eyes. Five persons mentioned itching of their buttocks and legs and sometimes their head.

DISCUSSION

The results of this study point to the appearance of physical complaints related to increasing duration of the disease combined with a more severe disease course. There are differences and similarities in the patterns of physical complaints between SMA 1–2 and 3+.

The response rate for the questionnaires was 52%. The non-responders reported more SMA type unknown, and had a shorter duration of the disease. The SMA type unknown can be regarded as SMA type 3 (see methods/analysis), and the disease course of SMA 3 is generally less progressive (2, 3). The possibility of a selection bias is likely, however, the bias may work positively for the study by increasing the chance of the detection of new physical complaints (since the aim was to explore persons with SMA with the longest disease duration and a severe disease course). The number of the participants in the structured interviews is very small, but all selected persons can be regarded as being at risk for developing late (new) complaints. Their distribution of SMA type was comparable to the primary responders group.

SMA is divided into 3 types according to the onset of the first symptoms (1). However, nowadays SMA is regarded as a disease with a gradual severity related to the onset of the symptoms: onset at a young age predicts a more severe course (2, 3). Although classified in 3 types there are no strong cut-off points and the manifestation of the disease is regarded as a range. Thus it can be expected that the appearance of physical complaints is also gradual with a wide range of time of appearance.

When we compare SMA 1–2 with SMA 3+, a similar pattern of complaints can be found, but there are also differences. The group with SMA 1–2 can be regarded as the group with a more severe disease course. This is reflected in the higher prevalence of lung complaints in the co-morbidity questionnaire for SMA 1–2. Respiratory muscle involvement is known in SMA, and thus it is not a co-morbidity. However, the used co-morbidity list makes it possible to compare SMA with the general Dutch population. Significantly different for SMA 1–2 are the higher percentages of kyphoscoliosis, joint contractures, difficulty in coughing and speech and voice problems. This can be explained by the fact that in SMA 1–2 the back muscles are already (very) weak in youth. During growth a kyphoscoliosis can develop that influences the functioning of the lungs. The restricted lung function combined with the weakness of thorax muscles thus can give rise to more difficulty in coughing. In the most severe course of SMA, namely type 1, bulbar problems such as swallowing problems are well known (17) and they are also described in SMA type 2 at a lower frequency (9, 18). The high percentage speech and voice problems in SMA 1–2 may be related to bulbar involvement or to the restriction in lung function. The cause cannot be deduced from the questionnaires.

A wide range of duration of the complaint is reported for all physical complaints, including the more recent complaints. The fact that persons are asked to recall the time of appearance introduces possible bias. Another possible bias is that the grouping was done based on the person's own reported SMA type. The interviews showed that this is not a very reliable way for correct typing. Furthermore no DNA confirmation of the diagnosis was requested, again a possible source of bias.

