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The Management of Children with Spinal Muscular Atrophy Type 1 in Australia

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ABSTRACT

Aims: To (1) estimate the prevalence of Spinal Muscular Atrophy Type 1 (SMA 1); (2) describe what practices characterise end-of-life care of patients with SMA 1; (3) ascertain whether a consistent approach to the management of these patients exists in Australia.
Methods: An audit of the Australasian pathology laboratories offering the diagnostic *SMN1* deletion test was conducted for patients diagnosed with SMA in Australia for 2010 and 2011. In addition, a retrospective clinical audit was conducted in eight major Australian paediatric hospitals of the end-of-life care provided to children with confirmed SMA 1 from 2005 to 2010.
Results: 35 children were included in the clinical audit, accounting for an estimated 61% of children diagnosed with SMA 1 from 2005-2010. 26% were ventilated invasively, only two of whom were intubated after the diagnosis was confirmed. No children were ventilated long-term (>90 days) or had a tracheostomy performed. Nasogastric tube feeding was a common measure to support adequate nutritional intake. Total parenteral nutrition, gastrostomy and fundoplication were not provided for any children. Conflict over end-of-life care decisions was documented in one instance, without the involvement of a guardianship tribunal.
Conclusion: There appears to be a consistent approach in the management of children with SMA 1 in Australia, which can be characterised as 'actively managed dying.' This study could contribute to the development of Australian consensus guidelines for the management of these children. These results also highlight a number of ethical issues related to the management of children with SMA 1.

INTRODUCTION

Improvements in medical technology over the past several decades have extended clinicians' capacity to prolong life – both in acute care settings and where patients are suffering from chronic or progressive disease. While these advances have provided immense benefit, they also raise difficult issues regarding the appropriate goals of therapy and the ethics of withholding or withdrawing life sustaining treatments. These issues are perhaps most difficult in children. The management of infants diagnosed with Spinal Muscular Atrophy Type 1 (SMA 1), in particular, has highlighted important ethical issues.

SMA 1 is the most severe form of an autosomal recessive motor neuron disease associated with *SMN1*, a gene required for motor neuron survival, and has a reported incidence between 1 in 6000 and 1 in 10 000 live births [1,2]. Onset occurs within the first 6 months of life and progressive muscular weakness, including of respiratory, facial and ocular movements eventually lead to children becoming effectively 'locked in' [3]. SMA 1 is rapidly progressive and, without ventilatory support, death from respiratory complications usually occurs within the first year of life [4,5]. As there is no cure for SMA 1, management is centred on treating or preventing complications of weakness and maintaining quality of life – primarily through provision of temporary respiratory and nutritional support [6,7].

Management decisions regarding respiratory and nutritional support inevitably require weighing the burdens of therapy against possible or likely benefits. Three options exist in regards to respiratory support: non-invasive ventilation via facemask or nasal prongs combined with airway clearance techniques; invasive ventilation, with or without a tracheostomy; or no ventilatory support [3, 8-10]. The decision to ventilate these children invasively is of great import as few children are successfully weaned from ventilators following initiation of respiratory support [11]. The available evidence provides limited guidance as to the optimum feeding method in these infants, as complete oral restriction has not been found to alter the clinical course of SMA 1 and neither nasogastric nor gastrostomy feeding eliminates the risk of aspiration from gastro-oesophageal reflux [7,12].

There is limited empirical data specific to current Australian practices. One survey published in 2007 found significant variation in opinion between treating subspecialists regarding prognosis and appropriate management of these infants [13]. While consensus statements on the management of SMA have been published internationally, there is currently no Australian consensus statement available to guide clinicians and families in making treatment decisions regarding children with SMA 1. This paper presents the results of a clinical and laboratory audit that sought to address the following questions:

1. What is the estimated prevalence of SMA 1 in Australia?
2. What practices characterise the end-of-life care of patients with SMA 1 in Australia?
3. What appear to be the goals of therapy for these patients?
4. How frequently does conflict arise regarding these goals and practices?
5. Is there a consistent approach to management of patients with SMA 1 in Australia?

PATIENTS AND METHODS

Australasian pathology laboratory audit

An audit of all Australasian pathology laboratories that offer *SMN1* deletion testing was conducted for patients who were diagnosed with SMA in Australia for 2010 and 2011.

Patients were excluded if their age at the time of sample collection was less than 0 months (i.e. prenatal diagnosis) or more than 6 months.[1] Loss of the *SMN1* gene is essential to the pathogenesis of SMA 1 and homozygous deletion of *SMN1* is used as the diagnostic test in infants with suspected SMA 1. This test has a reported 95% sensitivity and nearly 100% specificity [14].

Clinical audit

The specific aim of this audit was to describe current practices regarding management of infants diagnosed with SMA 1. ICD-10 searches were conducted on medical records from the eight major paediatric hospitals in New South Wales, Victoria, Queensland, South Australia, Western Australia and Tasmania for SMA 1 cases from 2005-2010. Consultant paediatric neurologists and intensivists were then contacted to provide details of known SMA 1 cases not identified by the ICD-10 search. Only children with a clinical diagnosis of SMA 1 and laboratory confirmation of SMA 1 were included in this audit.

