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Paediatric palliative care: Coming of age in oncology?

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ABSTRACT

Palliative care in children has been emerging as a clinical subspecialty of paediatrics for many years. It requires the knowledge and experience of a paediatrician, combined with the skills of a palliative care specialist. Both are essential, as a paediatrician may not have advanced knowledge of palliative care and a palliative care specialist is unlikely to be familiar with the complexity of working with families where the child is the patient. This paper reviews recent literature and discusses advances in the development of palliative care services for children and young people with incurable cancer. It highlights key areas where paediatric palliative care differs from that of adults and outlines the barriers to providing palliation and conducting evidence-based research in children and young people dying from cancer.

1. Introduction

Over the last twenty years there has been steady growth in the field of paediatric palliative medicine. As in the adult sector, paediatric palliative care originated within the oncology setting. As the obvious benefits of palliation were recognised, the need for professionals experienced in symptom control emerged. Formal recognition of this new subspecialty within paediatric regulatory bodies all over the world has encouraged the emergence of dedicated teams and a growing body of supportive evidence. There is now a skilled body of professionals committed to teaching and training, with formal channels for education within the specialty world-wide.

In England, a detailed and specific training curriculum for all doctors working in the field, from general practitioners working in children's hospices to specialist paediatric palliative care consultants, has recently been developed. Creating an official career pathway for doctors, nurses and allied health professionals has given paediatric palliative medicine the professional credibility it deserves.

Within the UK, most paediatric palliative care teams manage a significant number of patients with non malignant dis-

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ease; children with cancer comprise approximately 40% of the average case load. In 2007 the Great Ormond Street Palliative Care Team received 186 referrals and cared for 127 children/ young people at the end of life; of these 42% had malignant disease.

Over recent years there has been an increase in the number of children's hospices, community and specialist teams providing paediatric palliative care, although there remains considerable geographic variation in the services available. An independent review of paediatric palliative care services in England, commissioned by the Department of Health in 2007, highlighted gaps in service provision, alongside poor access to specialist care, as essential areas for improvement. It stressed that choice of place of care at the end of life should be mandatory, not an optional extra.[1]

It is important to emphasise that palliative care for children and young people is not just about end of life care and symptom management; it is a continuum of care from provision of responsive services (e.g. education, respite, transport and social services) to access to specialist services (e.g. specialist paediatric palliative care teams, a paediatric palliative care consultant). It is about providing choice to the patients and families based on individual needs assessment at a local level.

The core principle of palliative care involves provision of physical, psychological and spiritual support around the requirements of the child, young person and family. The report from the Department of Health proposed that every child/ young person with palliative care needs should have access to universal paediatric services, core palliative care services (hospice, community palliative care nurses) and specialist palliative care support when required (Fig. 1). It emphasized the need for coordinated, seamless care for these children and their families.

Despite advances in the provision of services, evidenced-based practice is limited. Practice has evolved through clinical experience, anecdotal evidence and modification of adult palliative care management. It is well established that babies, children and young people are not 'little adults' and should not be treated as such. There are many differences between adults and children not only in their physiological make-up but also in their psychological and spiritual being. Infants, children and young people experience considerable variation in types of malignancy and disease trajectory both within these age groups and compared to adults. Future research should focus specifically upon the different age groups and all aspects of the symptoms they suffer. Care must be age appropriate, taking into consideration emotional development and levels of understanding.

2. Differences between adult and paediatric palliative care

Although the principles of palliative care in adult practice are relevant to paediatrics, the adult model cannot be applied directly to children. There are several key areas where this is most relevant:

- The types of malignancy and disease trajectory seen in children are different from those in adults
- Factors that influence prescribing are quite distinctive from adults: metabolism; renal clearance; changing size and surface area; the ability to manage medication
- Access to services unique to the paediatric population: paediatricians; specialist tertiary services; community paediatric services; child development teams; schools; respite; holiday clubs

