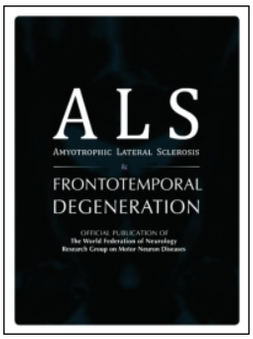

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THEME 10 RESPIRATORY AND NUTRITIONAL MANAGEMENT

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THEME 10 RESPIRATORY AND NUTRITIONAL MANAGEMENT

P239 EFFECT OF INSULIN SUPPLEMENTATION ON BODY COMPOSITION AND HAND GRIP MUSCLE FORCE IN ALS PATIENTS

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Keywords: body composition, fatigue index, muscle force

Background: Amyotrophic lateral sclerosis (ALS) is a progressive and fatal neurological disease caused by the degeneration of motor neurons. The appearance of so-called "bulbar" weakness can occur at any time during the clinical course of ALS and carries an adverse prognostic implication for patients' survival. Surprisingly, the nutritional consequences of ALS have received poor attention. Some authors found that 70% of ambulatory ALS patients consumed less energy than the recommended dietary allowance based on 24h dietary recall (1). The reduction in energy intake correlated with increased weight loss, the degree of dysphagia reported by the patient, and a reduction in muscle wasting and triceps-skinfold thickness. Most authors recommend nutritional supplementation only after dysphagia and weight loss become prominent (2).

Objectives: We evaluated the effects of insulin supplementation in ALS patients on body composition (BIA method), muscle force fatigue index (20 sec^{-1} fatigue hand grip force/time curve), arm muscle areas (AMA) and nitrogen balance.

Results: Twelve non-obese women with ALS were recruited for this study. Patients were staged clinically according to the Norris Scale. During the week immediately preceding the study, each patient recorded food intake with the assistance of a digital photography system. Seven patients received 0.3 $U.I.Kg^{-1}$ crystalline zinc insulin s.c. infusion three times a week (insulin group, IG), five patients no additional insulin (control group, CG). BIA analysis system (RLJ-system inc. Detroit), nitrogen balance, muscle hand grip force/time, AMA (3) were assessed at the 60^{th}, 120^{th} and 180^{th} day. Data were analysed at the baseline and at the 180^{th} day. BIA and triceps-skinfold thickness by Desport's equations in ALS patients (4) were used for FFM_{50Hz}: there was a decrement in all groups, but less in the IG (4.8%: 44.0 ± 9.1 vs 42.1 ± 7.8 Kg) than in the CG (10.6%: 44.6 ± 9.8 vs 39.7 ± 7.5). Changes in the fatigue index were significantly ($p = 0.05$) higher in the CG than in the IG (5.1 vs 3.7 with polynomial 2^{nd} degree index). AMA showed no significant decrements in IG (24.2 ± 5.6 vs 23.9 ± 4.7 cm^2), but in the CG muscle loss was 25 ± 3.7 vs 21.2 ± 2.2 cm^2 (at the end of the protocol). No significant changes in 24-h nitrogen balance were found in both group (CG $<8\%$ and IG $<10\%$).

Conclusion: Our data showed that insulin supplementation is somehow able to counteract muscle mass and functional deterioration over time in ALS patients.

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P240 LEPTIN AND GHRELIN SERUM CONCENTRATIONS IN PATIENTS WITH ALS

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Keywords: leptin, ghrelin, T lymphocytes

Background: Leptin, an adipocyte-derived hormone of the cytokine family and ghrelin, a gastric-derived hormone, represent a link between body energy metabolism, nutritional status and immune and inflammatory response. Leptin promotes CD4+ T cell proliferation, whilst it can act as a negative signal for the expansion of human naturally occurring CD4+CD25+ T regulatory (Treg) cells. Ghrelin inhibits release of pro-inflammatory cytokines from LPS-stimulated macrophages. ALS patients are known to develop changes in their nutritional status and alterations in their metabolism; moreover, important changes occur in their innate or adaptive immune responses.

Objectives: In this study we examined the serum levels of leptin and ghrelin in a cohort of ALS patients with reference to their nutritional status and disease severity. In addition, we analysed a possible correlation between the percentages of CD4+ T lymphocytes, Treg cells and leptin serum levels.

Methods: Serum leptin and ghrelin levels were measured by immuno-ELISA assay in 41 ALS patients and 40 healthy donors. We also collected data on nutritional status using bioelectrical impedance analysis. Nutritional evaluation included: body weight, body mass index, fat mass, fat free mass.

Results: Serum leptin is proportional to the body fat mass in both genders of ALS patients and controls. However, although both males and females with ALS showed higher body fat mass compared to the healthy controls, only females with ALS exhibited remarkably and significantly higher serum leptin concentrations than respective controls. Serum ghrelin, which as expected is higher in females than in males, did not differ between ALS patients and healthy controls or correlate with body fat mass in ALS patients and controls of both genders. No significant correlations were found between serum leptin or ghrelin concentrations and disease duration and progression rate, or with the ALSFRS-R score in all patients.

Discussion and Conclusions: Body fat mass increases in ALS patients as consequence of muscle mass reduction. Although the serum leptin levels are proportional to the fat mass in both ALS patients and controls, the ALS females exhibit much higher circulating leptin than the other groups.

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Whether such effect has possible implications for the immune-inflammatory response in ALS females remains to be elucidated.

P241 NUTRITIONAL MANAGEMENT AND SURVIVAL IN ALS PATIENTS

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Keywords: PEG, bulbar onset, nutritional problems

Background: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease caused by a selective loss of motor neurons leading to progressive muscle weakness and muscle atrophy. ALS patients develop dysphagia and have nutritional problems. Recently, it has been reported that early percutaneous endoscopic gastrostomy (PEG) placement is beneficial for ALS patients with bulbar palsy.

Objectives: ALS patients with nutritional problems were provided with information about how early PEG placement might be beneficial. Some patients still hesitated to go ahead with the PEG, and sometimes the opportunity passed because of the progress of respiratory failure. In this study, the correlation of survival with PEG placement was analysed.

Methods: We evaluated 33 consecutive ALS patients with nutritional problems (22 men and 11 women; mean age $\pm$SD: 68.0 $\pm$ 13.1 years (yrs), 21 spinal onset and 12 bulbar onset) from April 2006 to April 2008. We followed their survival for one year after the day when patients, together with their practitioners, made the decision on how to manage nutritional problems.

