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Palliative care for patients with motor neurone disease: current challenges

David J Oliver

¹Wisdom Hospice, Rochester,

²University of Kent, Canterbury, UK

Abstract: Motor neurone disease is a progressive disease, and the patient and his/her family face many challenges during the disease progression, with increasing weakness and multiple losses of function. The provision of care for these patients and their families is equally challenging, anticipating and responding to the person's needs. There are increasing challenges as more is understood about the disease and its management, including the genetic basis, cognitive change, the use of interventions such as ventilatory support, and gastrostomy. There is also an increasing need to ensure that the later stages are recognized so that all can be more prepared for the end of life, including recognition of deterioration and end of life, advance care planning, symptom management and psychosocial care at the end of life, and coping with requests for assisted dying. Careful assessment and good multidisciplinary team (MDT) work can enable patients and their families to have as good a quality of life as possible, and allow a peaceful death of the patient.

Keywords: Amyotrophic lateral sclerosis, end of life care, cognitive change, noninvasive ventilation, gastrostomy, advance care planning

Introduction

Patients with motor neurone disease (MND) and their families face many challenges, along with multidisciplinary teams caring for them. MND is a progressive disease, the etiology of which is usually unknown, although there is increasing evidence of a genetic component.¹ There is progressive loss of neurones – both motor neurones and within the brain – leading to progressive muscle loss and dysfunction. This is very individualized and varies from person to person but may present as follows:

- Amyotrophic lateral sclerosis, with both upper and lower motor neurone loss, leading to a mixed pattern of weakness, spasticity, and wasting. This is the commonest form of the disease, affecting ~66% of patients at diagnosis.
- Progressive bulbar palsy, affecting ~20% of patients at diagnosis, with the bulbar area being primarily affected initially, leading to speech and swallowing problems.
- Progressive muscular atrophy, affecting only 10% of patients, with primarily lower motor neurone damage, leading to weakness of arms or legs, affecting more commonly men in their 50s and with a slower progression and a longer prognosis of up to 10 years.²
- Rarely, MND may present as a respiratory failure due to respiratory muscle and diaphragmatic weakness. The diagnosis of MND may be made after the start of respiratory support.³

Correspondence: David J Oliver
Wisdom Hospice, High Bank, Rochester
ME1 2NU, UK
Tel +44 1634 83 0456
Fax +44 1634 84 5890
Email drdjoliver@gmail.com



- MND may present as frontotemporal dementia (FTD) with the cognitive changes presenting before the physical changes of MND; dementia may occur in up to 15% of all patients.

At present, there is no curative treatment, although riluzole has been shown to extend life by a few months.⁴ More recent evidence shows that MDT support⁵⁻⁷ and noninvasive ventilation (NIV)⁸ will extend life. The prognosis is often 2–3 years, although 25% live for 5 years and 10% will be alive at 10 years.² As there is no curative treatment, palliative care can be considered as appropriate at the time of diagnosis, which can be defined as follows: “An approach that improves the quality of life of patients and their families facing problems associated with life-threatening illness, through the prevention and relief of suffering, early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.”⁹

There is increasing awareness of the role of palliative care in MND, and the European Guidelines on MND care¹⁰ and the American Practice Parameters¹¹ press for improved care throughout the disease progression and at the end of life. A recent Consensus Document from the European Association for Palliative Care and the European Academy of Neurology has also stressed the role of palliative care for all neurological diseases.¹²

Moreover, there is increasing evidence that palliative care is effective in improving quality of life. A study of patients with neurological diseases showed that there was improvement in overall quality of life and in the symptoms of patients with MND, multiple sclerosis, and Parkinson’s disease.¹³ This has been supported by other studies with multiple sclerosis and other neurological diseases where symptoms and quality of life are seen to improve with a palliative care approach.^{14,15} However, there are increasing challenges with the provision of palliative care for people with MND, as there is increasing recognition of certain aspects of the disease progression – genetics, cognitive change, respiratory dysfunction, new interventions in management (gastrostomy, respiratory support), issues toward the end of life, recognition of the end of life, advance care planning, care at the end of life, requests for assisted dying, and the increasing complexity of multiple team involvement. The aim of this review is to summarize some of these issues and look ahead into the future.

