Implementation of “the consensus statement for the standard of care in spinal muscular atrophy” when applied to infants with severe type 1 SMA in the UK

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ABSTRACT

The diagnosis of severe type 1 spinal muscular atrophy (SMA) should be confirmed by an expert in paediatric neuromuscular disease. Invasive investigations are not usually necessary as the diagnosis is confirmed with a DNA blood test. Care thereafter should be delivered close to home by a multidisciplinary team with a clear point of access during times of crisis. The aim of care is to keep the infant as well as possible with the best possible quality of life. There are many forms of active respiratory management which can help maintain the well-being of infants with severe type 1 SMA. These include approaches to reduce the risk of infection and aspiration and appropriate techniques of airway and secretion clearance. The use of non-invasive ventilation may be helpful for some, usually less-severely affected infants, particularly to assist extubation. Long-term invasive ventilation is not recommended. Active assessment of feeding and nutrition is vital, and most babies can be managed well with nasogastric feeds. Gastrostomy may be considered for some infants, but the benefits should be carefully weighed against the risks. It is vital to share information and formulate an anticipatory care plan with the infant’s parents from the point of diagnosis.

Type 1 spinal muscular atrophy (SMA) is a rapidly progressive life-limiting disorder which results in bulbar and respiratory insufficiency. Many affected infants will be cared for by clinicians who have little experience or knowledge of the condition. Caring for such infants can pose specific difficulties for medical teams which can lead to ethical dilemmas.

In 2007, a Consensus Statement for Standard of Care in Spinal Muscular Atrophy was published.1 This was produced by a multidisciplinary group of experts who formed “The International Standard of Care Committee for SMA” (SCC). It was identified that no common care pathway for the management of SMA existed, and the SCC convened to identify the available published evidence for all aspects of care. Where evidence did not exist, the group used a Delphi process2 to determine the opinions of known experts in the field.

The published consensus document has been summarised by TREAT-NMD and has been widely disseminated across Europe through their website (http://www.treat-nmd.eu/). A lay version of the document entitled “A Family Guide to the Consensus Statement” has also been produced (http://www.treat-nmd.eu/). These comprehensive documents are very useful; however, they relate to all people affected by SMA with no differentiation between the severe (type 1) and the milder (types 2, 3) forms of the condition.

The workshop participants were either parents of affected children or professionals involved in the care and support of infants with SMA. Due to the severity and rarity of the condition, there is a dearth of published evidence on the management and care of babies with type 1 SMA. This report draws on the extensive literature review and Delphi process undertaken by the SCC and on the wealth of experience of the professionals and parents involved in both workshops. It provides the basis from which to develop a uniform standard of care across the UK, the objective of which is to ensure that all infants with type 1 SMA receive the best possible care, enabling them to live as well as possible, with the best quality of life.

Background

Type 1 SMA has an incidence of about 1:10 000 live births. It is an autosomal recessive disorder, with a carrier frequency as high as 1 in 40.3 Muscle weakness in SMA is secondary to anterior horn cell loss. This is determined by loss of function of the survival motor neuron 1 (SMN1) gene; 95% of all people affected with SMA, regardless of severity, have a deletion in exon 7 with or without a deletion in exon 8. Other diagnostic investigations should be considered only if the DNA test shows no deletion and should be guided by an expert in neuromuscular disease.

A second gene, SMN2, can partially compensate for the absence of SMN1. Individuals have a variable number of copies of the SMN2 gene. Transcription of the SMN2 gene produces only 10% full-length SMN protein. There is an inverse relationship between the severity of the disease and the SMN2 copy number, with fewer copy numbers present in individuals with type 1 SMA compared with types 2 and 3.4 Investigations to determine the SMN2 copy number are not widely available, and this finding is anyway more applicable on a group rather than single-patient basis. Hence, assessment of the severity of SMA in an individual child is determined purely on clinical grounds by a clinician experienced in the field.
Review

Infants with type 1 SMA present with profound hypotonia, muscle weakness and delayed motor development. The onset may be before birth or within the first few weeks or months of age. Generally, the younger the age of onset, the more severe is the phenotype. Children with type 1 SMA never achieve independent sitting, have poor head control, develop bulbar weakness and intercostal muscle weakness with diaphragmatic paradoxical (seesaw) breathing. Most affected infants with type 1 SMA have a severe form with onset before 6 months of age and usually by 3 months; in these studies, 95% of these babies have died by 18 months of age. A recent study from Holland, of infants with severe type 1 SMA who had onset before 6 months, showed that in this cohort, the median age at death was 176 days (25 weeks); 74% of these infants died by the age of 12 months. All deaths were attributed to respiratory insufficiency with or without pulmonary infection.

