Chronic stress and quality of life in muscular dystrophy patients using ventilatory support in different medical care environments

Suzuki, Tomiko

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Chronic stress and quality of life in muscular dystrophy patients using ventilatory support in different medical care environments

（異なる療養環境において人工呼吸器を使用する筋ジストロフィー患者の慢性ストレスと QOL）

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鈴木智子

Doctoral thesis

Chronic stress and quality of life in muscular dystrophy patients using ventilatory support in different medical care environments

Tomiko SUZUKI1) 2)

1) Division of Family Health Care Nursing, Kobe University Graduate School of Health Sciences

2) Faculty of Health and Welfare, Tokushima Bunri University

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Contents

Abstract

Living at home enables Muscular dystrophy (MD) patients to maintain family and social relationships, and to make decisions regarding their lifestyle. Consequently, it is considered that patients living at home have an improved quality of life (QOL) and reduced chronic stress levels when compared to patients confined to a hospital. The study aims to compare the relationships between chronic stress and QOL of hospitalized MD patients vs home-care MD patients using non-invasive positive pressure ventilation (NPPV). It is hoped that these findings will support the transition of medical care to the home. Results of the study show that the cortisol awakening response (CAR), an index of chronic stress, was significantly attenuated in the inpatient and home-care patient groups, compared with the healthy control group, and that in SF-36 Health Survey the general health perceptions (GH) concept was significantly higher in the inpatients than in the home-care patients. Therefore, it can be surmised that muscular dystrophy patients using NPPV are in a state of chronic stress, irrespective of the care environment. Also, nursing is still required even for patients who are cared for at home in order to improve their sense of well-being.

Keywords: salivary cortisol, home-care, muscular dystrophy, chronic stress, SF-36

Introduction

Muscular dystrophy (MD) is a chronic disease that causes progressive skeletal muscle weakness in the entire body and for which no cure exists. Since the late 1980s, mechanical ventilators have been gradually introduced; the average life expectancy of patients with MD has been extended by nearly 10 years to approximately 30 years, particularly owing to the adoption of Noninvasive Positive Pressure Ventilation (NPPV). This has led to more transfers of medical care from medical institutions to the home1). However, since muscle weakness continues to progress, daily activities become increasingly difficult, and although patients and their families generally prefer living at home, the deterioration of muscular and cardiorespiratory functions require many patients to be hospitalized for an extended duration in order to receive intensive medical care. With home-care, patients can spend their daily lives maintaining relationships with family members and interact with society. Within these relationships, patients can fulfill their own roles and live at their own pace in accordance with their desires. In this manner, living at home is the preferred pattern of living for many MD patients, and from reports indicating that self-efficacy is improved2), we postulated that the home environment leads to improvement in quality of life (QOL) and reduction in chronic stress.

Studies have been conducted in Japan to assess the QOL of MD patients 3)4). However no studies have been performed, in Japan or elsewhere, that simultaneously evaluated both MD patients' psychological stress and QOL. Therefore, through this study, we assessed the differences in chronic stress levels between MD inpatients and home-care MD patients, comparing health-related QOL using Short Form 36 Health Survey version 1.2 (SF-36)5) with salivary cortisol as an endocrine index. As an objective index of chronic stress, salivary cortisol has been validated in fields such as industrial health sciences. Recently, chronic stress-induced allostatic load such as hypothalamic-pituitary-adrenal axis (HPA) dysfunction has been reported6). One of the evaluation indices for this allostatic load is the cortisol awakening response (CAR) by which cortisol increases 20 to 40 minutes after awakening. CAR is one of the allostasis responses that influences the switch from resting to active states, and has been noted as a sensitivity indicator of HPA activity7). In this study, measurements were performed four times: immediately upon awakening, and then again after 30, 45, and 60 minutes.

The maximum increased amount of salivary cortisol was considered to be the CAR.

This study compared the health status of hospitalized MD patients vs. home-care MD patients using NPPV. The health-related QOL5) was surveyed using SF-36, while the salivary cortisol level upon awakening was used as an endocrine index to assess the status of chronic stress. The objective was to utilize the findings as a nursing practice to support the transition of the medical care location to the home.