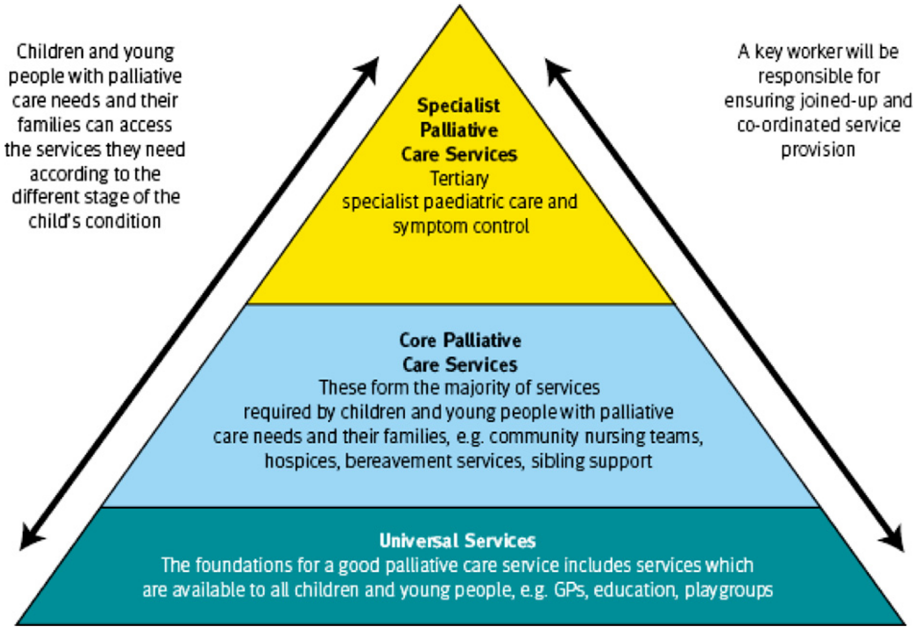

Fig. 1 – Different levels of palliative care service which should form the basis of a children's palliative care service. From: Palliative care services for children and young people in England: an independent review for the Secretary of State for Health by Professor Sir Alan Craft and Sue Killen. May 2007. Permission requested from Professor Sir Alan Craft.

- Children, however ill, have a continued need for education and supportive development
- A child's family and social structure is obviously dissimilar to that of an adult. Relationship with parents and siblings; child's school and friends; extended family networks; cultural role
- Psychological factors are complex. A child's understanding of death changes with age, cognitive development and life experiences. The approaching death of a child generates complex emotions, both from the child and those who care for them
- The legal position regarding decision-making ability of both those with parental responsibility and the child/ young person themselves is very different to that of an adult.

3. Prescribing in children

Children represent a variable and diverse subset of individuals from the neonate through to the fully grown, sexually mature, young adult. Physical development and age influence both drug effect and drug disposition, with age-related changes in pharmacokinetics and pharmacodynamics. Particular care is needed when prescribing for specific groups of children. Neonates, for example, have inefficient renal filtration, relative enzyme deficiencies, differing target organ sensitivity and inadequate detoxifying systems, which cause delayed excretion. They have reduced gastric emptying which can make the oral route less reliable, but transdermal absorption is greatly increased so there is a greater risk of toxicity via this route than in older children or adults. Some specific drugs should be avoided in children, for example: chloramphenicol can cause 'grey baby' syndrome in neonates and aspirin can cause Reyes syndrome in children of any age.

Many of the drugs used routinely in adult palliative care are unlicensed for use in children or need to be prescribed outside the terms of the product license. The risks and benefits of these drugs in children have not been scrutinized by the licensing body, so there are often no age-related profiles of adverse drug reactions, no age related profiles for dosing and medication may not be available in appropriate strengths and doses for a child. Despite this, there is often huge practical experience of the use of some of these drugs in specialist paediatric palliative care centres.

Compliance with medication can often be a problem in paediatrics. Children may refuse medication due to the formulation, volume, taste, appearance or because they are angry, or just don't feel like taking it. Parents are often reluctant to start opioids, due to fear that this will hasten their child's death, or because they feel starting opioids is acknowledging that their child is going to die. It is essential that the reason for medication is explained fully to parents and children. Parents/carers and, if possible, the child should be involved in planning what medication should be given, the frequency, route of administration and, in some cases, even the colour.