The role of genetics

Over the last 20 years, the role of genetics in the etiology of MND has been recognized. Although 5%–10% of people with MND have a clear family history, until recently, it was

possible to identify gene mutations in only a small minority. However, there are now more than 15 genes recognized, many with multiple mutations, and recently, it has been shown that in people with familial MND, a gene abnormality can be found in 60% – most commonly the *C9orf72* gene (often with associated FTD, or some family members may only have FTD), and also the *SOD1*, *TDP*, and *FUS*.² Moreover, within the population with no family history, ie, “sporadic” MND, there is evidence of gene mutations, particularly *C9orf72*.² It would seem that there may be complex genetic and environmental factors involved in MND, with much still to learn.¹

Thus, there is a new challenge that people with MND, whether they have a family history, or not may request gene testing. This has great implications for patients and their families. The majority of gene mutations show autosomal dominance, although the penetrance of the gene mutation is not always clear, so not all carriers of the gene mutation may develop the disease. The identification of people with abnormal genes, and thus with a very high risk of developing MND, will have many implications for families and individuals. There may be decisions taken not to have children, or to consider alternative complex in vitro fertilization and reimplantation of unaffected zygotes. There may also be complex psychosocial reactions and family interactions after the genetic basis of the disease has been identified.

Although a gene mutation may be identified in ~50%–60% of patients with familial MND, it may not be possible to identify any abnormal gene mutation at the present time. Thus, this leaves further uncertainty and unresolved issues for all involved. Consideration of genetic testing is complex and should be taken after careful consideration and discussion with experienced genetic services.

Cognitive change

There have been similar developments in the awareness of cognitive change in MND over the last 20 years. Although dementia was originally described in the early descriptions of MND, it was always stated that there was no evidence of brain changes. However, in the last 20 years, there has been increasing evidence of cognitive and behavioral change, and several forms can be identified:

- ALSci – cognitive impairment 28%;
- ALSbi – behavioral impairment 39%;
- ALS-FTD – frontotemporal dementia 15%.¹⁶

These changes can have a large influence on the care and quality of life of both the patient and family carers. The behavioral changes can be very hard for families and carers,

as there are issues of safety and decision making. Although FTD may be more obvious and have a major influence on the care provided and the ability of family carers to cope at home, the less pronounced frontal changes can greatly influence decision making and forward planning. These may affect day-to-day care, and help may be needed for all carers, family, and professionals to ensure that any discussions and decision making is kept as simple as possible – for instance, presenting a range of options may be too complex and it may be necessary to have a simple decision between two clear options to facilitate the patient's involvement.¹⁶

This awareness is increasing, and there are new assessment tools to allow professionals to recognize cognitive change.^{17,18} These often include both patient and family carers, who may recognize earlier changes in behavior. The Edinburgh Cognitive Assessment Scale includes all involved and can be helpful in identifying cognitive changes, although there is complexity in analyzing the results and assessing how relevant these changes are in the day-to-day care of patients.¹⁷ The ALS-Cognitive Behavioral Screen has also been used to help assess cognitive function.¹⁸ The recognition of possible change may be helpful in ensuring that advance care planning is undertaken earlier in the disease progression while the patient can express his or her views clearly.