Methods

Participants

The patient group consisted of MD patients on NPPV who were either inpatients at a hospital or home-care patients receiving care at a hospital on an outpatient basis. Patients were referred to the study by their attending physicians after confirming their physical conditions. Researchers provided written and verbal explanations of the study objectives to these referred patients, and written consent was obtained from those who gave consent to participate in the study.

The control group consisted of healthy young individuals who were attending a four-year university program, do not take steroids, and do not smoke. Written consent was obtained after both written and verbal explanations of the study objectives were provided.

The study was conducted from February to September, 2011.

Measures

Salivary cortisol. Saliva samples were collected using a saliva collection-specific device (Salivette, Sarstedt K.K.). A cotton swab was placed in the patient’s mouth for one minute, then removed and frozen at −20°C. The collection time for each participant was fixed. All saliva samples were thawed on the same day, centrifuged at 3,000 rpm for 10 minutes, pre-processed with a salivary cortisol kit (Salimetrics, LLC), and finally analyzed via enzyme-linked immunosorbent assay (ELISA) method9). Measurements were conducted using the same measurement kits and reagents for all of the samples. Salivary cortisol concentration was expressed as μg/dl. In general, salivary cortisol concentration is at its highest upon rising, and subsequently decreases with time. We calculated the maximum increase in cortisol levels after awakening, and it was concluded that the CAR was attenuated when the amount of increase diminished7). This was interpreted to indicate that the level of chronic stress was high.

Health-related QOL. In order to evaluate the latent impact of psychological stress in daily life, we used SF-36, a comprehensive health scale that is the most widely used in Japan as well as in many other countries. As the survey duration was about 10 minutes, the burden among participants was minimal. Moreover, it could be carried out in either a self-report style or through an interview style for patients who had difficulties in completing the survey. Permission to use SF-36 Japanese version and its user manual were obtained from the Institute for Health Outcomes and Process Evaluation9). SF-36 consists of 36 questions to measure eight health concepts, which are: physical functioning (PF), role-physical (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH). Replies to all 36 questions are given in accordance with a 5-level response scale. Based on the Japanese national standard value8), the survey was scored from 0 to 100, with higher scores indicating fewer problems.

Data collection procedures

The researcher visited the inpatient on routine days, on which saliva samples were collected four times: once upon awakening, and 30, 45, and 60 minutes after awakening7). On the morning of saliva collection, the SF-36 survey was also conducted in the form of an interview by the researcher. Similarly to the inpatients, the SF-36 survey was conducted and saliva samples were collected four times a day by the caregiver at home. Saliva samples were frozen and shipped to the researcher. For the young individuals who gave consent to participate in this study, the saliva collection method and timing were explained. After self-collection at home, samples were frozen in a refrigerator and brought to the researcher in a frozen state, together with the questionnaire.

Statistical analyses

Participants were divided into inpatients, home-care patients, and controls, and compared using SPSS for statistical analysis. For the comparison of SF-36 scores among groups, One-way ANOVA was used for comparison, and the Tamhane’s post hoc test used for multiple comparisons. For the comparison of time-dependent changes in salivary cortisol concentration between the three groups, one-way ANOVA was performed. The maximum increased amount of salivary cortisol concentration was also analyzed using one-way ANOVA and Dunnett's post hoc multiple comparison test. Pearson correlation coefficient was calculated to assess the relationships between the maximum increased amount of salivary cortisol concentration and eight subscale scores of SF-36. In all analyses, a *p* value of less than 0.05 was considered statistically different.

Ethical considerations

Prior written informed consent was obtained from each of the participants. For home-care patients, the study participants received an explanation when they visited the outpatient clinic and those who gave consent were established as study participants. The study protocol was approved by the Institutional Review Board of the university and the hospital.

Results

Characteristics of the participants

Twenty MD patients (12 inpatients and eight home-care patients) and 20 individuals or the controls (19 men and one woman) were investigated (Table 1). The mean ages of the participants were: 26.5 years old for inpatients, 23.4 years old for home-care patients, and 22.8 years old for the controls. The level of physical activity for the MD patients was operating of an electric wheelchair. They could remain seated with assistance when getting into the wheelchair. As a part of recuperation, some were able to operate a personal computer on their own. Eight of the inpatients practiced wheelchair football two days per week. When the home-care patients were taken to the hospital by car, they remained connected to the NPPV. Only one home-care patient was able to walk on her own, and could also perform some housework. All of the control participants were able to lead healthy lives as university students.