Results: Seventeen patients (7 spinal onset and 10 bulbar onset) chose PEG placement, and the others (14 spinal onset and 2 bulbar onset) chose to receive nutrition via nasal tube feeding or intravenous drip (non-PEG). The average age of those who chose the PEG was 65.6 yrs, while the average age of non-PEG was 70.6 yrs. One year later, 14 of the 17 PEG patients were living without ventilator support, while 10 of the 16 non-PEG patients had died or needed ventilator support.

Discussion and Conclusion: Our study supports the benefit of PEG replacement for ALS patients with bulbar palsy. The difference in age and onset type of the patients must be considered.

P242 GUIDELINE FOR NUTRITIONAL CARE IN ALS

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Keywords: guideline, nutritional care, dieticians

Background: Most Dutch multidisciplinary ALS treatment teams have implemented the protocol for rehabilitative management in ALS (1). Although the ability to eat and drink are two of the most important functions in life and the progressive loss of these abilities has an immense impact on the patients and their families, the dietician was not always an integral member of the treatment team (2). It is known that optimal nutritional management by a dietician can positively influence survival and quality of life, but detailed evidence-based information for dieticians is lacking.

Objectives: To obtain a nutritional guideline in order to equip dieticians in helping to provide optimal nutritional care for ALS patients.

Methods: A guideline has been developed by reviewing the literature, in combination with practice-based experience from ALS dieticians. The guideline (3) has been written by Dieticians for Neuromuscular Diseases, an officially registered group of the Dutch Association of Dieticians.

Results: The guideline was published in the autumn of 2007. It is the initial step toward developing a national nutritional policy, for which the implementation continues.

Discussion and Conclusions: The guideline is a an instrument to initiate national and international discussion considering the statements of preventing weight gain, energy requirements influenced by progression and weight evolution, protein requirements, use of fibres during the course of the disease and defining palliative nutrition. Presentation of the statements will lead to discussion and establishing consensus on the nutritional requirements of ALS patients.

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P243 NUTRITIONAL PROGNOSTIC FACTORS IN AMYOTROPHIC LATERAL SCLEROSIS

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Rationale: It is well-known that hypermetabolism, weight loss, and cachexia are common phenomena in Amyotrophic Lateral Sclerosis (ALS) which contribute to prognosis. In this study we investigated the influence of Body Mass Index (BMI), serum glucose, serum cholesterol (LDL, HDL and LDL/HDL-ratio) and triglyceride levels on survival.

Methods: Over a time period of 10 years we prospectively and retrospectively investigated the course of disease of 419 patients (age = 58.4 $\pm$ 12.1 years). Among others we collected survival data, clinical scores and laboratory values, including nutritional factors, were collected. Cholesterol and triglyceride parameters were collected at time of diagnosis.

Results: We found that high serum levels of both cholesterol and triglycerides had a positive effect on survival ($p < 0.05$). We found a mean prolonged life expectancy of 21.6 months for patients with a serum triglyceride level $>$177 mg/dl. There was a highly significant correlation between triglyceride level and BMI ($p < 0.001$). We found that 11.8% of the subjects had a hyperglycemia, and 9.7% had a manifest diabetes mellitus which is above-average.

Conclusions: The results suggest that high triglyceride and cholesterol levels might be beneficial for ALS patients. Therefore, a diet rich in calories and lipids can possibly contribute to a favourable course of disease. The prescription of statins should be approached cautiously although further studies are necessary in this regard.

P244 ALS-CACHEXIA IS AN EARLY SIGN OF MOTOR NEURON DISEASE WITH TRUNCAL ONSET – RESULTS FROM A RETROSPECTIVE CLINICAL STUDY

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Keywords: ALS cachexia, truncal onset, ventilatory insufficiency

Background: Significant weight loss is common in amyotrophic lateral sclerosis with bulbar onset and in late stages of motor neuron disease. In patients without bulbar onset, it rarely occurs in the initial stages of the disease. F. Norris used the term ALS cachexia for severe early weight loss in patients with nonbulbar disease and considered it a poor prognostic sign.

Objectives: The purpose of this study was to identify clinical characteristics of patients with early severe weight loss in nonbulbar motor neuron disease and compare them to patients with bulbar and other nonbulbar disease.

Methods: In a retrospective clinical study we screened all ALS patients presenting to our clinic during a 2 year period with a disease duration of less than 26 months. Seventy-three patients were included, for whom weight and spirometry data were available.

Results: The study population comprised 45 patients with limb onset and 21 patients with bulbar onset. Seven patients presented with truncal onset, both with weakness of the paravertebral muscles and with early weakness of the respiratory musculature. In patients with truncal onset, vital capacity was reduced to a mean of 50.3% (minimun 33%, maximum 72%). Capillary blood gas analysis showed carbon dioxide retention (mean 55.7%).
All patients with truncal onset suffered from significant weight loss amounting to a mean of $19.9 \pm 7.1\%$ of the body mass index (BMI). Marked weight loss resulted in an extended tumor search in two of the seven patients prior to the diagnosis of motor neuron disease. None of the seven patients had significant bulbar involvement during their initial evaluation in our institution. Patients frequently complained of an early satiety feeling which limited their caloric intake. In some patients, the early weight loss was partially reversible after initiation of non-invasive nocturnal ventilation, thus suggesting a causal link between ventilatory insufficiency and weight loss. In contrast, weight loss in the limb and bulbar onset groups was much less pronounced (mean $2.5 \pm 5.6\%$ and $6.0 \pm 5.1\%$, respectively). A few patients with limb onset (6 of 45) also lost 10% or more of their BMI in the early disease stages; in some cases this was due to other causes such as dieting, active colitis etc.

Conclusion: ALS cachexia is commonly observed in motor neuron disease with truncal or respiratory onset. Thus, it may be an indicator of hitherto undetected respiratory muscle involvement which may also in part explain the poor prognosis associated with this finding. Early severe weight loss in ALS patients without significant bulbar involvement should therefore prompt screening for ventilatory insufficiency.

P245 DECISION MAKING FOR GASTROSTOMY AND RESPIRATORY SUPPORT – VARIATIONS ACROSS UK HOSPICES

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Keywords: gastrostomy, non-invasive ventilation, hospices

Background: UK hospices are often involved in the care of people with ALS/MND. However over the last 10 years there has been increasing use of interventions of gastrostomy and non-invasive ventilation, and there is evidence that the use of these interventions varies across the country.

Objectives: The aim of the study was to ascertain the use of the interventions in several hospices and the attitudes of consultants in palliative medicine across the country to the use of these interventions.

Methods: An audit of notes of 60 patients who had died under the care of 6 hospices in the UK and Ireland allowed a comparison of the use of these interventions. A telephone audit of consultants in palliative medicine was undertaken, using a structured questionnaire, to ascertain their attitudes and their involvement in the decision making for the interventions.

