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The development of the UK National Institute of Health and Care Excellence evidence-based clinical guidelines on motor neurone disease

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Abstract

The care of people with motor neurone disease / amyotrophic lateral sclerosis is often complex and involves a wide multidisciplinary team approach. The National Institute for Health and Care Excellence (NICE) in the UK have produced an evidence based guideline for the management of patients. This has made recommendations, based on clear evidence or consensus discussion. The evidence is often limited and areas for further research are suggested.

Introduction

The care of people with motor neurone disease (MND / amyotrophic lateral sclerosis (ALS)) is complex. Individuals who are affected experience multiple symptoms and issues that may change quickly, with a pattern of deterioration that can be difficult to predict. Guidelines for the care of people have been produced – both in Europe with the European Federation of Neurological Societies Guideline on ALS (1) and in the USA the Practice Parameter from the American Association of Neurology (2). Within the UK the National Institute for Health and Care Excellence (NICE) had published guidelines on the use of riluzole for MND (3) and the use of non-invasive ventilation (NIV) (4) but there was no overall guideline on the clinical care of people with MND. It was felt that the care of people with MND across the UK was very variable. Although there are multidisciplinary team clinic and networks providing co-ordinated multidisiciplinary care many patients are isolated and their care is less than ideal. Thus a a guideline on the care and management of MND was developed in early 2016 to consider the clinical and cost effectiveness of the care of people with MND from diagnosis to death(5) . The earlierguideline on NIV was updated and incorporated within this new Guideline. . The Recommendations shown below reflect those in the Guideline, and fuller versions are available in the main Guideline documents (5).

Methods of developing the Guideline

NICE commissioned the National Clinical Guideline Centre, based at the Royal College of Physicians, London to undertake the development of the guideline. There is a rigorous process for all stages of guideline development as there is a requirement for recommendations to be based the assessment of the best available evidence.

An initial scoping exercise was undertaken using interested stakeholders including professionals and organisations representing people with MND. The scope defined the guideline population and specific areas that would be considered. There were 21 clinical questions in the guideline, each of which was addressed through a systematic review of the literature. The reviews were developed in accordance with the methods outlined in the NICE guidelines manual (6). This guideline included intervention (treatment) reviews, prognostic reviews, and qualitative reviews. A protocol was formulated for each clinical question indicating the objective of the evidence review and stating, a-priori, criteria of the studies to be included, what data would be extracted from the studies, and how the data would be analysed. For example, for prognostic reviews, studies were only included if the risk factors pre-specified by the Guideline Development Group (GDG) were adjusted for each other using multivariate analysis. Studies not meeting this requirement were not included.

A comprehensive literature search was undertaken for each question using MEDLINE, Embase, and The Cochrane Library. Additional subject specific databases (CINAHL and PsycINFO) were used for some questions. An initial search of abstracts identified papers judged relevant to the review and full text of these were then subject to a definitive assessment. For some questions no published evidence was found.

Once the studies to be included were determined their data was extracted and, where possible, evidence was synthesised. For intervention and prognostic reviews, meta-analyses were conducted using Review Manager (RevMan) 5 software. Dichotomous outcomes in intervention reviews, such as mortality, were meta-analysed via risk ratios (relative risk). For continuous outcomes, such as quality of life, results were meta-analysed using weighted mean differences. For data synthesis in prognostic factor reviews the odds ratios, risk ratios or hazard ratios for the effect of the pre-specified prognostic factors were extracted from the studies. Qualitative reviews were synthesised by thematic analysis, identifying sub-themes from the included papers and linking them to a generic theme and allowing a summary evidence table of generic themes and underpinning sub-themes to be produced.

Where possible the quality of the evidence was assessed using Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (7). For the intervention questions, overall quality assessments were made for each outcome. This included an appraisal of the risk of bias, indirectness (relevancy to the clinical question) and imprecision for each outcome in each included study. It also required a judgement of "inconsistency"; the heterogeneity of effect estimates between studies, and the possibility of publication bias. The quality rating for each outcome was determined to be high, moderate, low, or very low. A modified GRADE methodology was utilised for prognostic studies with the risk of bias rating assigned to each study for each combination of risk factor/outcome. For both intervention and prognostic reviews, randomised controlled trial (RCTs) began at high quality and were downgraded whilst observational studies began at low quality and downgraded from there. Observational studies could be upgraded for quality if the evidence presented determined this. In terms of qualitative reviews, the methodological quality of each study was assessed using an NCGC-modified NICE checklist and the quality of the evidence was assessed by a modified GRADE approach for each outcome, taking into account the applicability and theme saturation/sufficiency of the evidence. The evidence was graded 'applicable' if the evidence was directly applicable to the question, and graded partially applicable if it was related but not sufficiently.