Comparison of health-related QOL (SF-36)

The SF-36 scores for health-related QOL were lower in patient groups compared to the control group for all 36 items, and the subscale concepts that demonstrated significant differences between the 3 groups were: PF (F = 1880.2, $p < 0.001$), RP (F = 10.2, $p < 0.001$), BP (F = 5.2, $p = 0.01$), GH (F = 8.9, $p = 0.001$), and RE (F = 3.5, $p = 0.037$). After the Tamhane's post hoc multiple comparison test, PF, RP, BP, and RE were significantly lower in inpatients compared to controls. PF, RP, BP, and RE scores, while not statistically significant, were higher in the home-care patients than the inpatients. VT, SF, and GH were higher for the inpatients compared with the home-care patients, and the results for GH were significantly higher (F = 5.1, $p < 0.05$, Table 2).

Comparison of CAR

Salivary cortisol of the controls demonstrated a pattern that significantly elevated after awakening ($p < 0.05$, Table 3). CAR was observed where cortisol increased from the time of awakening to 60 minutes after awakening. Regarding changes in salivary cortisol in home-care patients and inpatients, home-care patients showed a CAR pattern with the mean of 0.32 μg/dl, 0.50 μg/dl, 0.56 μg/dl, and 0.51 μg/dl for the respective collection time points; however inpatients did not show changes between the four saliva collection time points with the mean levels being 0.39 μg/dl, 0.43 μg/dl, 0.37 μg/dl, and 0.36 μg/dl, respectively. Both groups had attenuated CAR. We then conducted one-way ANOVA followed by a Dunnett's post-hoc comparison test to compare the maximum increased amount of salivary cortisol and observed significant differences between the 3 groups (F = 4.6, $p = 0.016$). The controls (mean = 1.60 μg/dl) had significantly greater elevation than the home-care patients (mean = 0.32 μg/dl, $p = 0.04$) or inpatients (mean

= 0.09 μg/dl, *p* = 0.01) (Table 4).

Related health-related QOL and CAR

In terms of Pearson correlation coefficient between all participants' (*n* = 40) maximum increased amount of salivary cortisol concentration and eight subscale scores of SF-36, a significant relationship was only observed in terms of BP (r = 0.59, *p* = 0.006) (Table 5).

Discussion

Health-related QOL in inpatients and home-care MD patients

In all subscales of SF-36 evaluating health-related QOL, the mean scores were lower in the patient groups compared to the control group. However, no significant differences were observed in the VT, SF, and MH subscales. It has been reported that no correlation was observed between physical impairment and QOL when QOL of MD patients using ventilators was evaluated with SF-36$^{10)}$. In this study, we observed a significant difference in physical health-related QOL between patient groups and the control group, but did not observe differences in the subscale that measures the degree of mental health. MD patients exhibit physical symptoms such as difficulties in walking from approximately 10 years of age, and have required assistance of others[11)]. It is considered that accepting a lifestyle that is adjusted for their surroundings eventually led to living independently while still receiving assistance, and could lead to greater independence. A new health concept proposed by the British Medical Journal in 2011 aims to ascertain health through the abilities to adapt and self-manage when patients are faced with social, physical, and emotional problems[12)]. Even if a patient is physically impaired, medical care that encourages the independence of patients who confront their issues appears to lead to improvements in health. When comparing the two patient groups, home-care patients had greater PF, RP, and RE scores than inpatients. However, VT, SF, and GH scores were higher in inpatients. These point to vitality, social functioning, and mental health, and indicate that patients perceive that they can lead a mentally healthy social life even if they are hospitalized and receiving medical care. In a study that investigated the changes in subjective QOL in MD patients during hospitalization, the subjective QOL including medical care satisfaction and psychological stability significantly improved in 2004 compared to 1992[13)].