Results: The audit of 60 patients showed variation from hospice to hospice: the use of percutaneous endoscopic gastrostomy (PEG) varied from 0% to 50% of patients, with a mean of 32%, and non-invasive ventilation varied for 10% to 50% with a mean of 18%. The questionnaire of over 20 consultants showed that they were rarely involved in the referral for either PEG insertion or non-invasive ventilation. They were concerned that the interventions could lead to distress to patients and families if they were used inappropriately and without clear discussion beforehand. There was need to provide clear and helpful information for patients and families and for the discussion to take place over a period of time, as a "process" rather than on a single occasion. They gave examples of the inappropriate use of interventions.

Discussion: Although UK hospices are often involved in the care of people with ALS/MND this may often be only for end of life care. There is limited involvement in the decision making for interventions that may promote quality of life and potentially extend life. These decisions may occur before hospice teams are involved and there are concerns that the information provided for patients and families may not always be adequate. The study shows that there may be a need for specialist palliative care teams to be working in a more collaborative way with neurology, rehabilitation and MND teams to facilitate decision making for the difficult decisions of interventions.

P246 "INSPIRATIONAL" – INSPIRATORY MUSCLE TRAINING IN AMYOTROPHIC LATERAL SCLEROSIS

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Keywords: inspiratory muscle training, clinical trial, respiratory function

Background: Respiratory impairment, due to respiratory muscle weakness, is a major cause of morbidity and mortality in patients with amyotrophic lateral sclerosis-motor neuron disease (ALS-MND). Threshold loading may strengthen the inspiratory muscles and thereby improve patient prognosis.

Objectives: To determine whether a 12-week inspiratory muscle training (IMT) program would strengthen the inspiratory muscles and improve respiratory function in ALS-MND patients.

Methods: Nine patients were randomised to inspiratory muscle training and 10 to sham training. Primary endpoints were respiratory function (forced vital capacity, vital capacity), lung volumes and inspiratory muscle strength. Patients were assessed before, during and immediately after a 12-week training period, and at eight weeks follow-up.

Results: Although improvements in inspiratory muscle strength were observed in both treatment arms, there was a non-significant increase in maximum inspiratory pressure of $6.1 \pm 6.93\%$ in the experimental group compared to controls (95% confidence interval, $-8.58 - 20.79$; $P = 0.39$). The gains in inspiratory muscle strength were partially reversed during a period of training cessation. Similar trends were observed in respiratory function after the 12-week training period, with forced vital capacity $4.59 \pm 3.02\%$ (95% confidence interval, $-1.85 - 11.02$; $P = 0.15$) higher in the experimental group than control group. No serious adverse side effects were reported by patients.

Discussion and Conclusions: The present clinical trial is the first to evaluate the effects of IMT in ALS-MND patients in the context of a double-blind, randomised-controlled trial. Consistent trends for improvement were demonstrated across all respiratory parameters over multiple occasions. Measures of respiratory function suggested that IMT may have partially ameliorated the restrictive defect that develops in ALS-MND. In addition, measures of inspiratory muscle strength suggested that IMT was efficacious in strengthening the inspiratory muscles. As such, the results of the present trial would tend to support the hypothesis that despite an environment of ongoing denervation, the inspiratory muscles of ALS-MND patients are capable of responding favourably to a strength-training program.

P247 CAPNOGRAPHY AS A SCREENING TOOL FOR NOCTURNAL RESPIRATORY DISTRESS IN PATIENTS WITH ALS

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Keywords: capnography, pulse oxymetry, non-invasive ventilator

Background: Patients with amyotrophic lateral sclerosis (ALS) suffer from hypoventilation which can be worsened during sleep.

Objectives: To evaluate the efficacy of capnography monitoring for screening nocturnal hypoventilation in patients with ALS.

Methods: Thirty eight definite or probable ALS patients with subjective symptoms of hypoventilation or decreased vital capacity (<80% of normal) were included. Patients underwent nocturnal capnography and pulse oximetry monitoring, daytime arterial blood gas analysis (ABGA), measurement of forced vital capacity (FVC) and ALS functional score revised (ALSFRSr). Patients with subjective respiratory symptoms or decreased vital capacity were treated with non-invasive ventilation (NIV). Spearman's correlation test was used for statistical analysis.

Results: The degree of nocturnal hypercapnea was measured as duration of nocturnal hypoventilation, average level of $ETCO_2$, and maximal level of $ETCO_2$, using capnography. Those three values correlated well with degree of respiratory distress during sleep (scores to 'orthopnea' questionnaire in ALSFRSr; $r = -0.627 \sim -0.491$, $P = 0.004 \sim 0.033$) and compliance to NIV treatments ($r = 0.539 \sim 0.649$, $P = 0.001 \sim 0.012$). However the degree of nocturnal hypoxia, measured as duration of nocturnal hypoxia (defined as % of sleep when $SaO_2 < 95\%$ per total sleep), average nocturnal SaO_2, and minimal nocturnal SaO_2 had no significant correlation with nocturnal respiratory symptoms or compliance to NIV treatment.

Conclusion: Nocturnal capnography is a simple, efficient tool in screening hypoventilation and detecting respiratory symptoms in patients with ALS. Moreover, this can also be useful in predicting future compliance to NIV treatment.

P248 EARLY START OF NON INVASIVE MECHANICAL VENTILATION IN ALS PATIENTS

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Keywords: non invasive ventilation, disease severity, survival

Background: Many studies have shown improvement in survival for mechanically ventilated amyotrophic lateral sclerosis (ALS) patients. However, there is no consensus as to when non invasive ventilation (NIV) has to be started. One criterion is a vital capacity (VC) lower than 50% of predicted value.

Objectives: To compare the survival of NIV-treated ALS patients in early (VC >50%) vs late (VC <50%) disease stages.

Subject and Methods: Since 2004, 165 ALS patients (mean age: 63.7 ± 11.2 years) have been assisted. Thirty-three of 55 (33%) who died used NIV. Among these, only 24 patients,

with a diagnosis of ALS confirmed no longer than 12 months before, were studied. In particular, they were subdivided into two groups: twelve patients (mean age: 66.0 ± 9.1 years) who started NIV at a VC < 50% (mean VC: 35.5 ± 12.8%), and 12 (mean age: 58.5 ± 7.4 years) who began NIV with a VC > 50% (mean VC: 94.7 ± 23.3%).

Results: In the former group survival was 21.4 ± 12.2 months from diagnosis and 13.2 ± 8.0 months since using NIV; whereas in the latter group survival times were 18.7 ± 8.8 and 11.5 ± 7.2 months, respectively. Values did not differ significantly between groups.