The multidisciplinary Guideline Development Group (GDG), including 2 neurologists, 2 palliative care consultants two respiratory consultants, physiotherapist, occupational therapist, community matron, nurse specialist, general practitioner, speech and language therapist, patient and carer representatives and co-opted neuro-psychologist, dietitian and social worker, made recommendations from the highest quality evidence that was found. In the absence of evidence expert opinion recommendations were made by consensus.

For all questions the evidence for cost-effectiveness was considered. The health economist identified potentially relevant studies and reviewed, critically appraised and extracted key information from them, as described for the reviews above. NICE has set out principles to be used in these assessments and an intervention is considered to be cost-effective if the intervention dominates other strategies (is less costly in the use of resources and more clinically effective) or the intervention costs less than £20,000/ QALY compared to the next best strategy (6). When no relevant studies were found the GDG made a qualitative judgment based on the expected differences in resource use together with the clinical review of effectiveness.

Reviews were undertaken looking at information, prognostic factors, organisation of care, psychosocial support, end of life care, symptom management, nutrition, communication, respiratory impairment and non-invasive ventilation.

The Recommendations shown below reflect those in the Guideline, and fuller versions are available in the main Guideline documents (5). The recommendations vary in their strength, taking into account the benefits and harms of an intervention and the underpinning evidence. Strong recommendations are stated as "offer" when it is felt that for the majority of patients the intervention will do more good than harm and are cost effective, and "consider" is used when the intervention is felt to do more good than harm and is cost effective but other options may be similarly cost effective (6). In this paper the strength of the recommendation is not given, but further information and the full recommendations are available within the main Guidleine document (5)

Recommendations

Recognition and referral

MND is a rare disease and as symptoms may be vague initially the diagnosis is often delayed. Qualitative studies, of medium quality, were reviewed and showed that there were many reasons for delay in diagnosis: patients often did not perceive the physical changes as significant and did not ask for help, when they did present to health care professionals the significance of the symptoms was not recognised and a variety of medical specialities could become involved as the wider significance of symptoms was not recognised, such as referral for leg weakness to rheumatology or orthopaedics rather than neurology (8,9,10).

Recommendations

- A protocol and pathway for referral should be available in all healthcare regions)
- Awareness of possible symptoms should be encouraged
- If MND is suspected a referral should be made without delay
- Information should be provided for patient and family at all stages

Information and support at diagnosis

As MND is rare the General Practitioner and other health and social care professionals may have little understanding and knowledge of the condition, but patients and families may have many concerns they wish to discuss. There is a need for careful and considered communication, with professionals who are able to respond to patient and family concerns (9, 11, 12). Qualitative studies were considered and were of moderate quality and were evaluated together with the GDG experiences and knowledge when formulating the recommendations.

- *Recommendations*The diagnosis of MND should be given by a consultant neurologist with knowledge and expertise in MND
- It is important to ensure:
  - People are asked about their wishes for information and involvement of family / carers
  - Information on MND is provided as they wish
  - A single point of contact for the MND Multidisciplinary Team (MDT) should be available
  - Follow up appointment with a MDT member within 4 weeks

- A referral for social care should be made
    - If there are social care needs
    - To ensure carers are aware of Carer's Assessment, and assessments are made financially and for care

Organisation of care

A person with MND has diverse and complex symptoms, necessitating the involvement of a variety of different specialists and services. Moreover the disease progression varies greatly and there may be rapid change, with different symptoms adding to the complexity. The GRADE review identified several papers of low or very low quality, largely because they were cohort studies and at risk of bias. The evidence was overall in favour of a co-ordinated team approach that appeared to increase survival, the use of riluzole and NIV (13, 14, 15, 16). The GDG concluded that the evidence demonstrated that a clinic based MDT with involvement of professionals, who could see patients at home, was both clinically and cost effective. The GDG acknowledged other models of care organisation and recommended further research establishing whether benefits were maintained in other care models, such as a network based team.