Table IV. *Physical complaints group SMA 1–2 and group SMA 3+*

	Group SMA 1–2			Group SMA 3+		
Physical complaints	Mean years (range)	No. (%) (n=29)	>10%=*	Mean years (range)	No. (%) (n=29)	>10%=*
Hearing	3.5 (1–6)	2 (7)		37.5 (15–60)	2 (2.9)	
Sleepy during day	4.4 (1–10)	7 (24)	*	8.2 (1–25)	13 (18.6)	*
High blood pressure	5.3 (3–10)	3 (10)		6.5 (2–10)	3 (4.3)	
Neck pain	5.8 (3–10)	11 (38)	*	10.5 (2–25)	24 (34.3)	*
Periods	6.0 (6)	2 (7)		18.2 (3–29)	7 (10.0)	
Excessive perspiration	7.3 (2–15)	7 (24)	*	23.6 (2–55)	14 (20.0)	*
Palpitations	7.3 (1–18)	3 (10)		17.3 (1–36)	13 (18.9)	*
Joint pain	7.5 (1–22)	9 (31)	*	11.8 (2–30)	17 (24.3)	*
Concentration	7.8 (5–10)	4 (14)	*	2.7 (1–5)	10 (14.3)	*
Speech/voice	8.5 (1–23)	13 (45)	*	12.2 (1–27)	12 (17.1)	*
Skin pressure problems	8.6 (6–15)	5 (7)		15.2 (2–40)	14 (20.0)	*
Opening mouth	9.1 (2–20)	12 (41)	*	16.7 (10–43)	8 (11.4)	*
Muscle pain	9.4 (2–25)	10 (34)	*	19.1 (1–44)	22 (31.4)	*
Swallowing	9.6 (2–20)	12 (41)	*	11.8 (1–26)	17 (24.3)	*
Sleep problems	9.7 (4–15)	3 (10)		14.8 (1–35)	12 (17.1)	*
Intestinal	9.8 (4–15)	5 (17)	*	11.7 (2–33)	12 (17.1)	*
Headache	10.8 (4–21)	4 (14)	*	9.7 (1–25)	17 (24.3)	*
Muscle cramps	11.0 (2–20)	2 (7)		18.4 (1–44)	20 (28.6)	*
Back pain	11.3 (5–20)	9 (31)	*	12.9 (4–26)	19 (27.1)	*
Dental	11.3 (2–16)	3 (10)		16.0 (5–25)	3 (4.3)	
Overweight	12.0 (4–20)	3 (10)		15.9 (2–40)	16 (22.9)	*
Defecation	12.5 (4–27)	11 (38)	*	16.1 (1–37)	16 (22.9)	*
Muscle trembling	13.3 (2–25)	16 (55)	*	21.3 (2–50)	33 (47.1)	*
Fatigue	13.4 (3–24)	10 (34)	*	17.8 (1–54)	43 (61.4)	*
Hyperventilation	13.5 (2–25)	2 (7)		8.7 (10–43)	9 (8.7)	
Diaphragmatic	14.0 (10–18)	3 (10)		18.3 (10–30)	5 (7.1)	
Eczema	14.1 (5–25)	8 (28)	*	15.3 (1–40)	7 (10.0)	
Muscle stiffness	14.6 (1–30)	9 (31)	*	17.1 (1–44)	23 (32.9)	*
Short of breath	14.9 (4–24)	10 (34)	*	10.7 (1–20)	10 (14.3)	*
Choking	15.0 (5–25)	13 (45)	*	10.1 (1–27)	15 (21.4)	*
Chewing	15.6 (2–21)	11 (38)	*	12.8 (5–30)	16 (22.9)	*
Tasting	16.0 (16)	1 (3)				
Cold calf/knee	16.1 (2–27)	14 (48)	*	25.1 (3–60)	34 (48.6)	*
Bladder voiding	16.3 (9–25)	3 (10)		7.2 (1–20)	11 (15.7)	*
Stomach	16.8 (8–40)	6 (21)	*	16.4 (6–30)	9 (12.9)	*
Underweight	17.2 (8–25)	5 (17)	*	19.9 (1–30)	8 (11.4)	*
Swollen feet/legs	17.3 (5–35)	13 (45)	*	19.5 (4–47)	40 (57.1)	*
Pulmonary infections	18.2 (6–24)	5 (17)	*	15.0 (3–27)	5 (7.1)	
Cold hands/feet	18.5 (2–35)	27 (93)	*	23.1 (4–60)	58 (82.9)	*
Kyphoscoliosis	19.4 (2–34)	26 (90)	*	27.5 (3–51)	25 (35.7)	*
Joint luxation	20.0 (15–23)	3 (10)		26.5 (1–50)	5 (7.1)	
Difficult coughing	20.4 (5–37)	22 (76)	*	21.7 (5–50)	29 (41.4)	*
Joint contractures	21.5 (10–45)	18 (62)	*	27.6 (2–47)	26 (37.1)	*
Seeing	21.0 (18–25)	3 (10)		12.3 (2–48)	13 (18.6)	*
Muscle paralysis	22.2 (20–27)	8 (28)	*	23.5 (1–50)	18 (25.7)	*
Catarrh/bronchitis	22.0 (16–27)	5 (17)	*	25.1 (1–40)	14 (20.0)	*
Muscle weakness	23.6 (3–50)	28 (97)	*	30.3 (4–55)	62 (88.6)	*
Rest group						
Potency	Not mentioned	1 (3)		4.0 (3–5)	2 (2.9)	
Low blood pressure		0		3.7 (5–8)	7 (10.0)	
Menopause		0		8.5 (2–15)	4 (5.7)	
Joint inflammation		0		3.0 (3)	2 (2.9)	

No significant correlation could be found between the duration of the complaints and disease duration, probably due to the wide range of time for all the physical complaints. We matched the physical complaints with the shortest mean time of appearance as indicated in the questionnaire with the interviews. The swallowing and sleeping complaints stand out, indicating that the concentration complaints and sleepiness during the day revealed in the questionnaires may be highly related to the sleep complaints reported in the interviews. It is striking that all 9 persons with the longest disease duration and most severe disease course had swallowing and sleeping complaints. In the interviews all phases of sleep and swallowing were investigated, which is different from the questionnaire in which the questions were more general. This can give rise to different prevalence numbers. Sleep investigations involving SMA revealed periods of hypoxaemia (19–21). Whether this is the cause of the waking up sweating and the concentration problems and feeling sleepy during the day is likely, but needs to be established.

Table V. *Physical complaints, less than 10 years in SMA 1–2, less than 15 years in SMA 3+, and more than 10%*

	Time (years)	
	SMA 1–2	SMA 3+
Physical complaint	Range (average) %	Range (average) %
Concentration	5–10 (7.8) 14	1–5 (2.7) 14
Sleepy during day	1–10 (4.4) 24	1–25 (8.2) 19
Neck pain	3–10 (5.8) 38	1–25 (10.5) 34
Intestinal	4–15 (9.8) 17	2–33 (11.7) 17
Swallowing	2–20 (9.6) 41	1–26 (11.8) 24
Joint pain	1–22 (7.5) 31	2–30 (11.8) 24
Speech/voice	1–23 (8.5) 45	1–27 (12.2) 17

The interviews also revealed new problems: hypermobility in the joints of the hand, problems with the suffusion of the eyes and itching. Thus structured interviews elicited information about complaints that were not noticed in the questionnaires.

Identification of complaints is useful information for use in developing interventions. For example, for the hypermobility in the joints of the hands stabilizing orthoses can be tried out for a functional gain in hand function. More insight into the pathophysiological mechanisms of sleep problems and swallowing problems can give clues for therapy.

Further research is needed to establish the extent of these complaints for the whole population of persons with SMA and to guide the therapeutic approaches.

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