Conclusions: These data show that in early NIV-treated ALS patients severity of respiratory impairment does not influence survival.

P249 EFFECT OF A MULTIDISCIPLINARY ALS CLINIC ON NIV TOLERANCE AND SURVIVAL IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS AND BULBAR IMPAIRMENT: A PROSPECTIVE STUDY

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Keywords: non-invasive ventilation, survival, bulbar impairment

Background: The effect of non-invasive ventilation (NIV) in prolonging survival and improving quality of life in ALS patients with respiratory failure (RF) has been largely demonstrated, but it is currently under-prescribed. One restricting factor to the efficacy of NIV is bulbar involvement, but little is known about predictors of NIV tolerance.

Objectives: To evaluate the factors associated with NIV tolerance and survival in ALS patients.

Methods: All consecutive ALS patients who came to the Center between January 2001 and December 2006 were prospectively monitored with RF and indication to NIV. NIV was offered according to current guidelines. Patients were assessed by: demographical and clinical characteristics, pulmonary function and disability (as measured by ALS Functional Rating Scale (ALS FRS)). After NIV indication, subjects were followed-up in the ALS Clinic regularly at three-month intervals. According to current accepted criteria, the tolerance to NIV was defined as the ability to use the ventilator for more than 4 consecutive hours/day.

Results: A total number of 115 ALS patients (75 males and 40 females) with indication to NIV were enrolled. Among them, 33 patients had a bulbar disease onset, but 38 had developed severe and 65 mild/moderate bulbar impairment at NIV initiation. Sixty patients (52.2%) were tolerant to NIV. As expected, the majority of the intolerant patients had mild/moderate (47.3%) or severe (43.63%) bulbar impairment at NIV initiation. Survival analysis (total survival and survival from the time when NIV was indicated) demonstrated a longer survival in the tolerant group ($P < 0.001$). Interestingly, among the group with severe bulbar impairment, patients who tolerated NIV survived longer than those who were intolerant ($P < 0.001$). Further, we found that the bulbar patients tolerant to NIV come to the ALS Clinic more often than those intolerant after NIV indication ($P = 0.0001$).

Conclusions: This study shows that a regular follow-up in a multidisciplinary ALS Clinic after NIV indication could increase tolerance to NIV and survival, even in patients with severe bulbar impairment. The effect of clinical type must be considered in management of respiratory failure.

P250 FACTORS ASSOCIATED WITH NON-INVASIVE POSITIVE PRESSURE VENTILATION COMPLIANCE IN ALS/MND PATIENTS

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Keywords: non-invasive positive pressure ventilation, compliance, BIPAP

Background: Despite Class I evidence that non-invasive positive pressure ventilation (NIPPV) improves both survival and quality of life (QOL), compliance with the intervention remains low.

Objectives: To prospectively examine factors which influence NIPPV compliance.

Methods: Seventy-three ALS patients with a forced vital capacity (FVC) > 50% were enrolled in the multi-center pilot study of Early Nutrition and NIPPV. Patients with a FVC over 80% at baseline were initiated on NIPPV when their FVC was 75–85% (Group1 – Early intervention). Patients with a FVC between 50–80% were started when their FVC was 45–55% (Group 2 – Standard of Care). Patients were educated about NIPPV prior to initiation. Respiratory therapist visits were made three times the first week, twice the second and once in the third and fourth weeks with monthly visits during the rest of the study. NIPPV compliance was defined as > 4 hours of use on 60% of days based on computer downloads 4 weeks after initiation of treatment. Patients were followed over 12 months and were asked to complete a 17 item "symptom score" after initiating NIPPV. The instrument asked patients: "While using NIPPV, how often do you experience the following symptoms?" and patients completed a scale from 0 (never) to 10 (all the time) for each symptom.

Results: Of the 73 participants in the NIPPV arm of the study, 57 subjects were offered NIPPV (36 in Group 1 and in 21 in Group 2). Objective data from downloads were available from 47 of the 57 participants offered NIPPV (30/36 Group 1 and 17/21 Group 2). By day 28 (week 4) after initiation of NIPPV, the compliance rate was 53.3% for Group 1 and

70.6% for Group 2. For the non-compliant patients in both groups, the most frequent symptoms included: excessive dryness of the nose or throat passages (mean score 3.67), mask discomfort (3.28), air leakage from the mask (3.11), waking up frequently during the night (2.78), a sense of suffocation or claustrophobia (2.39), and soreness in the nose or throat passages (1.78). The remainder of symptoms did not appear to be related to non-compliance: running nose, headaches, ear pain, marks or rash on face, complaints from partner about noise from the machine, or bloating. Interestingly, when this non-compliant group was asked, "Do you believe there has been an improvement on your QOL?", 72% responded "yes".

Discussion and Conclusion: The majority of symptoms reported by patients within the first 4 weeks of initiating NIPPV are related to issues that are potentially resolvable with aggressive respiratory therapy intervention. Ensuring proper humidification and finding an interface that is comfortable and seals properly are imperative to improving compliance.
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P251 NON-INVASIVE POSITIVE PRESSURE VENTILATION IN AMYOTROPHIC LATERAL SCLEROSIS: PREVALENCE, APPROACH AND BARRIERS TO USE AT CANADIAN ALS CENTRES

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Keywords: NIPPV, prevalence, initiation

Background: Non-invasive positive pressure ventilation (NIPPV) has become the standard of care in the initial management of respiratory insufficiency in ALS (1,2). Nonetheless, considerable variability in the prevalence of NIPPV use has been reported in the European and U.S. ALS patient populations (3).

Objectives: To evaluate: 1) the prevalence of NIPPV and invasive mechanical ventilation via tracheostomy (TV) therapy, 2) the approach to NIPPV use, focusing upon the currently employed initiation criteria and 3) the barriers influencing NIPPV utilization in Canada.

Methods: A descriptive survey research design aimed to acquire quantitative data and open-ended responses from an active physician at each of the 15 multidisciplinary Canadian ALS centres.

Results: The principal findings were: 1) NIPPV and TV therapy are used in 18.3% and 1.5% of Canadian ALS centre patients, respectively. 2) Symptoms of respiratory insufficiency, namely orthopnea (clinical importance rated at 9.00/10 $\pm$1.48, mean $\pm$SD), dyspnea (8.27 $\pm$1.95) and morning headache (7.55 $\pm$1.21) are the most significant indicators for NIPPV initiation. 3) Secondary to symptoms, nocturnal oximetry, then forced vital capacity (FVC) and morning blood gases, are the investigations most important to NIPPV initiation. 4) The primary barriers to NIPPV utilization are patient intolerance (70% of centres) and lack of access to respirologists and/or ventilation technologists (50% of centres).