A minority of affected infants with type 1 SMA are less severely affected, and their clinical phenotype is borderline with type-2 SMA; these babies are more likely to have onset of symptoms after 6 months of age and develop respiratory involvement later. There are a number of studies which have demonstrated prolonged survival in type 1 SMA patients with interventional respiratory management including the use of cough assist machines, non-invasive ventilation (NIV) and invasive ventilation including tracheostomy. These studies included infants who were less severely affected and who had developed the onset of symptoms after 6 months of age.9–12 The inclusion of these less severely affected infants in some research studies of type 1 SMA can lead to difficulties in interpreting data on outcome and survival. In addition, there may be factors other than ventilation which contribute to prolonged survival, for example, vaccination and respiratory physiotherapy.13 14

This workshop focussed on the care of those infants with the severe form of type 1 SMA whose parents report the onset of symptoms before 6 months of age. The age of diagnosis should be considered unreliable as a measure of severity because of discrepancies in time to diagnosis from onset of symptoms. Clinical assessment of these infants by an experienced neuromuscular clinician is essential to differentiate severely affected infants from the few milder cases.

MULTIDISCIPLINARY CARE FROM THE TIME OF DIAGNOSIS

Once the diagnosis of severe type 1 SMA has been confirmed, the baby and family should be supported by a multidisciplinary team. Accurate information for parents is essential to aid informed choices about their child’s future care. Parents should be offered referral to the Jennifer Trust Outreach Workers, who provide information and emotional support to distressed parents of infants with type 1 SMA. All parents should be offered referral for genetic counselling.

The initial assessment and diagnosis should be undertaken by a consultant with experience and training in paediatric neuromuscular disease with the infant’s care subsequently being shared with local services. Babies with severe type 1 SMA deteriorate rapidly and may not tolerate long journeys to hospital; it is vital that local contacts are established as soon as possible. The multidisciplinary team should include a consultant paediatrician and/or a paediatric palliative care consultant, consultant paediatrician with respiratory expertise, General Practitioner, paediatric community or palliative care nurses, paediatric physiotherapist and a feeding team including dietitian and speech and language therapist.

Palliative care has many aspects, including providing psychological support and active management of symptoms; it should be seen as commencing at the time of diagnosis and continuing throughout the infant’s life. Each family should be allocated a key worker to coordinate the multidisciplinary aspects of care. There should be clarity of emergency access through a single contact point, for example the local children’s ward or community/palliative care team. A written anticipatory care plan should be agreed with parents to decide levels of care in advance of any crisis and how medical services should be accessed in case of an acute deterioration. The anticipatory care plan is likely to evolve with time and should be regularly reviewed.

RESPIRATORY CARE

Respiratory muscle weakness is an inevitable feature of type 1 SMA, with early intercostal weakness being particularly prominent. Infants should be examined regularly to review cough effectiveness, work of breathing, presence of paradoxical (diaphragmatic) breathing and evolution of chest deformity. Assessment of safety of swallow should be undertaken by a speech and language therapist to reduce the risk of aspiration.

Prevention of infection

Infants should receive all standard immunisations. Flu immunisation should be given to infants over the age of 6 months and palivizumab considered for protection against respiratory syncytial virus during the winter months, although there is no evidence that it alters outcome in the severe form of type 1 SMA. There is no evidence to support or refute the use of prophylactic antibiotics.

Airway clearance and secretion mobilisation

Physiotherapy

Although there is no published evidence, clinical experience is that physiotherapy assists with secretion clearance in babies with severe type 1 SMA. Intermittent clapping, positioning and nasopharyngeal suctioning may provide symptom relief. Parents can be taught these techniques by a paediatric physiotherapist experienced in respiratory management. Other techniques of airway clearance such as breath stacking with bag, mask and one-way valve and manually assisted coughs can be very useful in older children who are able to understand commands but are not applicable to infants with severe type 1 SMA. Saline nebulisers have been demonstrated to aid symptom relief in paediatric palliative care settings15 16 and can be helpful in alleviating symptoms in babies with type 1 SMA when combined with physical methods of airway clearance.

Cough assist

The use of a mechanical insufflator/exsufflator via a face mask increases peak cough flow and aids airway clearance. These devices have been demonstrated to be effective in reducing infection in older children with neuromuscular conditions.17–20 They are not useful in young infants because patient cooperation is essential for success.19 20 Those experienced in its use find that cough assist devices may be used in some infants from 6 months of age but not with maximum pressure settings. Cough assist needs to be used after secretion mobilisation and does not negate the need for nasopharyngeal suction. There needs to be a careful risk assessment by an experienced respiratory paediatrician or specialist.
physiotherapist before the use of cough assist at home in any infant with type 1 SMA.

**Oxygen**

Low-flow home oxygen should be considered for symptom relief for babies who have acute cyanotic attacks. However, practitioners should be aware that oxygen may mask worsening hyperventilation in the presence of hypercapnia by reducing respiratory drive.