If patients are to be included in decision making, it may be necessary to consider advance care planning, such as an advance directive or the definition of a proxy for decision making, to ensure that their wishes are known and can be respected. This is now a clearer challenge, as the patient may be facing increasing cognitive change, as well as increasing problems with communication.¹⁶

Interventions

There are now interventions that may improve either the quality of life and/or prognosis, including gastrostomy for the continuation of feeding when someone cannot swallow effectively, or NIV or invasive ventilation, with a tracheostomy, for respiratory failure due to diaphragmatic and respiratory muscle weakness. These do present further challenges in the assessment and recognition of the need for intervention, the issues of discussion about the benefits and problems, and the consideration of withdrawal at the end of life.¹⁹

Gastrostomy

Gastrostomy has been used to help people with swallowing and nutrition issues for many years.²⁰ For people with MND, there is evidence that gastrostomy may improve quality of life and reduce stress on patients, families, and professionals

in the administration of fluid and medication, even at the end of life, but there is little convincing evidence that there is increased survival with gastrostomy.²¹ Moreover, there is some limited evidence that, if the patient has compromised respiratory function, there may be increased mortality and morbidity.¹¹

The discussion of gastrostomy – either as percutaneous endoscopic gastrostomy (PEG) or percutaneous radiologically inserted gastrostomy (PRG or RIG) – can be complex.^{20,21} It has been suggested that a gastrostomy should be considered if there is a 10% loss of weight, although even a 5% loss has been recently shown to have increased mortality.²² It is also helpful to start discussion when there are signs of swallowing problems, as the discussion should be considered as a process over several weeks or months, rather than a sudden decision based just on weight loss.²⁰ However, patients, and often their families, find discussion of interventions difficult and may put off decisions. As the decision is influenced as much by respiratory muscle function – if the forced vital capacity is <50%, the mortality rises for the insertion of a PEG¹¹ – the patient may not see a need for PEG and put off decisions until it is no longer possible as sedation is necessary for a PEG and the risk increases greatly. It may still be possible to consider a PRG, as this is inserted using X-ray monitoring and the patient can remain more upright and even use the NIV.

The use of gastrostomy as the person deteriorates may also be complex. Families and carers may wish to continue a full nutritional feeding regime, even though this may no longer be appropriate. However, for most patients, the gastrostomy is used less as the disease progresses and can be used just to maintain hydration and the administration of medication even near to the end of life.²⁰

Ventilatory support

The cause of death in the majority of patients with MND is respiratory failure. There is increasing evidence that the recognition of early respiratory failure can allow consideration of respiratory support, usually NIV, which may improve the quality of life and extend survival.⁸ There is a challenge to ensure that respiratory function is regularly assessed – asking for symptoms, in particular orthopnea, poor interrupted sleep, morning headache, increased dreaming or nightmares, lethargy, anorexia, breathlessness – and checking respiratory function and blood gases – using sniff nasal inspiratory pressure, measurement of forced vital capacity, and checking oximetry, at rest or overnight if there is suspicion of nocturnal respiratory insufficiency.

There are guidelines suggesting assessment regimes,²³ but it may be a challenge to help patients and families see the importance and significance of regular supervision and testing. Moreover, it has been suggested that throughout the disease progression, even from diagnosis, there is the need to explain the reasoning behind the monitoring of respiratory function.^{23,24}

The majority of patients will cope well with NIV, but some find it particularly difficult – if there are bulbar symptoms with drooling into the mask – or some people with feelings of claustrophobia.²⁵ With perseverance, many can continue with NIV, but for those for whom it is too difficult, other ways of helping the symptoms – such as raising the head of the bed and helping the patient to be less supine, or opioids, such as oral morphine, to reduce the sensation of dyspnea.^{26,27}

Symptoms are often managed very effectively by NIV, with improved sleep, reduced fatigue, and improved appetite. Survival may be increased, and the one trial of NIV showed a survival advantage of over 200 days – from 11 days without NIV to 216 days for the people tolerating NIV.⁸ However, there will be disease progression and many patients find this deterioration difficult, as they face increasing disability and dependency and often increasing speech and swallowing issues.²⁴ Although most patients require the NIV only to support breathing at night initially, as the disease progresses there is often the need to use NIV in the day, and some patients become dependent on continuous respiratory support, with severe breathlessness when they are not receiving NIV. Thus, many patients may feel that the burdens of continuing NIV are too great and they may wish to withdraw from this treatment. Although this decision may be taken by anyone who has the capacity to do so and is acting autonomously, there may be many issues raised – for patient, family, and professional carers.