3.1. *Barriers to Paediatric Palliative Care in Oncology*

Although survival rates for paediatric malignancy are now in the region of 70% in the western world, there remains a significant number of children and young people who die from incurable disease.[2] Historically, there has been a point in the disease trajectory of a child/ young person where the focus of care has moved from a curative to palliative approach. In some, this is quick and well-defined; in others that point is less clear, with further options and treatments offered despite disease progression. It is common for many parents not to accept palliative care as a mutually exclusive option to treatment-oriented care. A persisting unrealistic drive to cure can create a barrier to symptom control and the benefits of palliative care.

In more recent years this required change in goal is no longer recognised as a prerequisite to access palliative care services. Indeed there is a much greater understanding of the processes that occur with the recognition that a child/ young person has an incurable malignant disease. A recent study has described parents' approaches to treatment when cancer therapy has failed. Bluebond Langener et al. found that parents want and will seek cancer cures whilst expecting symptom control and supportive care to be delivered concurrently.[3] In other words, the hope of cure and the need for palliation are not mutually exclusive.

The certainty that a paediatric cancer patient would not get better factored strongly in health care workers decisions to enter into discussions about palliative care.[4] Uncertainty of prognosis was highlighted as a frequent barrier to initiating palliative care by over 50% of nurses and physicians in a large American paediatric tertiary centre.[5] This need for absolute prognostic certainty in diagnosis discourages the concept that palliative care can coexist with other treatment therapies. It also limits the potentially positive experience of supportive care from which the patient and family can both benefit. Other frequently occurring barriers to initiating paediatric palliative care cited by health care professionals in the same study, included the family not being ready to acknowledge an incurable condition, language barriers and time constraints of the professionals involved. This is in contrast to our colleagues working with adults who describe fear of opioid addiction and hastening death as more common barriers in providing palliative care to adults.[6]

4. General symptoms

The burden of symptoms in dying children is high.[7–10] The effective management of distressing symptoms is pivotal to the role of the palliative care team when caring for a child/ young person with cancer. Increasing prevalence of symptoms may be the trigger of referral for palliation.

A large multicentre prospective trial recently assessed the prevalence of symptoms in the last months of life in 162 children/young people (aged 4 months to 19 years) across the UK.[9] Although other studies have reported on symptoms at the end of life in paediatric patients, this was the first study to document the frequency with which symptoms occur in relation to disease type. Across all malignancies symptoms increased in prevalence towards the end of life. According to nursing observation, the major symptoms that were present but responded to treatment included pain, vomiting, nausea and constipation. Specific symptoms which were present with high frequency but were less responsive to intervention included weakness, anorexia, weight loss, reduced mobility and poor speech. Neurological symptoms, including headache, were universal in children with tumours of the central nervous system. The study also showed that although many symptoms were present in all three malignant disease groups (CNS tumour, solid tumours and leukaemia/ lymphoma) the importance of the symptoms differed according to disease type.

It is of note that the paediatric oncology outreach nurse (POON) was responsible for assessment and report of symptoms in the above study. Other studies interviewing parents of deceased children showed that the parents recalled a similar array and frequency of symptoms; fatigue, pain, nausea, vomiting and constipation in the terminal stage of life.[7,8] In both studies the parents recalled that successful treatment of symptoms had occurred in less than 30% of children/young people. This in an interesting contrast to the prospective observation of the healthcare professional.

Research studies investigating the child/young person's perspective on symptoms is sadly lacking. A report by Hinds has highlighted the lack of patient-reported outcomes (PROs) in end of life care in paediatric oncology.[11] PROs are defined as the measurement of any aspect of the patient's health status as defined by the patient themselves. It is common sense that management goals should be directed towards the concerns and issues expressed by the patient. Obviously there has to be an objective measurement in the younger age groups. However, children over the age of 5 years are able to use visual analogue scales and those as young as 10 years old have discussed end of life decisions when asked in a sensitive manner.[12–14] As Hinds suggests, an important step forward for paediatric oncology patients would be the development of validated symptom assessment tools which were culturally sensitive, related to cognitive ability and clinical context. This is imperative to tailor individual management and focus research and attention upon the concerns of the patient.