Discussion: These data may reflect an international trend towards an increased use of NIPPV therapy and a concurrent restriction of TV application in ALS patient care, which for some represents a translation of evidence into clinical practice. In addition, the results provide support for the primary importance of symptom assessment in the decision to institute NIPPV therapy. Subsequently, greater weight is being placed on investigations that may facilitate an earlier implementation of NIPPV (i.e. nocturnal oximetry over FVC). Nevertheless, similar to previous international analyses, inter-centre variability persists with respect to NIPPV utilization (3).

Conclusions: As this variability has an impact upon the management of ALS patients, future studies should focus upon: the continued establishment of more definitive NIPPV initiation criteria, with an emphasis upon respiratory symptoms; and the attenuation of barriers to NIPPV use, so as to ensure optimal care for all ALS patients.

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P252 VENTILATORY SUPPORT IN ALS: TIMING, CHOICE AND OUTCOME IN A MULTI-ETHNIC POPULATION

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Keywords: ventilatory support, BiPAP, multi-ethnic

Background: Amyotrophic lateral sclerosis (ALS) frequently causes death within 5 years of onset. Almost all deaths in ALS are due to pulmonary complications resulting from respiratory muscle weakness and bulbar involvement. Timely ventilatory support can reduce the work of breathing and dyspnea, can improve gas exchange, improve quality of life and it can prolong survival in patients with ALS. The timing, choice and outcome of ventilatory support in a cross-ethnic population of ALS remain unexplored.

Objectives: To study the timing, choice and outcome of ventilatory support in an ethnically diverse ALS population.

Methods: The results of ventilatory use was retrospectively analyzed in an ethnically diverse group of 205 patients who were seen and followed up at the Kessenich Family MDA-ALS Center from 2002 through 2007 and in whom clinical records were available from diagnosis to death.

Results: The cohort of 205 patients (male 122, female 83; mean age at death 64.9 years (yr), range 34–91 yr) comprised of 128 White Caucasians (W, 62%), 61 Hispanics (H, 30%), 12 African Americans (AA, 6%), and 4 Asians (A, 2%). 139 patients (68%) elected to receive BiPAP (W 60.2%, H 80.3%, AA 83.3%, A 75%). In BiPAP group, 93 patients (67%) had limb-onset and 46 patients (33%) had bulbar-onset ALS.

Acceptance of BiPAP showed a steady increase in all groups during the study period (61% in 2002, 72% in 2007). Survival from the onset of the disease was 41.2±26 months (mo) (mean and SD; BiPAP group 45.1±28.6 mo, non-BiPAP group 36.7±22.7 mo). 11 patients (5.4%) opted for invasive ventilation (W 4%, H 8%, AA 8%, A 0%). 66 patients (32.3%) received a feeding tube before or soon after ventilatory assistance (W 26%, H 41%, AA 50%, A 50%). 102 patients (50%) died in the hospice program (W 48%, H56%, AA 58%, A 0%). Age of onset, gender, site of disease-onset and mean survival were comparable across the ethnic groups. Tolerance and quality of life following ventilatory assistance was generally good in all groups of patients.

Discussion and Conclusions: Acceptance of non-invasive ventilation showed a steady increase during the study period and BiPAP significantly prolonged survival in all ethnic groups. The findings of relative under utilization of BiPAP ventilatory support among ethnic groups require prospective studies to determine the underling cause(s). Patients with ALS rarely elect invasive ventilation.

P253 COST-EFFECTIVENESS OF HOME TELEMONITORING NON-INVASIVE VENTILATION IN ALS PATIENTS

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Keywords: cost-effectiveness, telemonitoring, wireless solution

Background: A prospective trial of home-ventilated ALS patients was recently conducted documenting less healthcare utilization and a trend towards better quality of life and survival outcomes. Nevertheless, no study has yet evaluated healthcare costs associated with telemetry for assessing compliance to non-invasive ventilation (NIV). Home telemonitoring of NIV by modem communication may substantially cause a significant impact on total cost of care.

Objectives: To analyse direct (hospital and NHS) and indirect (patient and caregiver) costs of following-up NIV compliance via modem.

Methods: A prospective controlled trial of consecutive ALS patients, randomly assigned according to their residence area to G1 (patients nearby hospital; office-based follow-up) and G2 (patients outside hospital area; telemetry device based follow-up) was performed. Total NHS direct cost of care was determined by summing medical costs related to General District Hospital (GDH)-based outpatients visits and hospitalizations. Hospital direct costs included transportation to/from hospital, office visit per hour cost and daily maintenance of equipment (with/without modem). Non-medical costs were considered as days of wage lost due to caregiver absenteeism. Annual costs analysis with all variables adjusted to the survival period with NIV in days was performed.

Results: G1 included 20 patients aged 60±10 (14 males, 16 spinal-onset and 4 bulbar-onset) and G2 included 19 patients aged 62±13 (13 males, 11 spinal and 9 bulbar-onset forms). No statistically significant differences were found among the two groups regarding clinical and demographic characteristics at admission. (i) NHS costs evaluation showed a 55% reduction on average total costs (G1: 19,665±23,507€ vs G2: 8,909±4,619€; P=0.05) with a statistically significant decrease of 81% on annual costs (G1: 44,134±50,607€ vs G2: 8,186±6,553€; P=0.005) in G2. (ii) Hospital costs were found to be significantly higher in G2 regarding to the total costs (64% average increase, P=0.008) but not annual costs (7% average increase, P=0.36). (iii) No statistical difference was found concerning caregiver expenses from abseentism due to office visits or hospitalizations (P=0.15).

Conclusion: At the expense of an initial financial constraint to the hospital per year (non-significant), this telemonitoring instrument for NIV compliance in ALS patients has proved to be cost-effective along with survival with NIV, thereby representing major cost savings to the NHS in the order of €700,000 per year.

P254 DESCRIPTIVE STUDY OF A HIGH RESOLUTION NEURO-RESPIRATORY UNIT

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Keywords: non-invasive ventilation, multidisciplinary, tracheostomy

Background: Patients with Amyotrophic Lateral Sclerosis (ALS) need multidisciplinary care. The development of Multidisciplinary Units may develop and provide better assistance to patients. The aim of this study is to evaluate the results of the early respiratory intervention during the first two years of an ALS Unit.

Methods: Observational study of the patients attended in the ALS Unit during the period from March 2006 to December 2007. The following information has been recorded: age, gender, ALS initial form (bulbar or spinal), months of evolution up to non-invasive ventilation (NIV), adjustment to NIV, type of ventilator, tolerance to the ventilation and tracheostomies.