In Japan, home NPPV was introduced in 1999, enabling patients to live a lifestyle at home similar to inpatients. NPPV users have since been able to opt for medical care at home. In 2006, the Services and Supports for Persons with Disabilities Act was enacted with the objective of enabling people with disabilities to live independently. Consequently, hospitalizations have shifted from a welfare placement system to a contract system, which has greatly encouraged the transition to home-care living. In a study that compared health-related QOL in home-care patients with severe disabilities before and after the enactment of the new law, it was demonstrated that PF, GH, and MH significantly decreased following enactment of the law, compared to before enactment14). With the revision in the system, it is also thought that the QOL of home-care patients had temporarily improved. In addition, the overall sense of well-being evaluated in GH was significantly higher in inpatients compared to home-care patients, showing that patients feel they lead a healthier life in a hospitalization environment. This indicated that these results are perhaps associated with the fact that there are medical staff members close by who can deal with physical problems, and that social activities using personal computers are possible with inpatient living. It is difficult, however, engage in simple comparisons of inpatient and home-care environments because they are largely impacted by family environment and social support. It is therefore, essential to consider the location of medical care on an individual basis. Especially, for adolescent inpatients who are at a stage when individuals are trying to develop their own physical and psychological capabilities for independence, it is important to provide patients with thorough explanations in order to encourage them to make decisions while considering their individual physical risks and test results.

Chronic stress as determined by salivary cortisol measurement in inpatients and home-care MD patients

The CAR is a discrete phenomenon superimposed on the circadian rhythm characterized by a sharp increase in the morning7). The maximum increase in salivary cortisol from the time of awakening was significantly lower in patient groups compared to the control group. It has also been reported that chronic stress and chronic fatigue conditions attenuate CAR8). The attenuation of CAR among the inpatient and home-care patient groups was similar to those of patients with depressive symptomatology15), and those with heavy burdens from caring for a family member with dementia[16)], and such a condition is believed to indicate the burden of chronic stress. Moreover, among the eight subscales of SF-36 among all participants, a significant relationship was observed in the maximum increased amount of salivary cortisol concentration only for BP. As this can be understood to indicate that physical pain causes chronic stress, it suggests the possibility that chronic stress can be reduced through control of physical pain. In addition, the level of cortisol itself increases in response to acute stress[17)]. In research directed at healthy adolescents[6)], the salivary cortisol concentration upon arising was approximately 0.5μg/dl, which increased to approximately 1.0μg/dl after 30 minutes. These values were lower than the values of control group used in this study, but were higher than the values of the inpatient and home-care patient groups. It is surmised that the high values for salivary cortisol in the control group was due to such factors as the participants' collection of the saliva by themselves at home, and that the collection took place just prior to their sitting for national examinations. However, further study is needed to determine any specific factors.

The study suggested the possibility of a chronic stress condition in patient groups with regards to CAR. It was considered that chronic stress was due to decreased physical function over an extended duration. The mean hospitalization period of the inpatient participants was long (mean = 9.4 years), an indication that hospitalization of 10 years or more can be longer than the time living at home with their family, and that in the interim they may have formed a new community. Many inpatients played wheelchair football twice weekly and engaged in communication using personal computers. Numerous patients were satisfied with hospital life. Tatara18) reported that cardiac failure is a common cause of death of MD patients in Japan and that the survival rate is greater in inpatients compared to home-care patients. Hospitalization forces the patients to live away from home and family. However, many MD patients have decreased respiratory function and started using NPPV in their adolescent years when they acquired their own identity. Thus, living together in a community with other patients suffering from the same disease, in an environment where they can consult with others and feel secure being supervised by medical staff, were considered necessary for providing psychological and physical support.

Implications for nursing practice

Even if a patient desires medical care at home, family cooperation is required for this to be realized. Bothwell et al.[19)] questioned family members of children with MD about what they desire in an institution. Their results showed that while parents of children younger than six years old wished to extend the duration that the child can walk as long as possible, parents of children age six and above primarily desired psychological assistance for the patient's caregiver in order to cope with social isolation. Furthermore, support is provided for the risks associated with assisted breathing as well as the economic independence of the patient. Medical and social support must also change as the disease progresses. In terms of respiratory care for pediatric neuromuscular diseases, adapting to the use of NPPV has been encouraged recently, and NPPV has been listed as the first choice of respiratory care under the international care guidelines for congenital MD even in patients who cannot express their own will[20)]. Evans et al.[21)] stated that home caregivers of ventilator-assisted progressive neuromuscular disease patients experience an enormous physical and mental burdens and that alleviating these burdens is important to enable the continuation of home life.