5. Fatigue

Fatigue has been reported as one of the most frequently occurring symptoms in the last weeks of life of children/ young people who died of cancer.[9,15] It is one of the most distressing, pervasive and persistent symptoms, is disproportionate to activity undertaken, does not respond to rest, persists despite attempts to overcome it and impacts significantly on daily living. The causes of fatigue are multifactorial and may include: anaemia, pain, 'hang-over' effects from opioids and other medication, tumour degradation products, cytokines and numerous psychological factors. A study showed that adults with cancer felt that fatigue affected their daily living more than pain (61% vs. 19%) whereas their oncologists believed that pain would have affected them more than fatigue (61% vs. 37%).[16]

The question we must address is whether fatigue is amenable to intervention in an attempt to improve quality of life. Fatigue in adults with cancer may be improved with methylphenidate, a stimulant, and a case series has supported this in adolescents.[17–19] As methylphenidate is used to treat attention deficit and hyperactivity disorder(ADHD) in children, its safety and pharmacokinetic profile is well-established in paediatrics.[20–22] However, no studies have evaluated the use of methylphenidate, or other stimulants in the treatment of fatigue in children.

In recent years, there have been several tools developed to measure fatigue in children and adolescents with cancer.[23–25] These must be tested in larger prospective trials and then used readily in palliative care if scientific evaluation of psychological and pharmacological treatment intervention is to be made.

6. Pain

The high prevalence of pain in paediatric cancer patients has been known for many years. It is well-documented that children/ young people with cancer suffer from pain related not only to disease but also to treatment and procedures. Pain is the symptom that many parents and carers fear most for their children.

Wolfe et al. interviewed 103 parents of children who had died from cancer. The parents reported that 76% of their children suffered from pain at the end of life and felt that only 37% of the pain was successfully 'treated'. The authors found that children who died from treatment-related complications were less likely to have their pain managed successfully than those who died from progressive disease. Despite this, 81% of parents rated the care provided by their oncologist as 'very good' or 'excellent'.[7]

This discrepancy of parental satisfaction with end of life care despite uncontrolled pain and continued suffering has been reported in other studies. The same parents who reported that their child experienced substantial pain also felt that their pain had been managed 'adequately' or 'well'.[26] An explanation may be that parents needed to feel that everything possible had been done for their child prior to death and that the symptoms were purely 'unmanageable'. Parents, as advocates for their children, must feel a great responsibility for ensuring that suffering is kept to a minimum and the thought that a child has suffered unnecessarily is maybe just too hard to bear. Whatever the complex reasons behind the discrepancy, parental satisfaction is clearly not a good indicator of quality of palliative care.

In a prospective study of children/young people dying from cancer, Goldman et al. found that over 90% of children suffered from pain in the last month of life. According to nurse observers the majority of pain reported responded to treatment interventions.[9]

With the same cohort of patients, Hewitt et al. found that 120/144 patients had escalating analgesic requirements in the month preceding death. Of 164 patients receiving opioids in the last months of life, 34 required what was deemed by the authors to be high dose (over 20mg/kg/day oral morphine equivalent (OME)). Of these, 30 reported pain to be a major problem and in three children/ young people it was a major unresolved problem. Eleven individuals received extremely high doses (over 50 mg/kg/day OME). This study observed that children/ young people dying from solid tumours outside the central nervous system were particularly likely to receive higher doses of opioid. It was in this group that opioid switching and drug combination was also more likely.[27]

The suggestion that pain in solid tumours is more difficult to treat relates to the fact that tumour progression often involves infiltration of nerves and bones. Both neuropathic pain and bone pain are known to present a challenge if managed with opioids alone and may also remain uncontrolled even with appropriate adjuvant treatments. Other investigators have also found that it is in this group of patients that extraordinary measures are sometimes required to control pain.[28]

The assumption that pain will be well-managed in an inpatient environment is not substantiated by a study that interviewed staff members in a US tertiary paediatric centre. Thirty percent of 191 nurses interviewed reported that they felt inexperienced in managing patients' pain at the end of life. They also described feeling distress that the child suffered when appropriate analgesia was either not available or not being delivered.[29] This mirrors other reports in the literature which describe paediatric health professionals' inexperience, discomfort and lack of confidence in dealing with the symptoms of dying children.[30]

Pain is a complex phenomenon and management must involve thorough assessment and measurement of pain within the context of the child and family. There are many modifying factors which contribute to the experience of pain. These factors include the cultural, behavioural, cognitive and emotional elements of an individual and must be considered in order to manage pain effectively.