The withdrawal of NIV may be seen as a challenge in the care of patients with MND. A survey of palliative medicine specialists showed that the process and discussion of withdrawal of NIV was a source of ethical debate, emotional stress, and team stress,²⁸ particularly as it was not a common event within their practice. Other studies of doctors and professionals and families have shown that there are often many debates and discussions of the ethics and practicalities of withdrawal – with concerns that withdrawal would be seen as assisting suicide/dying or even euthanasia.^{28,29} However, the ethical position can be seen to be clear if a patient with capacity makes the autonomous decision to refuse a treatment, which he or she feels is burdensome, or there is actually an imperative to ensure that this occurs.³⁰

In many cases, there may be doubts and conflicts with the patient, family, and the professional team.^{28,29} As a patient deteriorates, the assessment of capacity may be more complex and, as communication becomes more difficult, these discussions can be challenging. On occasions, patients may have made their wishes clear with an advance directive stating that they do not wish to continue with NIV in certain circumstances. Even then, it may be complex assessing whether the person has reached the situation that they envisaged and there may be a lack of clarity in such advance directives.³⁰ Moreover, there are often disagreements within families and the caring professional teams, as everyone has his or her own particular ethical standpoint, the understanding of which may be inaccurate and not reflect the true ethical and legal aspects.

There are now clearer guidelines on the withdrawal of NIV,³¹ and these stress the need for clear communication with patient, family, and all the team involved, a clear plan for withdrawal – what medication to give to ensure that distress is minimized, who will give medication, who will remove the mask, and who will support the family – and with a clear ethical and legal explanation. If a patient is completely dependent on NIV, he or she will need to have medication to prevent distress, as the patient is very likely to become very breathless when NIV is reduced or removed. If a patient is not totally dependent on NIV, it may be possible to give medication if there is distress, although some anticipatory medication may be helpful to cope with the anxiety of patient, family, and professionals. Usually, an opioid, such as morphine or diamorphine, a benzodiazepine, such as midazolam, and an antimuscarinic, such as hyoscine hydrobromide or glycopyrronium bromide, is given, as a continuous subcutaneous infusion, with extra medication available to give intravenously or subcutaneously if there is distress with the procedure.³¹

With careful planning and discussion with all involved, NIV may be withdrawn without distress for the patient. However, there is a need for discussion of these issues of NIV to be undertaken before there is disease progression and dependency on NIV. It has been suggested that the discussion of disease progression and the management of dependency – using medication to reduce distress rather than NIV – should be undertaken at the time NIV is started and at regular intervals as the disease progresses.^{23,24} In this way, all can become aware of the issues, and advance care planning can be instigated, so that the patient's wishes are known even if communication, cognition, or capacity becomes compromised.

Tracheostomy ventilation may be possible and has been shown to extend life further, even for many years or decades.^{24,32} However, disease progression may lead to a patient becoming totally locked in with no way of communication.²⁴ In the UK, tracheostomy is rarely performed as a planned procedure, although some patients, who present with acute respiratory failure, may receive a tracheostomy and start on ventilation before the diagnosis of MND is made. In other countries, tracheostomy is used more commonly, and in Japan up to 33% of all MND patients have full ventilation with tracheostomy.³² There are many ethical issues raised with the continued ventilation for a patient when he or she cannot communicate, and great care is needed in discussing these options. Studies have shown that Japanese neurologists would be less likely to have a tracheostomy if they developed MND, although this is often offered to their patients.³³

Recognition of the end of life

A patient with MND is facing a short prognosis and usually dies from respiratory failure, often associated with a respiratory infection. This may follow a slow decline but may be a sudden decline over only a few days.³⁴ The recognition that the patient is now at the end of life may be a challenge, particularly as the patient, family, and professionals may all see the gradual deterioration and not notice the final changes that may herald the end of life. It has been suggested that there are certain triggers that may be used to recognize this phase. For all neurological patients, these are the following:

- swallowing problems;
- recurring infection;
- marked decline in functional status;
- first episode of aspiration pneumonia;
- cognitive difficulties;
- weight loss;
- significant complex symptoms.³⁵

For patients with MND, there may also be

- respiratory failure or increased breathlessness;
- reduced mobility;
- dysphagia.³⁵

These triggers have been initially assessed, and a group of neurological patients were found to have an increased number of triggers as death approached, and aspiration pneumonia was particularly significant, and was often within 6 months of death.³⁶

The importance of the recognition of the end-of-life phase may be in allowing the preparation of the patient, and often, more importantly, the family and carers, that time is

limited, and in preparation for the dying phase. This may include the provision of anticipatory medication – morphine, midazolam, and glycopyrronium bromide injections, and/or buccal midazolam or sublingual lorazepam – that could be given if there is a sudden deterioration or development of breathlessness, pain, or distress. This has been developed within the “Just in case kit” by the MND Association in England,³⁷ and has been supported for patients at the end of life by NICE.³⁸ Careful discussion about the wishes of the patient and family – of place of death, funeral arrangements, will, and care at the end of life – may be important so that all are prepared as much as possible.^{18,30}

Before the last stages of life, there is a need to consider planning ahead – advance care planning. This may be of particular importance in MND, and there is a challenge in enabling these discussions when the patient is still able to communicate and has not developed cognitive change.³⁰ Thus, discussion of wishes, including will, funeral, place of death, resuscitation, and use of invasive procedures such as gastrostomy, NIV, or even tracheostomy, will allow the patients to express their wishes and enable the family and professional carers to follow their wishes, even if they are no longer able to communicate them.³⁰

Advance care planning may be ensuring that the wishes are clearly known, but there are specific ways to express these views such as the following:

- Advance directive (in England an Advance Decision to Refuse Treatment), which may record measures a patient does not wish at the end of life, such as resuscitation or ventilation. This may be a legally binding document if correctly completed and specific in its wording.
- Advance statement – a nonspecific document expressing the general wishes of a person, such as their wish not to have life extended if they are no longer able to communicate.
- The appointment of a proxy – who would be able to make decisions on the person’s behalf if he or she has lost capacity. In England, this Power of Attorney can be for property or health issues.
- A will that allows the person to clearly state his or her wishes for the belongings and monies.³⁰

The discussion of these issues may be complex and difficult, especially because on occasions there may be an imperative to discussing and completing these documents if the person has reduced communication or has increasing cognitive change. However, with careful communication it is usually possible to raise these issues and ensure that patients are able to express their wishes and their autonomy, so that

if they do lose the capacity to make or express their views, these are still clearly known and can be acted on.^{18,30}

Care of the dying

When death is expected, there is an even greater need to ensure that symptoms are managed effectively, especially pain, breathlessness, and fear. Careful assessment is essential, and consideration of all aspects of care, including psychological, social, and spiritual issues. If a patient is frightened about death, this may be the process of dying – fearing breathlessness or distress – or fear of death itself, as a deeper spiritual fear.^{39,40} Both these issues need to be addressed appropriately, and may include other members of the wider MDT, including a spiritual care adviser or priest/spiritual leader.⁴⁰ As someone becomes more ill, the oral route for medication may become more difficult. If the patient has undergone gastrostomy, this may be used to administer medication until near to death. For many patients, parenteral medication may be necessary, using subcutaneous injections or a continuous subcutaneous infusion using a syringe driver.⁴¹ It is essential to continue opioid medication until death because, although a patient may become unrousable, he or she may still perceive pain or dyspnea and need to have appropriate medication.