A review was also undertaken looking at the optimum frequency of assessment. No relevant literature was found and the GDG agreed on discussion that assessment every 2 to 3 months was appropriate, but more or less frequent review may be needed according to patient need.

Recommendations

- Co-ordinated care should be provided from a clinic based MND multidisciplinary team
    - Based in hospital or community
    - Including health and social care professionals
        - With expertise in MND
        - Staff able to see people at home

      Ensuring communication to all health and social care professionals / Family / carers
- The skills of the multidisciplinary membership would include:
    - Neurologist
    - Specialist MND nurse
    - Dietitian
    - Physiotherapist
    - Occupational therapist
    - Respiratory healthcare professional
    - Speech and language therapist
    - Palliative care expertise – may be one of the team members. Referral to specialist palliative care should be considered if there are complex needs

- Co-ordinated assessments should be undertaken every 2-3 months according to the person's needs and they could be seen earlier if there are changes in condition. If person cannot attend clinic care should be facilitated within the community. It is important to ensure all are informed of key decisions, with close liaison with General Practitioner.
    - The multidisciplinary team should assess, manage and review
        - Weight, nutritional intake, feeding, swallowing
        - Muscle problems –weakness , stiffness, cramps
        - Physical function

- Saliva problems – drooling, thick saliva
- Speech and communication
- Cough effectiveness
- Respiratory function

Psychological care

Psychological distress is an understandable response to the diagnosis of MND and progressive deterioration. No RCT's or cohort studies were identified. A large qualitative literature was reviewed consisting of a number of high and moderate quality studies. The main themes that were derived from the evidence were:

- Coping with the diagnosis
  Reactions to the diagnosis, making sense of the diagnosis and support following diagnosis
- Understanding the disease
  Information seeking behaviour, sources of information and filtering of information
- Acceptance
  Accepting the disease, coping and gaining control, finding meaning in life
- Coping with a changed life
  Maintaining and coping with "normality", hope, living for the moment and looking to the future
- Changes in relationships
  Changes in identity and role, reduction in intimacy and the importance of touch (11, 12, 17)

The evidence suggested that the psychological support provided needs to adapt through the disease course and regular assessment of psychological needs was important (17). Informal support may often be helpful but referral for formal psychological assessment and management may be necessary.

Recommendations

- The MDT assessment should include discussion of the psychological / emotional impact of MND
- Information on support should be offered to the person with MND and their family / carer
- Social care should be discussed with experienced social care worker – considering the need for personal care (with continuity of carers), finances, enabling social activities, hobbies and social media and respite care.

Social care

The diagnosis and management of MND takes place within health services and in the UK social care is provided by local authorities, who have a duty to assess their needs and those of their carers. As MND causes many different issues there is overlap with other areas of care. A review was undertaken to consider the social care support needs of patients and their families. Six qualitative studies were analysed and were felt to be of moderate or high quality and two main themes were identified - social care needs and the delivery of social care. The GDG concluded that regular assessment of social care needs was important, as the situation was continually changing. There was a need to ensure that care teams were aware of the specific issues of MND and the individuality of the issues patients faced. There was also a need to ensure continuity of care, so that carers providing

personal care were aware of the patient's specific needs and could provide effective care (12, 18, 19, 20).

Recommendations

- A social care practitioner with knowledge of MND or rapidly progressive complex disabilities should discuss the needs and support information and access to personal care, equipment, financial support, support to engage in work, social activities and hobbies and respite care X
- As MND progresses people may develop communication problems and have difficulty assessing support or services, such as accessing a call centre. It is important to ensure people are given different ways of getting in touch with support or services, with a designated contact if possible.

Planning for end of life care

MND is a life shortening illness with an average survival of 2 to 3 years following symptom onset, although 25% of individuals survive 5 years and 10% are alive at 10 years. A review was undertaken into the most appropriate ways of communicating and supporting people with MND and their families to help them anticipate and prepare for the end of life.