In order to maintain the patient's living at home, families, in addition to their own limitations of daily life and medical care, require information regarding NPPV and responsive care in emergencies. The results of this study showed that GH of the home-care patients was significantly lower than that of the inpatients. In order to ensure that a high level of medical care is maintained at home, it is necessary to enhance the health care. Also, since MD often has its onset during childhood, with gradual deterioration of physical functions, as the parents age a need exists to establish a society-based system that provides aid in addition to the family's efforts. Even if outside the family, when NPPV management becomes possible in at-home care, it can become easier for patients themselves to choose the site of their medical treatment.

This study revealed that patients experience chronic stress, irrespective of whether they are cared for in a hospital or at home. No differences were observed, in terms of CAR, in the comparison between living at home with the family and the hospital environment. It can be thought that prolonged living in a physically challenged state is stressful. However, it is necessary to investigate when the state of chronic stress began, determine whether alleviation is possible, and continue follow-ups.

It is hoped that, as home nursing support increases in the future, technological improvements in advanced medical care and upgrading of the home-care assistance system to support the long-term NPPV life of muscular dystrophy patients will also evolve.

Limitations

The authors used CAR as an index of chronic stress. However, because this was limited to salivary cortisol collected in a non-invasive manner, we could not assess the correlation with blood cortisol. Also, the study was carried out at a single institution with a disease specialty division that enrolled only twenty patients in the patient groups, limiting the ability to make generalizations based on the results. Therefore, it will be necessary to investigate a larger number of patients and perform evaluations using other objective stress indices.

Conclusions

Assessments of health-related QOL, using SF-36 and CAR, were made on 20 MD patients on NPPV who were either an inpatient or home-care patient. The results showed that the score from the health-related QOL subscale GH, which measures overall sense of well-being, was significantly greater in inpatients compared to home-care patients, indicating that inpatients were likely to have a greater perception of ability to lead a healthy lifestyle compared to home-care patients. CAR was significantly attenuated in the patient groups compared to the control group. Although no significant differences were observed in the maximum increased amount of salivary cortisol between inpatients and home-care patients, both patient groups had significantly lower increases compared to the control group, indicating that patient groups were under conditions of chronic stress. Our results suggest the necessity of comprehensive and continual nursing care in order to improve the sense of well-being for patients who receive medical care at home.

Acknowledgments

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Table 1 Characteristics of sample of patients with muscular dystrophy and controls

		Inpatients	Home-care patients	Controls
		$n = 12$	$n = 8$	$n = 20$
Age (years)				
	mean (SD)	26.5 (5.4)	23.4 (6.6)	22.8 (5.9)
	range	20-37	17-35	19-27
Hospitalized period (years)				
	mean (SD)	9.4 (6.1)	nothing	nothing
	range	1.4-18.5		
Use of NPPV support (years)				
All day	mean (SD)	8.1 (4.5) ($n = 7$)	8.2 (4.5) ($n = 5$)	nothing
	range	4.5-17.1	4.0-13.2	
Sleep only	mean (SD)	5.5 (3.8) ($n = 5$)	4.5 (2.3) ($n = 3$)	
	range	3.1-12.2	2.0-6.6	
Social activity		wheelchair football ($n = 8$)	vocational aid center ($n = 3$)	student ($n = 20$)
		chorus ($n = 2$)	student ($n = 2$)	
		nothing ($n = 2$)	nothing ($n = 3$)	