There is also the need to support family and carers,³⁹ and often professional carers who may have known the patient for some time. It is important that all involved in the patient's care are aware that death is near and expected, so that they all act appropriately and support the patient, family, and each other.^{39,40}

Assisted dying

Patients with MND often fear a distressing death, and the media often discuss the distress of dying with MND, talking of breathlessness, pain, and loss of control. This has led many people to consider an assisted death – according to their country of residence. This may be assisted suicide – when the doctor provides medication for them to take with the explicit aim of ending life – or euthanasia – when a patient is given an injection of medication with the aim of ending life.⁴² This may be possible in the Netherlands (euthanasia and assisted suicide), Belgium (euthanasia), Luxembourg (euthanasia and assisted suicide), Switzerland (assisted suicide), Columbia (euthanasia) and several states in the US (assisted suicide).⁴³ Patients with MND are often one of the patient groups more likely to ask for an assisted death – 22% of patients in the Netherlands received euthanasia and 10% terminal sedation.⁴⁴

Thus, there is increased awareness of the issues of assisted dying, and there has been pressure across the world for increased access to assisted dying, often using a person with MND as an example of why this should be allowed – often exaggerating the fears of dying and of distress.⁴¹ The evidence from many studies is that death from MND is peaceful when there is good palliative care – with good management of both symptoms and the support of patient and family.^{34,45} For many people, this information can be reassuring and reduce the wish for an assisted death, but a small minority may still wish to keep control and wish to choose their mode of dying. Within countries where there is no legislation allowing assisted dying, there will be the need to explain the position clearly and stress that actions can be taken to ensure that life is not unnecessarily prolonged – as many people fear prolongation by unnecessary intervention – and advance care planning can allow their wishes to be known and for these to be respected even if they are not able to communicate or have lost capacity to express their wishes.³⁰ A “Do Not Attempt Cardiopulmonary Resuscitation” (DNACPR) order can also be helpful in showing that a natural death would be allowed, and the provision of anticipatory medication shows that if there are difficult or distressing symptoms, these will be managed effectively and speedily.^{30,41} Some patients may still request assisted dying and may even seek this in another country – for instance, traveling to Switzerland and receiving an assisted suicide at Dignitas.

Team issues

The management of a person with MND will often need the involvement of an MDT, and this has been suggested as the aim in the provision of care.^{5–7} Moreover, there is evidence that the MDT approach improves both quality of life and the length of survival – one study suggesting that the 1-year mortality was decreased by 29.7%⁵ and another suggesting that the median survival was 19 months for the MDT group compared to 11 months for standard care⁶ and a further study showing a survival difference.⁷

However, there may also be other issues arising within any MDT – as there may be differences of opinion or even conflicts between team members. This has been highlighted in the issues of withdrawal of NIV, as there were often different understanding of the ethical issues – as one consultant in palliative medicine talked of “walking onto the ward at the allocated time and being treated like an executioner is not easy” and another spoke of the “nurses need emotional and ethical support.”²⁸ These issues may take time and careful discussion, and one of the main roles of the MDT meeting

may be to allow these discussions and the support of the team.

These issues may be even greater when several teams are involved in the patient's care. It may not be unusual for other teams – respiratory teams looking at NIV, gastroenterology considering PEG, neurology team, specialist palliative care, primary care. All of these teams may have different standpoints, with different ways of working, varying ethical systems, and ways of working as a team.⁴⁶ These issues can lead to conflict between teams and understanding the different ways of working, and the differing pressures and stresses on team members and team dynamics are important if the care of the patient and family is not to be compromised. As the care of the patient with MND becomes more complex – perhaps with psychological services assessing cognition, genetic counseling services providing advice – the need of a clear lead is important. An MDT should define, if at all possible, a key contact – although a single team contact is often suggested, a “team contact” may be more realistic to cover leave and sickness absences of a single person.⁴⁶ The MDT should ensure that there is clear coordination and the contact(s) are able to liaise with other teams and provide a clear pathway for the patient and family.⁴⁶

Conclusion

The care of a patient with MND, and their family, is becoming more complex as further information about the disease and its effects are found and further interventions are used to improve the quality and length of life. Careful coordination is essential, and the MDT needs to be there to help patient and family meet all these challenges.

Disclosure

The author reports no conflicts of interest in this work.

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