Nine qualitative studies were analysed thematically and the evidence was mainly assessed as being of moderate or high quality. The key themes that emerged were: a need for information (what happens at the end of life), the importance of choice and control (through advance care planning) and the need for specific support (timely involvement of specialist palliative care) (17, 19, 21).

Recommendations

- All professionals should be open to discuss end of life care whenever the person asks and provide advice on
    - The discussion of their preferences and concerns about care at the end of life at trigger points such as diagnosis, interventions, respiratory function changes (Strong recommendation)
        - Support and advice on advance care planning – including what may happen and the consideration of advance care plans
        - Anticipatory medication at home
        - Specialist palliative care involvement
        - The person's wishes
            - Place of care
            - Place of death
            - What to happen if deterioration / other illness
        - As end of life approaches
            - Provision of additional support so family are able to reduce responsibility and spend time with the person
            - Ensure prompt access to
                - Communication aid to allow communication
                - Specialist palliative care
                - Equipment - syringe driver, beds, commodes, hoist
        - Bereavement care for families / carers

Provision of equipment to aid activities of daily living and mobility

MND leads to significant physical disabilities, many of which require aids and adaptions to enable the person with MND to continue to function and undertake activities of daily living. These changes

are usually progressive over time. A review was undertaken of the equipment needs of people with MND and two qualitative studies of moderate or acceptable quality were found which considered the devices most used by people with MND and the level of satisfaction with this equipment (22, 23).

The recommendations were based on the evidence and the discussions of the GDG. There were concerns that any equipment should be provided in a timely fashion and, as the disease was progressive, equipment should be adaptable to cope with further changes and this would help maintain quality of life and reduce the risk of adverse events such as falls and hospital admission. Co-ordination of the assessment and provision of all equipment was felt to be very important, including ensuring equipment was suitable for any adaptions to the environment and housing.

Recommendations

- Physiotherapy and occupational therapy assessments should be undertaken with regular review
- Activities of daily living, mobility and prevention of falls, the home environment and adaptation and assistive technology – environmental control – should undertaken
- Equipment should be provided without delay to allow maximise daily living and independence
- Equipment should be able to change as deterioration occurs and be integrated with other aids – eg AAC devices

Nutrition

Nutritional issues usually occur in MND, due to problems with feeding, and swallowing. A review was undertaken exploring the clinically and cost effective methods of maintaining nutritional intake and managing weight for whom a gastrostomy is not possible or appropriate. Two studies were found, both of very low quality. The GDG made consensus recommendations having found little evidence supporting the use of any supplement feeding regimes (24). It was felt important that weight was maintained and weights should be checked regularly. Quality of life is often related with fluid and nutritional intake and it was felt that enrichment of food and careful consideration of feeding and nutrition, including palatability and psychological issues were important.

A further review considered the most appropriate timing for a gastrostomy tube placement. No literature was found and the GDG agreed by consensus. It was felt that regular review and discussion of both nutritional and respiratory aspects was essential and there should be regular and careful discussion of the benefits and problems of gastrostomy placement with the person with MND and their family. If a person with MND declined gastrostomy placement there should be discussion of the risks of late placement or no placement. For patients with frontotemporal dementia a careful assessment of whether the person could cope and accept a gastrostomy was important, in collaboration with the family, carers and MDT.

Recommendations

- From diagnosis assess weight , nutrition and swallowing
- Assess ability to eat and drink
    - Aids to help plate to mouth
    - Food / drink preparation

- Advice on positioning / seating / posture
- Coping with social situations

- If there are suspected swallowing problems ensure a swallowing assessment
  - Discuss gastrostomy early and regularly
- If gastrostomy is needed this should be placed without delay

Communication

Speech problems are common in MND and articulation and voice quality may be affected. Moreover upper limb weakness may reduce the ability to use technology. Speech loss affects social relationships and engagement with health and social care. Augmentative and alternative communication (AAC) is highly individualised and involves the use of gesture, symbols, boards (low technology) and more complex computer based (high technology) systems. No studies were identified in this area and consensus was used by the GDG to make recommendations. It was felt that enabling people with MND to communicate was very important for quality of life and often for survival, being able to call for assistance, as well as to maintain the person in their role in society and at work. Different forms of AAC may be needed and there was the need to be able to respond to changes in ability. There is a need for careful assessment, in collaboration with the person with MND, and ensuring that the person with MND, their family and carers and the professional carers are all aware of the use and have been trained in their use.