Each file was analysed retrospectively by a reviewer (BT) using an audit tool designed specifically for this study. Data were extracted regarding patient demographics, intensive care admissions, methods of ventilatory and nutritional support, discussions and decisions to limit treatments and end-of-life care.

Ethics and governance approvals for the audit were given by each of the eight participating hospitals.

RESULTS

Australasian Pathology Laboratory Audit

There are four laboratories in Australia that offer *SMN1* gene deletion tests. All provided the number of positive test results in 2010 and 2011 for patients aged less than 6 months at the time of testing, enabling assessment of incidence rates of SMA 1 in Australia. In 2010 there were 8 patients with confirmed SMA 1 and in 2011 there were 11 patients. This data makes an calculation of the incidence of SMA 1 in Australia as 1 in 31 553 live births for this time period [14]. As homozygous deletion of *SMN1* is able to identify 95% of cases of SMA 1 and all pathology laboratories in Australia offering the *SMN1* homozygous deletion test participated in our audit, we were able to estimate the total number of children who would likely have had a confirmed diagnosis of SMA1 from 2005-2010 (n=54) [14,15]**.** This, in turn, enabled validation of our clinical audit, which, with 35 cases included, captured clinical data from an estimated 64.8% of all children born with SMA 1 between 2005-2010.

Clinical Audit of Australian Paediatric Hospitals

All eight paediatric hospitals in New South Wales, Victoria, Queensland, Western Australia, South Australia and Tasmania, invited to participate in this study agreed to do so.

Forty-two patients were initially identified by an ICD-10 search of the period 2005 to 2010. One patient diagnosed with SMA 1 who was mechanically ventilated during 2005-2010, was excluded from this study as the diagnosis was confirmed before 2005. A further 3 patients were excluded because, while initially diagnosed as SMA 1, they were subsequently

[1] All four laboratories did not have data extending back to 2005, and the most recent full data set was chosen for the audit i.e. 2010 and 2011.

diagnosed as having SMA 2 as they were able to sit unsupported and were not ventilator dependent. The final sample, therefore, in the six years from 2005 to 2010 inclusive, included 38 infants diagnosed with SMA1. Of this sample, the clinical notes of three of these children could not be retrieved or located, leaving a total of 35 infants audited, all of which had died at the time of conducting the audit.

Specialist Care

Clinical specialties involved in the care of children with SMA 1 included paediatric neurologists in 32 cases (91.4%), clinical geneticists in 29 cases (82.9%), general paediatricians in 25 cases (71.4%), respiratory physicians in 21 cases (60.0%), palliative care physicians in 19 cases (54.3%) and intensive care specialists in 17 cases (48.6%). Specific clinical ethics consultations were sought in three cases (8.6%).

MET calls and PICU admissions

Medical Emergency Team (MET) calls were documented for 12 children (34.3%). In only one of these infants was a MET call made after the diagnosis was genetically confirmed.

Seventeen infants (48.6%) were admitted to a paediatric intensive care unit (PICU) on one or more occasions for a total of 22 PICU admissions in total. Of these 17 infants, 13 had a clinical diagnosis of SMA 1 at the time of PICU admission but were yet to have genetic confirmation. The remaining nine PICU admissions (in seven cases) occurred after the diagnosis had been confirmed. The average length of PICU admission was 10.6 days, median 6 days and a range of 1 to 68 days.

Ventilation

Twenty-two children (62.9%) were ventilated non-invasively at one point during their illness. Nine (25.7%) were ventilated invasively, all in PICU. There were no children identified who had ventilatory support at the time of their death. Of those who were invasively ventilated, only two were intubated after the diagnosis was confirmed – each by emergency services (ambulance officers and neonatal retrievalists). All children were ventilated in a hospital setting, although non-invasive home ventilation was considered in one cases on the basis of parental request but ruled out after a sleep study. No patients had a tracheostomy, and none were ventilated 'long-term' (>90 days). Eleven infants (31.4%) had no ventilatory support, nine of whom (25.7%) were provided with supplemental oxygen. Thirty-four children (94.3%) had suctioning for airway clearance.

Nutrition and hydration

None of the infants included in the audit were given total parenteral nutrition (TPN). Enteral feeds by nasogastric (NG) tube were provided for 30 children (85.7%). The remaining five children did not have NG tubes with explicit documentation of a decision not to insert an NG tube for one child. No children had percutaneous endoscopic gastrostomy performed and although gastrostomy and fundoplication was discussed for one child (due to poor tolerance of NG feeds) it was never performed. In no child was a decision made to withhold enteral feeds or to withdraw the NG tube as part of their end-of-life care.

Intravenous hydration was provided for 16 children (45.7%). There was no evidence that a decision was made to withhold or withdraw intravenous hydration as part of terminal care.

Advance care
Limits on acute care, including 'maximums' and 'minimums' were discussed for 26 children (74.3%) and a statement of parental wishes regarding care was explicitly documented in 19 cases (54.3%).