NPPV: non-invasive positive pressure ventilation

Table 2 Comparison of SF-36 profile scale among patients and controls

<table>
<tr><th>SF-36 profile</th><th>Inpatients
$n = 12$</th><th>Home-care patients
$n = 8$</th><th>Controls
$n = 20$</th><th>p value</th></tr>
<tr><td></td><td colspan="3">***</td><td></td></tr>
<tr><td></td><td></td><td colspan="2">***</td><td></td></tr>
<tr><td>PF</td><td>0 (0)</td><td>3.8 (3.8)</td><td>98.8 (0.6)</td><td>< 0.001</td></tr>
<tr><td></td><td colspan="3">***</td><td></td></tr>
<tr><td>RP</td><td>60.4 (5.0)</td><td>66.4 (8.6)</td><td>90.9 (4.2)</td><td>< 0.001</td></tr>
<tr><td></td><td colspan="3">**</td><td></td></tr>
<tr><td>BP</td><td>68.5 (5.0)</td><td>67.9 (8.5)</td><td>88.1 (4.5)</td><td>0.010</td></tr>
<tr><td></td><td colspan="2">*</td><td colspan="2">***</td></tr>
<tr><td>GH</td><td>63.3 (4.2)</td><td>50.9 (2.7)</td><td>76.2 (3.9)</td><td>0.001</td></tr>
<tr><td>VT</td><td>64.1 (3.8)</td><td>61.0 (6.7)</td><td>71.3 (3.1)</td><td>ns</td></tr>
<tr><td>SF</td><td>70.8 (5.9)</td><td>65.6 (10.0)</td><td>88.1 (4.1)</td><td>ns</td></tr>
<tr><td></td><td colspan="3">*</td><td></td></tr>
<tr><td>RE</td><td>66.7 (5.4)</td><td>76.0 (9.7)</td><td>86.7 (4.6)</td><td>0.037</td></tr>
<tr><td>MH</td><td>63.8 (4.8)</td><td>64.4 (8.4)</td><td>75.5 (3.6)</td><td>ns</td></tr>
</table>

Data are shown as mean (standard error). Possible score range is 0 to 100, with higher scores indicating fewer problems.

SF-36: Short Form 36 Health Survey, PF: physical functioning, RP: role-physical, BP: bodily pain, GH: general health perceptions, VT: vitality, SF: social functioning, RE: role-emotional, MH: mental health

One-way ANOVA or Tamhane's multiple comparison test: $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$

Table 3 Comparison of salivary cortisol awakening response of patients and controls

	Salivary cortisol (µg/dl)			
Time after awakening (min)	0	30	45	60
Inpatients (*n* = 12)	0.39 (0.28)	0.43 (0.29)	0.37 (0.32)	0.36 (0.24)
Home-care patients (*n* = 8)	0.32 (0.22)	0.50 (0.29)	0.56 (0.33)	0.51 (0.21)
Controls (*n* = 20) *	1.06 (0.89)	1.85 (1.39)	2.01 (1.37)	2.23 (1.59)

Data are shown as mean (standard error).

One-way ANOVA: *$p < 0.05$

Table 4 Comparison of salivary cortisol maximum increase among patients and controls

	Inpatients *n* = 12	Home-care patients *n* = 8	Controls *n* = 20
		**	*
Salivary cortisol maximum increase (μg/dl)	0.09 (0.08)	0.32 (0.13)	1.60 (0.46)

Data are shown as mean (standard error).

Dunnett’s post hoc multiple comparison test: *$p < 0.05$, **$p < 0.01$

Table 5 Correlation coefficients for the total sample

(N=40)	1	2	3	4	5	6	7	8	9
1. PF	1								
2. RP	0.62**	1							
3. BP	0.47**	0.42**	1						
4. GH	0.52**	0.46**	0.54**	1					
5. VT	0.28	0.36*	0.49**	0.53**	1				
6. SF	0.48**	0.68**	0.62**	0.45**	0.33*	1			
7. RE	0.42**	0.78**	0.54**	0.34*	0.29	0.72**	1		
8. MH	0.34*	0.64**	0.34*	0.40*	0.67**	0.55**	0.55**	1	
9. Salivary cortisol maximum increase	0.01	-0.04	0.59**	0.09	-0.04	0.33	0.21	-0.02	1

SF-36: Short Form 36 Health Survey, PF: physical functioning, RP: role-physical, BP: bodily pain, GH: general health perceptions, VT: vitality, SF: social functioning, RE: role-emotional, MH: mental health

Pearson correlation coefficient test: *p < 0.05, **p < 0.01