Recommendations

- Assess needs for communication, including face to face, telephone / email / social media
- Provide equipment and ensure it is integrated with other aids
  - Low level - alphabet board, picture board
  - High level – PC / Tablet based
  - Refer to specialised services if there are complex needs

Muscle problems

A review was undertaken for the pharmacological and non-pharmacological management of muscle symptoms (e.g. cramps, spasticity and weakness).

For pharmacological interventions one review for muscle cramps and two other papers for functional disability and muscle strength were considered but were of low or very low quality. The GDG therefore made consensus recommendations for pharmacological treatment based on clinical experience. For cramps quinine was felt to be the standard clinical practice and other medication were to be second line use. For muscle stiffness pharmacological medication – as in the recommendations below – should be used. Careful titration of medication, to the maximum tolerated dose, should be undertaken for each individual.

For non-pharmacological treatments physical therapy was considered in 2 studies of low or very low quality. There was some evidence of benefit of resistance exercise and range of movement exercise for muscle cramps, weakness and stiffness. It was also agreed that passive movement exercise for patients who have very limited movement may be beneficial. One study considered transcranial magnetic stimulation (TMS) but this showed no clinical benefit.

Recommendations

- Cramps
    - First line Quinine
    - Second line Baclofen, Tizanidine, Dantrolene, Gabapentin
    - Ensure medication is appropriate – eg swallowing issues
    - Review regularly for effectiveness / side effects
- Muscle stiffness/ spacticity /increased tone
    - Consider Baclofen, Tizanidine, Dantrolene, Gabapentin
    - If not effective / tolerated/ contraindicated, consider referral to a specialist service for the treatment of severe spasticity
- Use of physiotherapy
    - Aims
        - Maintain joint range of movement
        - Prevent contractures
        - Reduce stiffness and discomfort
    - Can be resistance / active-assisted / passive
    - Check to see if family / carers can assist in the programme
    - May need referral for orthotics

Saliva management

Swallowing problems may lead to difficulties with saliva, which may be watery or sticky. Drooling and feelings of choking may occur and are both distressing and embarrassing for people with MND. A review was undertaken into the interventions for saliva management and identified only 2 studies relating to MND and 14 studies for indirect populations with similar problems of drooling due to reduced swallowing, which were considered as the GDG agreed that they were relevant (25, 26). The majority of studies were of low or very low quality, with only three studies of moderate quality. The recommendations were made from the evidence and GDG consensus.

Recommendations

- For drooling:
    - Advice on posture / diet / swallowing / oral care
    - Antimuscarinic medication trial - Glycopyrrolate / glycopyrronium bromide, Hyoscine hydrobromide
    - Injection of Botulinum toxin A into salivary glands
- For thick saliva
    - Stop medication that may thicken saliva
    - Advice on diet / posture
    - Humidification / nebulisers/ carbocisteine may be helpful

Cough effectiveness

Effective cough allows clearance of secretions and reduces the risk of aspiration. People with MND often develop weak inspiratory and expiratory muscles that reduces cough strength and this increases the risk of respiratory tract infections that are a cause of morbidity and mortality. A review was undertaken of the clinical and cost effectiveness of cough augmentation techniques for people with MND who have an ineffective cough. 3 studies were identified, but all very of very low quality, due to risk of bias and imprecision.

As all these studies were of low quality the GDG made recommendations based on their experience to augment the evidence. There was no strong evidence that any cough augmentation technique was better than the others. However it was felt that techniques to augment cough were useful and should be attempted first. If the cough augmentation techniques were ineffective or inappropriate manual breath stacking and then assisted breath stacking and finally mechanical cough assistance devices should be considered.

Recommendations

- Cough augmentation techniques should be offered if the person cannot cough effectively
- Breath stacking and / or manual assisted cough should be tried
- If bulbar dysfunction / breath stacking ineffective
    - Assisted breath stacking – using lung volume recruitment bag
    - Mechanical cough assist considered
        - Breath stacking ineffective and /or
        - During respiratory infection

Respiratory function

Respiratory muscle weakness resulting in respiratory impairment is a major feature of MND. There was a previous Guideline 105 on the use of Non-invasive ventilation (NIV) in MND and many recommendations were updated and incorporated into this Guideline. Three new reviews were undertaken in areas not previously considered in Guideline 105 (3).