**Non-invasive ventilation**

Non-invasive ventilation is delivered via a mask attached with straps to the child’s face. This is described as an “interface”. CPAP delivers a continuous positive airways pressure while NIV provides continuous airways pressure, usually as bi-level cycling between a higher and lower positive pressure. CPAP is not useful in the management of infants with severe type 1 SMA because of their bulbar weakness. Likewise, NIV is ineffective and contraindicated in infants who have severe bulbar weakness, usually present in babies with severe type 1 SMA.

In older infants with intact bulbar function, NIV can be helpful in the management of acute infection or sleep hypventilation. Its use can reduce breathlessness and work of breathing and aid physiotherapy. NIV can extend life and facilitate discharge from hospital in infants who have presented acutely following emergency intubation and ventilation. There is also evidence that NIV may reduce the frequency of hospital admissions. The use of NIV can have a beneficial impact on chest shape, reducing the development of pectus excavatum.

A range of different interfaces are available, but sourcing different masks will often need consultation with others who have previous experience of their use. Even then, it can be very difficult to find an appropriate interface to fit some babies comfortably and to give the necessary seal for effective ventilation. Thus, NIV will not be suitable for all babies, especially those presenting at a younger age.

**Invasive ventilation**

The consensus of expert opinion is that once the diagnosis has been confirmed invasive ventilation is not appropriate for infants with severe type 1 SMA. These infants eventually become “locked in” with no voluntary body or facial movement including eye opening and with no hope of recovery. Furthermore, speech develops in babies treated with NIV, but not in those babies ventilated long-term by tracheostomy. All long-term survivors of type 1 SMA develop a severe scoliosis which can lead to pain. Initiation of long-term invasive ventilation in these infants is felt to be burdensome without hope for these babies to improve or survive in the long term.

Sometimes infants present acutely and the diagnosis is made after PICU support including invasive ventilation has been initiated. Under these circumstances, all efforts should be made to extubate the infant as soon as possible with the aid of NIV if feasible; in those infants where this fails, there should be careful consideration of all options, including withdrawal of active respiratory care, as quality of life is poor in these infants if long-term ventilation via tracheostomy is undertaken.

**Morphine**

Clinical experience suggests that oral morphine is helpful in relieving distressing symptoms of breathlessness which occur towards the end stage of the disease. If used, oral morphine should be started at 50% of the usual analgesic dose and administered on an “as required” basis; the dose can subsequently be titrated against symptoms. Some infants benefit from a long-acting morphine preparation to relieve their breathlessness. Occasionally, morphine can cause constipation, with a negative effect on respiratory function and then glycerine suppositories or gentle softening agents, such as docusate, can be a useful adjunct. Laxatives which cause bloating should be avoided as this may impair respiratory function.

**FEEDING AND NUTRITION**

In infants with type 1 SMA, the suck is weak, feeding is inefficient and the baby’s growth may be compromised. With progressive bulbar and respiratory involvement, there is an increased risk of aspiration of liquids, solid food and saliva. Cough strength is reduced, and poor head control may exacerbate swallowing difficulties; this may lead to silent aspiration, choking, distress and pulmonary infection. Feeding times become prolonged and increasingly difficult for the child and parent.

Videofluoroscopy can objectively assess the swallow and demonstrate silent aspiration. It is not usually a necessary investigation for babies with type 1 SMA as there is often clear observational evidence that these babies have significant bulbar involvement affecting swallow safety. Allowing oral fluids may not alter the respiratory prognosis and having no oral stimulation is more likely to lead to problems managing thick secretions at a later stage.

Babies’ feeding and swallowing should be assessed by a speech and language therapist who can offer advice on safe swallowing, including giving head support, positioning appropriately during feeds and texture modifications such as thickening feeds. Oromotor strengthening exercises are not advised. Infants with type 1 SMA frequently have gastro-oesophageal reflux which can exacerbate feeding problems and increase the risk of aspiration. These infants should be assessed for gastro-oesophageal reflux and symptoms managed appropriately.

Oral feeds alone will not usually be enough to sustain growth and should be supplemented via an indwelling nasogastric tube. Gastrostomy may be an option for some babies at the milder end of the spectrum, but the benefits of gastrostomy for babies with the severe form of type 1 SMA must be balanced against the risks of anaesthesia. Percutaneous endoscopic insertion under local anaesthesia allows a more rapid recovery with a low risk of complications: erythema at the insertion site develops in some patients and is manageable with topical care and antibiotics if necessary. The risk of procedure failure or the need for a laparotomy is low. An infant should first be established on a nasogastric feed to ensure optimal nutritional status prior to referral for a gastrostomy procedure. With appropriate gastrostomy-delivered feed management, it is rare to require fundoplication, a major procedure unlikely to be tolerated by babies with severe type 1 SMA.