Results: 45 patients diagnosed with ALS were checked, 24 men and 21 women, mean age of 65.88 years old (ranging from 41 to 91 years old). The mortality was 37.8%. 3 patients were lost in the follow-up. According to the initial form of ALS, 30 patients were spinal (66.7%) and 14 bulbar (31%), with a major mortality in the spinal group (46%) vs bulbar (21.42%). 20 patients were adapted to NIV (44.4%), with a major use of the volumetric ventilators (60%), than pressure ventilators (40%), leaving BIPAP for the patients who needed an orofacial mask. 53.33% of spinal ALS were adapted to NIV (37.5% to BIPAP and 62.5% to volumetric ventilator) and 28.57% of bulbar ALS to NIV (50% to BIPAP and 50% to volumetric ventilator). The evolution of the disease up to the start of using NIV was variable (35.88 months of average), which shows the variability of the disease. The tolerance to NIV was good at 66.7% of cases. Tracheostomies were performed on 5 patients (4 spinal and 1 bulbar).

Conclusions: During the first two years of the ALS Unit, the spinal ALS group was more numerous than the bulbar group, with a major adaptation to NIV. Volumetric ventilators were used more frequently and its tolerance was good. Tracheostomy was practised in more spinal than in bulbar patients.

P255 EFFECTS OF NIPPV INITIATION ON PULMONARY FUNCTION TESTING IN ALS SUBJECTS

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Keywords: NIPPV, FVC, respiratory failure

Background: Recent literature indicates a significant effect of non-invasive positive pressure ventilation (NIPPV) both on survival and quality of life in ALS patients who are compliant (NIPPV >four hours daily) leading to the present recommendation that NIPPV should be initiated when ALS patients are symptomatic and/or when the FVC declines to 50% of expected. While some studies have demonstrated a slowing of the rate of decline in FVC accompanying the survival benefit, others have demonstrated an initial deterioration in the FVC following the start of NIPPV leading to the concern that NIPPV may actually weaken respiratory muscles initially.

Objectives: To examine the early effects of NIPPV on respiratory function in compliant and non-compliant patients.

Methods: Seventy-three ALS patients with a forced vital capacity (FVC) >50% were enrolled in a multi-center pilot study of Early Nutrition and NIPPV. Patients with a FVC over 80% at baseline were initiated on NIPPV when their FVC was 75–85% (Group 1 – Early intervention). Patients with a FVC between 50–80% were started when their FVC was 45–55% (Group 2 – Standard of Care). NIPPV compliance was defined as consistent use of at least >4 hours per night based on machine downloads. Pulmonary functions (sitting and laying FVC, nasal inspiratory pressure (SNIP) and maximum voluntary ventilation (MVV), MIP and MEP) were measured before and 4–6 weeks after the initiation of NIPPV.

Results: Of the 73 participants in the NIPPV arm of the study, 57 subjects were offered NIPPV (36 in Group 1, 21 in Group 2). Objective data from downloads were available from 47 of the 57 participants offered NIPPV. The compliance rate was 53.3% for Group 1 and 70.6% for Group 2. FVC in compliant subjects dropped less then noncompliant subjects over the first two months ($71.8 \pm 1.4\%$ to $68.6 \pm 18.3\%$ vs $70.9 \pm 14.9\%$ to $63.5 \pm 19.7\%$ predicted) although it did not reach statistical significance. Similarly, the MVV declined less in compliant subjects (58.4 ± 34.5 L/min to 56.7 ± 38.3 L/min) compared to noncompliant subjects (52.9 ± 28.5 to 44.1 ± 26.5 L/min). The 7.4% drop in FVC between pre and post NIPPV in noncompliant subjects was statistically significant ($P = 0.003$) while the drop of 3.2% in compliant subjects was not. Similarly, the decrease in MVV was significant in noncompliant subjects (8.8 ± 10.5, $P = 0.003$), but not in compliant (3.9 ± 14.6). There was no immediate drop in FVC observed.

Discussion and Conclusions: There was less decline of both FVC and MVV in NIPPV compliant compared to noncompliant subjects observed within the 4–6 weeks following the initiation of NIPPV although the difference was not statistically significant. The drop of FVC between pre and post-NIPPV in compliant subjects was not significant and contrasts previous reports of a more rapid decline initially. This suggests that there is no initial weakening of the respiratory muscles.

P256 THE USE OF NON-INVASIVE VENTILATION DURING PERCUTANEOUS ENDOSCOPIC GASTROSTOMY INSERTION IN PATIENTS WITH IMPAIRED RESPIRATORY FUNCTION

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Keywords: non-invasive ventilation, PEG, RIG

Background: Percutaneous endoscopic gastrostomy (PEG) is the standard management of bulbar ALS patients at risk of malnutrition and aspiration. PEG is not recommended in patients with significantly impaired respiratory muscle strength (RMS) determined by a vital capacity (VC) below 50% predicted and/or a sniff nasal inspiratory pressure (SNP) below 40 cm water, although VC and SNP may underestimate RMS in bulbar ALS patients. Radiologically inserted gastrostomy (RIG) is well tolerated in patients with impaired RMS. However, RIG is not available throughout the United Kingdom. This necessitated the centre to develop a novel approach of performing PEG with non-invasive ventilation (NIV) available to be delivered before, during or after the procedure, if required.

Objectives: 1) To determine if the use of NIV permitted the insertion of PEG in bulbar ALS patients with significantly impaired RMS. 2) To determine if the above criteria were underestimating the patients RMS and if it was feasible to adopt less stringent threshold values to determine fitness for PEG.

Methods: The cases of patients referred for a respiratory muscle assessment were reviewed to determine fitness for PEG insertion over a 53-month period. Patients had VC, SNP, capillary blood gases and overnight pulse oximetry. 24 patients were identified that had inadequate respiratory function for PEG insertion as determined by the above criteria or already being established on NIV. These patients had a PEG insertion under sedation with the facilities and staff to provide NIV during the procedure or at recovery should it be required if the patient desaturated or developed respiratory compromise. If NIV was required during the procedure, the complications of PEG insertion and the date of death were determined.

Results: There was one death in the 24 patients within 30 days with all other patients surviving beyond this period following PEG insertion.
Eleven patients were already established on NIV. All required NIV during the procedure. PEG was successfully inserted in all but one patient who had significant desaturation and required a second attempt, which was successful.
Thirteen patients were not established on NIV. Three patients declined to have PEG under NIV cover, preferring to use local hospitals. None of the patients declining our service had complications during the procedure, but all patients had difficulty with respiratory tests and therefore their RMS may have been underestimated. Of the remaining 10 patients, 5

required NIV during the procedure. One patient required a second attempt for successful PEG placement and a PEG was unable to be placed in one patient due to a high stomach.