A review was undertaken on the experience of discontinuation of NIV following a request for NIV discontinuation by a patient. Two qualitative studies were found and the themes that emerged were: concerns about planning and timing; issues of where to undertake discontinuation and the avoidance of hospitalisation; concerns about how decisions were made; practical concerns as to how to turn off the machine; the differences in professional understanding of the ethical and legal aspects regarding withdrawal of NIV; concerns about the NIV use at the end of life; the emotional burden of these decisions and the involvement in discontinuation; and the need for team involvement and support (27, 28). The GDG agreed that NIV was one method of managing breathless towards the end of life and that patients should be made aware of other ways of managing these symptoms, including medication. It was felt that it was essential to have careful discussion before initiation so that people with MND should have a realistic understanding and expectation of NIV, as to its advantages and disadvantages, how it may help in managing symptoms and can be life prolonging but would not stop disease progression and how NIV may be withdrawn.

A review was undertaken on the most appropriate management of discontinuation of NIV. No studies were found and the GDG based their recommendations on their experience and the information from qualitative studies. It was agreed that ongoing discussion regarding the benefits of NIV was essential and this would include discussions of discontinuation. There are ethical and legal issues to be considered and advance care planning is very important in ensuring patients' wishes are known. As it is a rare event for many teams the wider team should be involved, with advice from

people with experience if necessary. The GDG also noted the guidelines on the withdrawal of NIV in MND that were available (29).

A review was undertaken of pharmacological treatments that could manage symptoms of breathlessness in MND but no studies were identified. The GDG, by consensus, agreed that opioids and benzodiazepines are recognised treatments for the management of these symptoms within palliative care.

Recommendations

- Assessment of respiratory function should be undertaken regularly
- Discussion of management of breathlessness
    - NIV has advantages and disadvantages
        - Dependency on NIV is possible
    - Options for treating infections
    - Support of how to cope if there is a distressing situation and deterioration
    - Effectiveness of medication in helping breathlessness – e.g. opioids
    - Psychological approaches and support
- Discuss use of NIV regularly at appropriate times , sensitively
    - Soon after diagnosis of MND
    - When monitoring respiratory function
    - When respiratory function deteriorates
    - If person asks
    - Discussion should provide information on
        - Possible signs and symptoms of respiratory impairment
        - Role of monitoring and explanation of results
        - The use of NIV to relieve symptoms and may prolong life, but does not stop the underlying progression of MND
- Offer non-invasive ventilation
    - If there is likely to be a benefit for the person
    - Consider trial of NIV in people with severe bulbar problems or severe cognitive problems - if it is thought they would cope with NIV and this may help in hypoventilation or sleep-related problems
    - Opioids / benzodiazepines may be used to relieve breathlessness
- Before starting NIV there should be risk assessment by the MDT
    - Most appropriate ventilator and interface
    - Tolerance to NIV
    - Risk of ventilator failure
    - Power supply needed - including need for battery back up
    - How easy for the person to reach a hospital for help
    - Risk of travelling abroad if they wish to do so
    - Need for humidification
    - Assessment of secretions / saliva management
    - Availability of help from carers
- Starting NIV
    - Initial acclimatisation in the day
    - Start regular use at night
    - Increase slowly in use
    - Training for person and family and carers is essential
    - The actions to be taken in emergency situations should be discussed
    - Secretion management is essential

        - Palliative care strategies should be in place – e.g. use of opioids and provision of "Just in case" anticipatory medication
- Stopping NIV
    - There needs to be careful consideration of the plan to stop NIV
    - Ensure there is support from professionals who have expertise in stopping ventilation, using palliative medication, supporting the person, family /carers / health and social care professionals and the legal and ethical aspects

Cognitive assessment

There is increasing evidence that over 50% of people with MND have changes in cognitive function, varying from subtle cognitive impairment to frank frontotemporal dementia (30). These changes have implications for communication, decision making and the care they may need. A review was undertaken looking at the optimum frequency of assessing cognitive function. No studies were identified and so the GDG, with a co-opted expert in neuro-psychology, used informal consensus to make recommendations. It was felt that if cognitive change occurs it often occurs early in the disease progression and assessment at diagnosis would help to plan further care. Ongoing enquiry of cognitive or behavioural change may be helpful. The GDG identified that this was an important area for further research.