More comprehensive end-of-life care plans, including documentation of a plan for resuscitation, fluid, PICU admission, ventilation and sedation were documented in the patient notes (n=14) or using a hospital proforma (n=7) for 21 children (60.0%). Of the advance care directives, none included an admission to a PICU as part of the plan. DNRs (or the equivalent) were documented for 29 children (82.7%), one of which was initially placed by the treating clinician unilaterally.

Place of death and sedation at the end of life
Eighteen infants (51.4%) died in hospital – three in a PICU, 12 on a general medical ward and two in an emergency department. One child died in an ambulance and three (8.6%) died in a palliative care facility. Thirteen children (37.1%) died at home. The records of one child did not specify the location of death.

Sedation for relief of respiratory distress was provided for 33 infants (94.3%) in the form of opiates (morphine or fentanyl) and/or benzodiazepines (midazolam) given orally, buccally, as an infusion or subcutaneously. Muscle relaxants (neuromuscular blockade) were not used at the end of life for any child. CPR was attempted unsuccessfully for one child.

Conflict
Conflict regarding end of life care was documented in only one case between the family and the treating team. No applications were made to a Guardianship Tribunal or equivalent body.

DISCUSSION

This research is the first empirical study to document end-of-life care in SMA 1 in Australia. Significantly, the data reveal that there is a high degree of consistency in the way that Australian clinicians manage children with SMA 1. It also paints a picture of the ethical issues that surround the provision of chronic and end-of life care for these children.

As our clinical audit included all major paediatric hospitals in Australia over six years, it is likely that our data provide a robust and generalisable description of how these children are managed in Australia. As a retrospective study, however, a limitation is that the data only represent what is included in the patient's medical notes. For example, the audit reveals how frequently decisions are made to ventilate these children, but cannot provide accurate information on rationales behind those decisions. A separate potential limitation of this study is that an estimated 35% of patients with confirmed SMA 1 were not included in this audit. Though proportionately high, this is unlikely to undermine the results obtained by the audit. It would be very unlikely for a patient with confirmed SMA 1 to be managed in a rural or regional hospital with aggressive interventions but without referral or admission to one of the hospitals audited.

While there was only one case of explicit moral conflict surrounding end-of-life care, many of the treatment decisions made for these children were of moral import, including those

surrounding admissions to PICU, the commencement, withholding or withdrawal of ventilation or nutritional support, and the use of DNR orders and advance care plans.

It is possible to infer from these results that the management of children with SMA 1 can characterised by 'managed dying' [16]. Active management of the dying patient has been described in terms of the following 'steps':

- a diagnosis that the patient is indeed dying;
- acceptance that death is an appropriate (and desirable – although this is more controversial) outcome;
- revision of the goals of therapy such that they aim to ensure comfort and dignity throughout the dying process and to provide support for the family and reassurance that the patient is not suffering;
- active clinical measures performed with the function of facilitating a 'good death' – where this may include knowledge of when death is approaching, being afforded dignity and privacy, relief from pain and other symptoms, and choice over location of death [16,17].

While this study revealed some variation in the way in which Australian children with SMA 1 are managed, for the most part, there appears to be consensus that affected children require palliation rather than prolonged medical interventions aimed at sustaining life. Australian clinicians caring for children with SMA 1 apparently eschew invasive options which prolong survival but may not (in their view) improve quality of life, such as mechanical ventilation, cardiopulmonary resuscitation and percutaneous endoscopic gastrostomy. These results stand in contrast to literature that describes a much broader spectrum of practice from the United States, France and Japan [11,17-21].

Despite SMA 1 having a well-described prognosis, approximately 40% of patients did not have a documented advance care plan, and 20% did not have a documented DNR. No association was found between the absence of advance care directives and having invasive interventions. Nonetheless, an advance care plan should be discussed and documented, with copies of the plan provided to the family and emergency services to ensure the best interests of the child remain at the centre of the goals of therapy.

In the United States, a consensus statement regarding SMA was published in 2007 claiming that clinicians had an obligation to present care options in an open, fair and balanced manner [7]. In contrast, a United Kingdom consensus statement recommended that invasive ventilation was inappropriate once a SMA 1 diagnosis had been confirmed [22]. Additionally, while a consensus exists to provide 'proactive nutritional supplementation as soon as inadequate oral intake is recognized', no consensus exists as to how supplemental nutrition should be provided [7]. Given the absence of Australian guidelines, this study may provide data to help development of a consensus statement for the management of children with SMA 1 in Australia.

The results of our study also raise a series of ethical questions about how these children are managed – questions that would best be explored through further qualitative studies and ethical analysis. Should any move be made to develop guidelines for practice, it will be important to gain a better understanding of the ethical dimensions of the care of children with SMA 1, the experiences and views of their carers/parents and the quality of their care. It is unclear, for example, how much parents are genuinely engaged in decision-making and the manner in which treatment options are framed by their physicians. It is also unclear how paediatricians incorporate futility and quality of life judgements into their management and

the degree to which these determinants are made unilaterally. And most importantly, we need to gain a better understanding of the quality of these children's dying and come to a considered judgement regarding the use of end-of-life therapies (including sedation) and end-of-life expertise in palliative care.

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