Conclusions: PEG with precautionary NIV available is a safe alternative procedure to RIG in patients with impaired RMS. PEG can be placed in patients currently using NIV.

P257 THE STUDY OF NIPPV USING FULL-FACE MASK REMODELED TO SUPPORT ENDOSCOPE IN PER-ENDOSCOPIC GASTROSTOMY IN ALS PATIENTS

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Keywords: remodeled mask, NPPV, PEG

Background: ALS treatment guidelines recommend performing PEG while the patient's%VC is greater than 50%. But sometimes PEG is required in patients already have respiratory dysfunction. In this case, the risk of worsening respiratory function during PEG is much higher. In 2005 the usefulness of NIPPV using a remodeled full-face mask to support endoscope during PEG was reported. We started to use this method in 2006.

Objectives: To evaluate usefulness of NPPV using remodeled full-face mask to support endoscope with larger number of patients.

Methods: Thirty-seven consecutive PEGs that were performed in ALS patients (14 men, 23 women) since March 2006 to February 2009 were studied. Seventeen patients were already on NIPPV (9 cases night-time only, 8 cases all day). Blood gas analysis, sniff nasal inspiratory pressure measurement (SNIP) and overnight SpO_2 monitoring were performed other than %VC prior to PEG. The condition of the patient, vital signs and SpO_2 were analyzed during PEG. PEG was performed using direct methods. Tentative criteria were used for indication of NIPPV to support endoscope as one of following 1) %VC less than 50%, 2) PCO_2 greater than 50 mmHg; 3) SpO_2 less than 88% lasts for more than 5 minutes during sleep. 4) Rapid decrease of SNIP. 5) Dyspnea. Pethidine Hydrochrolide and Midazolam injection were used as pre-operative medication.

Results: Only 11 cases had a%VC greater than 50% while 13 cases with 30% $<$%VC $<$50%, 4 cases with $<$30%, 2 cases were immeasurable. Only 22 cases have $PaCO_2$ less than 45 mmHg while 9 cases with 45 mmhg $<PaCO_2<$50 mmHG, 6 cases with $>$50 mmHg. Based on inclusion criteria, In 27 cases PEG with NPPV using remodeled full-face mask to support endoscope were performed. Despite two-thirds of patients having%VC less than 50%, PEG was safely performed in 26 out of 27 patients using NPPV using full-face mask remodeled to support endoscope. SPO_2 was temporally decreased in 12 patients but recovered with oxygen therapy. Only one patient had aspiration during preparation procedure and PEG was cancelled.

Discussion and Conclusions: PEG was safely performed even in ALS patients with respiratory dysfunction with NIPPV using full-face mask remodeled to support endoscope. Thus this method is very useful for patients that already have decreased respiratory function.

P258 STUDY RESULTS OF DIAPHRAGM PACING IN EXTREMELY LOW FORCED VITAL CAPACITY PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS/MOTOR NEURON DISEASE: IS THERE A ROLE AT END STAGE ALS?

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Keywords: diaphragm, diaphragm pacing, respiration

Background: Trials of diaphragm pacing (DPS) in ALS/MND had been limited to patients with FVC above 45% predicted at surgical implantation due to concerns of inability to extubate or tolerance of surgery. There is also concern of insufficient intact lower motor neurons with end stage ALS/MND and that remaining motor units are inadequate for pacing to have any effect on respiration.

Objectives: To assess the safety and efficacy of DPS in subjects with FVC below 45% predicted.

Methods: Prospective, nonrandomized, controlled, interventional feasibility trial assessing safety and efficacy through patient assessment of breathlessness, electromyography of diaphragm function and nocturnal oximetry with and without DPS.

Results: Subjects were enrolled between September 2007 and March 2009 with an average FVC at implantation of 28% predicted (range 14% to 36%). Subject 1 is still alive 19 months post implantation with benefits shown from increased diaphragm burst EMG activity, DPS overcoming nocturnal hypoventilation and Subject 1 is still not using non-invasive ventilation (NIV). Subject 2 survived 9 months post implantation and with benefits shown by increase in diaphragm EMG and decreased initial use of NIV. Subject 3 was initially extubated but rapidly tired out requiring re-intubation with subsequent withdrawal of life support. The patient had extreme malnourishment (BMI of 14) with significant weight loss awaiting DPS and gastrostomy placement. Although he had a stimulatable diaphragm at surgery, no benefit to DPS can be claimed. Subject 4 survived 10 weeks post implantation before withdrawing support and expiring. Surgical evaluation showed a significant loss of diaphragm motor units. Although survival was only 10 weeks patient benefits were seen by increased diaphragm burst activity during EMG, improved breathlessness scores, dependence on DPS to maintain night oxygenation and the need to turn off DPS to allow death. Subject 5 was able to be safely implanted and had a large amount of upper motor neuron involvement of the diaphragm manifested in substantial post-implantation tidal volumes and diaphragm movement under stimulation. While awaiting regulatory approval for implantation the patient had entered hospice, but decided to leave hospice to have the implantation. Within a week of implantation she decided to once again withdraw all life support and expired. Although DPS had the potential to improve ventilation, no beneficial outcome can be claimed for Subject 5 due to her decision to withdraw support.

Conclusion: DPS benefits can be seen in selected low FVC ALS/MND subjects. The societal expense of a surgical procedure has to be addressed with patient wishes preoperatively to prevent unnecessary expenses to the health care system. Patients must understand that DPS is only a

symptomatic treatment of diaphragm respiration. Presently, we only implant motivated patients with documented intact stimulatable diaphragm motor units through phrenic nerve conduction studies with diaphragm movement assessment.

P259 RESPIRATION AND AMYOTROPHIC LATERAL SCLEROSIS/MOTOR NEURON DISEASE: THE ROLE OF THE DIAPHRAGM AFTER A DECADE OF EXPERIENCE WITH DIAPHRAGM PACING

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Keywords: diaphragm, diaphragm pacing, respiration

Background: Diaphragm pacing (DPS) has been used in a series of trials to help respiration ranging from spinal cord injured (SCI) patients with pure upper motor neuron (UMN) loss of control to patients with pure lower motor neuron (LMN) loss from phrenic nerve transection along with direct analysis of stimulation of normal subject diaphragms. ALS/MND involves both UMN and LMN involvement of the diaphragm.

Objectives: To describe how ALS/MND diaphragm pathophysiology can affect respiration.

Methods: Prospective, nonrandomized, controlled, interventional trials under IRB and/or FDA approval for use of DPS in human subjects at a single institution. Comparisons of diaphragm function from normal to different diseases states were compared to ALS/MND.