There is no published literature to support gastrostomy over nasogastric feeding, although there is one report of a small series of babies with severe type 1 SMA having survived gastrostomy. Nasogastric feeding is non-invasive, and parents can be taught safely to replace dislodged tubes at home. Gastrostomy may reduce feeding times and in other conditions has been anecdotally reported to improve carer satisfaction and quality of life, although there is no data available for infants with severe type 1 SMA.
Tube feeds may be given as boluses or continuous overnight feeds, but there is no published evidence to support an optimum feeding method for these babies. Infants with significant respiratory impairment may tolerate only small volume feeds, and bolus feeds should therefore be given frequently. Overnight feeds may increase the risk of aspiration, and a naso-jejunal tube may be considered for overnight feeds to reduce this risk. Feeds given via a naso-jejunal tube should always be given by continuous infusion, not by bolus.

There is no evidence that infants with type 1 SMA need to be fed an altered or therapeutic feed. Anecdotal reports suggest that elemental feeds may be better tolerated by some babies. Nutritional support is as likely to be successful whether based on a polymeric, elemental or semi-elemental protein feed. Clinical experience suggests that high-fibre feeds may lead to abdominal bloating, which can interfere with respiration but are worth considering in some infants with constipation where they have sometimes been helpful. Constipation can interfere with respiration and can be managed with glycerine suppositories. The volume of feed depends on the infant's energy and protein requirements; various equations can be used to calculate energy expenditure, but none has been validated for infants with type 1 SMA. It must be remembered that these children have reduced lean body mass and lower energy expenditure compared with other infants of similar age and weight. It is also important to consider fluid losses by sweating and excess salivary losses, particularly if there is frequent suctioning.

EMOTIONAL AND PSYCHOLOGICAL CARE

The aim of all aspects of care is to allow the infant with severe type 1 SMA and their family to enjoy a good quality of life. Careful consideration of emotional needs will enable the well-being of the infant and family. The care of infants with type 1 SMA is likely to be very stressful for parents who have to cope with frightening symptoms as their baby's health declines.

The Jennifer Trust Outreach workers can provide support for families and should be contacted at the time of diagnosis. The palliative care team and community children's nurses will help provide emotional support. An early referral to a children's hospice should be offered. The palliative care team will advise on symptomatic treatment including secretion management, positioning and feeding difficulties. They will enable families to be supported at home, in hospital or in a hospice during their baby's terminal illness and can also signpost to appropriate bereavement follow-up as needed.

Toys and play form an important emotional and developmental role in the baby's care. The Jennifer Trust can advise on and often supply appropriate toys for the baby's developmental age and physical needs. It is important to recognise each infant's developmental progress and need for age-appropriate cognitive stimulation.

ORTHOPAEDIC CARE

Babies with severe type 1 SMA are too severely affected to be considered for orthopaedic management and referral to an orthopaedic surgeon is not appropriate. Supportive seating and passive stretching may be useful. A physiotherapist can advise on this and assess the need for splinting in babies who are more mildly affected. There is no role for spinal surgery in those babies who develop severe scoliosis. Spinal bracing will interfere with breathing in severely affected type 1 SMA babies and is not recommended.

POTENTIAL CONFLICT

Parents will be devastated to receive the news that their baby has type 1 SMA. They should be seen very soon for follow-up after the diagnosis has been given. Conflict between healthcare professionals and the baby's parents is best avoided at all costs. Close support with frequent and easy access to members of the multidisciplinary team may help reduce the chance of conflict developing, as does providing full and clear explanations and information about their baby's illness. Parents should be given honest and accurate information; if necessary, a second opinion should be sought early. Parents should be advised that the anticipatory care plan is not fixed and can be adapted as the baby's illness progresses. Parents should also understand that the anticipatory care plan is not binding should they change their mind in times of crisis. The care plan should be regularly reviewed with the parents and should be expected to evolve with time.

SUMMARY

- The diagnosis of severe type 1 SMA should be confirmed by an expert in paediatric neuromuscular disease. Invasive investigations are not usually necessary as the diagnosis is confirmed with a DNA blood test.
- Care thereafter should be delivered close to home by a multidisciplinary team with a clear point of access during times of crisis. The aim of care is to keep the infant as well as possible with the best possible quality of life.
- There are many forms of active respiratory management which can help maintain the well-being of infants with severe type 1 SMA. These include approaches to reduce the risk of infection and aspiration as well as appropriate techniques of airway and secretion clearance. The use of NIV may be helpful for some, usually less severely affected infants, particularly to assist extubation. Long-term invasive ventilation is not recommended.
- Active assessment of feeding and nutrition is vital, and most babies can be managed well with nasogastric feeds. Gastrostomy may be considered for some infants, but the benefits should be carefully weighed against the risks.
- It is vital to share information and formulate an anticipatory care plan with the infant's parents from the point of diagnosis.

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REFERENCES

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References
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