- At diagnosis or if there is a concern about cognition or behaviour explore these areas with the person and their family
- If necessary undertake a formal assessment
- Assess for capacity and adjust care accordingly
- Tailor discussions to the person's needs, taking into account their communication ability, cognitive status and mental capacity

Prognostic factors

The progression of MND for any particular patient is very variable. However patients and families may often wish to have a clearer idea of prognosis, as this could enable them to make plans for their lives, as well as enabling professionals to deliver more anticipatory management. A review was undertaken looking at the most accurate prognostic tools for estimating survival in MND. One study had produced an ALS Prognostic Index (31). A further 11 studies were found in a review of the risk factors that predict survival in MND. These varied in quality but in some there was serious imprecision and the quality of the evidence was rated at low or very low. The main risk factors that emerged were: ALS FRS scale, the higher at diagnosis, the longer survival; Forced vital capacity (FVC), higher values with longer survival; weight change at diagnosis, low weight at diagnosis, weight loss predicts shorter survival; older age at diagnosis predicted shorter survival; bulbar onset predicted shorter survival; longer time to diagnosis predicted longer survival.

The GDG felt that prognostication would be helpful for people with MND, their carers and professionals. The GDG considered that further research in this area would be helpful to be able to offer patients a more individualised prognosis.

Recommendations

- When planning care take into account that these factors are associated with shorter survival if they are present at diagnosis

- Speech and swallowing problems
- Weight loss
- Poor respiratory function
- Older age
- Lower Amyotrophic Lateral Sclerosis Functional Rating Scale (ALS FRS-R)
- Shorter time from developing symptoms to the time of diagnosis
- Cognitive change

Discussion

The development of this Guideline involved a close collaboration between the Guideline technical team and the professionals and carers within the Guideline Development Group. The evidence found was rarely from randomised controlled trials and so cohort studies or qualitative studies were used – further information on the searches are available from NICE (5). Consequently many recommendations were made by consensus from within the GDG.

The recommendations are similar to those in previous Guidelines (1, 2) although they do incorporate the updated evidence base since they have been written and published. There are still areas without evidence and the GDG have suggested research areas for consideration:

- What is the impact of assessing cognitive and behaviour change in people with MND on clinical practice, the person, their family and carers, and does repeated assessment provide greater benefit than at a single point at the point of diagnosis?
- Is the ALS prognostic Index an accurate predictor of survival in people with MND?
- How is excessive drooling of saliva (sialorrhoea) managed in people with MND?
- Does a high calorific diet prolong survival of people with MND if initiated following diagnosis or following initiation of feeding by gastrostomy?
- What is the current pattern of use of augmentative and alternative communication by people with MND in England?

The use of health economics assessment was considered for all the recommendations but there was little evidence for most reviews, except for the organisation of care. The GDG agreed that an in-depth economic assessment would be undertaken for the use of Multidisciplinary Team approach, as there was literature on the benefits of the approach (13, 14, 15, 16). This showed that MDT care was cost effective, with an Incremental Cost-Effectiveness Ratio (ICER) of £26,672 / QALY (Quality-adjusted Life-years). This study is to be presented as a separate publication (32). There were particular issues in calculating the cost effectiveness as the quality of life would appear to be undervalued, as the model used the EQ-5D scale, which is limited in assessing the quality of life in people with progressive disease as they reach the lowest level at an earlier stage of the disease progression and the quality of life may be adversely assessed. If a more sensitive assessment of quality of life had been used the effectiveness would seem to be greater and the ICER lower – for instance when the model was rerun adding a small increase in quality of life the ICER reduced to £20,469/QALY.

The aim of this Guideline is to improve the care of people with MND in England, Wales and Northern Ireland. However, it is hoped that they will be of interest to other areas and together with other guidelines help to improve care more widely.

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