Results: From 1999 to 2009 over 128 human diaphragms were surgically evaluated for motor point stimulation for ventilation with over 250 patient-years of DPS use. Subjects ranged from 12 weeks to 77 years old. Diaphragm evaluations included normal subjects undergoing elective laparoscopy to SCI patients on ventilators over 25 years. ALS/MND diaphragms evaluated varied from FVC of 89% predicted to continuous mechanical ventilation with tracheostomy for 18 months. Pre-operative pulmonary function tests do not predict surgical stimulation results. Patients can have high FVC but poor diaphragm function or low FVC and excellent stimulatable diaphragms. ALS/MND involvement of the diaphragm is heterogeneous. It can be visualized as radial bands or regions of loss of motor units and can functionally involve each hemi-diaphragm differently. Using frequency stimulation to differentiate muscle fiber type, ALS/MND diaphragms that had primarily UMN involvement or suppression of diaphragm function with NIV demonstrated conversion to fast twitch (type IIb) muscle fibers. DPS can convert ALS/MND diaphragms to more functional type I muscle fibers. Used in conjunction with NIV, DPS can prevent atrophy and conversion. Implanted DPS electrodes can be used to assess diaphragm burst activity which appears to correlate with strength of diaphragm contraction and can be serially followed. This has been utilized to identify and treat central sleep apnea in ALS/MND. ALS/MND patients with primary LMN involvement have diffusely thin non-stimulatable diaphragms. DPS increases respiratory compliance by 17% which decreases the work of breathing. ALS/MND patients may develop daytime hypoventilation leading to hypercarbia which DPS can overcome. During disease course use of DPS can go from several 30 minutes conditioning sessions a day to 24 hours continuous use to maintain ventilation with the need to turn off DPS if death is sought. In tracheostomy mechanical ventilated patients, some with intact phrenic motor neurons remaining, DPS decreases peak airway pressure and improves posterior lobe ventilation leading to less atelectasis and risk for pneumonia.

Conclusion: ALS/MND patients with respiratory complaints and intact phrenic motor neurons that the patient cannot control due to UMN involvement are candidates to improve diaphragm movement and ventilation with DPS.

P260 HYPOACUSIS IN ALS PATIENTS RECEIVING LONG-TERM VENTILATION

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Keywords: hypoacusis, long-term ventilation, decision-making

Background: ALS is defined as a degenerative disease that selectively affects motor neurons. In a subgroup of ALS there is evidence for non-motor involvement such as cachexia, ophthalmoplegia and autonomic impairments. Hypoacusis, however, has not been reported in ALS.

Methods: Three ALS patients, patient 1(P1) (32 year old female), patient 2 (P2) (47 year old female) and patient 3 (P3) (48 year old male) were retrospectively studied, who underwent tracheotomy after 35, 26 and 25 months of disease, respectively. All received continuous ventilation. 78, 33 and 31 months into the course of the disease these patients developed bilateral hearing impairment.

Results: Two cases (P1 and P2) were diagnosed as hypoacusis based on sensorineural hearing loss as demonstrated by audiometry (P1) and auditory evoked potentials (P2). A structural lesion in the middle ear was clinically and pathoanatomically excluded. In the third patient (P3), conductive hearing loss was identified, caused by chronic serous tubotympanal catarrh.

Discussion: Sensorineural hearing loss in the context of ALS is etiologically unknown. The reported cases (P1 and P2) suggest a neurodegenerative process involving the auditory system. By contrast, conductive hearing loss is presumably caused by bulbar symptoms, including paralysis of the tensor and levator veli palatini muscles. These symptoms disturb the equalization of pressure in the middle ear and can result in chronic serous tubotympanal catarrh.

Conclusion: Through altering the natural course of the disease, the administration of long-term ventilation leads to previously undiscovered aspects in patients and subsequently complicates patient management. Given the increasing use of long-term ventilation, atypical symptoms are of growing clinical relevance. Identifying hypoacusis is critically important in complex decision-making and particularly in the adaptation of electronic communication systems, in the withdrawal of therapy or palliative care.

P261 WITHDRAWAL OF INVASIVE HOME MECHANICAL VENTILATION IN ADVANCE STAGE ALS PATIENTS

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Keywords: withdrawal, invasive ventilation, advance stage ALS

Background: Due to the growing use of artificial respiration in amyotrophic lateral sclerosis (ALS), physicians are increasingly confronted with patients seeking discontinuation of therapy. Yet there are few systematic investigations of the withdrawal of invasive home mechanical ventilation (IHMV). IHMV in ALS varies greatly between centres and countries, depending on the physicians' attitudes. One of the controversial aspects of this procedure is the issue of life support withdrawal. According to Danish legislation patients must not only give informed consent to any therapy; they can also ask to have therapy terminated at a time when life has lost its meaning according to their own definitions.

Objectives: To describe and discuss the medical aspects of terminating IHMV in patients with advance stage ALS.

Methods: A retrospective, descriptive analysis was made of all 12 ALS-patients (4 females) median age 61 years (range 39–69 years) cared for at our centre from 2002 to 2009 and who decided to withdraw their consent of IHMV. All patients were on 24 hour IHMV. The time from initiation of IHMV to decision to terminate were recorded. The reasons for the request and the circumstances of the procedure of termination were obtained.

Results: In all cases withdrawal of treatment was discussed with the patient before the initiation of IHMV. All patients decided that treatment should be withdrawn should they develop a locked in state.
The median time from initiation of IHMV to decision of termination was 21.5 months (range 0.23–35 months). The reason for requests was for all patients a general loss of meaning in life, but in three patients additional factors were: recurrent infections, inability to speak and bleeding from colorectal cancer. In one case withdrawal was performed after the patient developed a locked in state. The final decision of withdrawal was taken after a median of 2 conversations (range 1–3) with median 10 days (range 1–87 days) interval to ensure the durability of the decision. According to the patients' wishes the procedure took place in the home in 8 cases and at the hospital in 4 cases. Deep sedation was achieved with high dose Morphine (median 100mg, range 50–460 mg), Diazepam (median 100 mg, range 20–260 mg), before disconnecting the ventilator. Median time from discontinuation to apnoea was 15 minutes (range 0–1080 min) and to death 30 minutes (range 5–1080 min). An exemplary case will be presented.

Conclusions: A majority of the patients decided that treatment should be withdrawn before they developed a locked in state. The reasons for the request for withdrawal of treatment were a general loss of meaning in life. Withdrawal of IHMV after deep sedation may be a medically, legally and for the patient justified procedure to ensure a peaceful death in patients with advanced stage ALS and 24 hour IHMV.