As in other paediatric practices, we have found that, in addition to opioids, children/ young people with cancer frequently require anticonvulsive agents, antidepressant agents and drugs with N-methyl-D-Aspartate (NMDA) receptor activity (for example Ketamine or Methadone) for effective pain management.[31] Anecdotally this medication seems to have an opioid sparing effect.

7. Psychological symptoms

Children with incurable cancer and their families are confronted with numerous psychological stressors including fear, anger, financial burden, disruption to normal social and family roles and the inevitable threat of death. Over the past few years many oncology departments have incorporated psycho-oncology services in the hope of supporting patients and their families through this ordeal. Whilst there is much literature now emerging regarding psychological input to children with cancer, there seems little robust data on the psychological issues surrounding the child/ young person facing incurable disease.

Often the focus of care revolves around the physical symptoms of the patient during the palliative phase of life. Attempts to assess the quality of life of children with cancer have been made.[25] Unfortunately, there has been no prospective data collection on the quality of life and psychological symptoms in children/ young people with cancer at the end of life. The multiple difficulties in addressing these issues openly and honestly with the child/ young person hinder research. Firstly, not wishing to upset the child/ young person would be the paramount concern of the professional and any ethics council. Secondly, approaching these issues at an appropriate emotional and developmental level with skill and care requires considerable expertise. The reluctance of some parents to allow professional psychological engagement with their child is an additional barrier to successful research.

A retrospective study interviewing parents of 32 paediatric cancer patients (average age 10.9 years) who died in Finland, found that psychological symptoms were more common over the age of 12 years then under the age of 7 years. Psychological symptoms suffered by the children/ young people as described by their parents included: sadness, fear of being alone, difficulty talking about feelings regarding illness and death to their parents, loss of perspective and loss of independence. According to the parents, 43% of these symptoms were addressed by health professions but in only 9% were the issues resolved completely.[8] This suggests that psychological symptoms are not readily addressed by professionals and that perhaps those who do address them may not have the appropriate skills to manage these difficult issues.

8. Place of death

There is much discussion in the paediatric palliative care literature about 'the right place to die'. Given the choice, the majority of parents will elect for their child to die at home, although it is likely that they are choosing 'place of care' rather than 'place of death'.[32,33] Care is often intense, requiring frequent assessment of needs and daily input from professionals as symptoms develop, yet with around the clock access to appropriate advice and support, parents are able and confident to care for their child at home.[34] Vickers et al. reported that in the UK, 132 of 164 families of children with incurable cancer stated a preference for home death in the last month of the child's life. Over a seven month period 120/155 (77%) children/ young people enrolled in this study died at home.[2]

Several studies have highlighted the relationship between type of malignancy and place of care at the end of life. Bradshaw et al. found that patients with a solid tumour or brain tumour who are dying of progressive disease are more likely to have time for end of life decision-making and more likely to die at home than those dying of leukaemia or treatment related toxicity. Patients with leukaemia received on average 11 days of palliative care compared to those with brain tumours who received an average of 29 days care.[35] These findings have been mirrored in other paediatric centres.[35–38] However the exact time spent in the palliative phase is often based on decision-making and acceptance, rather than defined clinical criteria, which makes data across studies impossible to compare. For example, a Dutch study reported that the terminal phase of 21 paediatric patients with brain tumours had a median of seven months duration.[8]

The UK model of home care is based around an identified key worker who supports local professionals and coordinates palliative care in the community. In children with cancer, the Paediatric Outreach Oncology Nurse (POON), Children's Community Nursing (CCN) teams and, in some areas, hospice outreach team are pivotal in this role. The importance of providing a seamless interface between tertiary centre, local hospital and primary care team (general practitioner, district nurse) is paramount to supporting the child and family at home. The establishment of palliative care networks throughout the UK will continue to aid this process.

The role of the children's hospice in end of life care for children with cancer is also developing. Historically, relatively few paediatric oncology children have accessed children's hospices for end of life care. The reasons for this are complex and beyond the scope of this article. However, as experience in symptom control increases and with new networks of care evolving, the numbers of children with cancer using these services is increasing. Often, once the families have been introduced to the hospice and become familiar with the facilities provided, the hospice provides a reassuring alternative to home care if the need arises. The experience of the paediatric palliative care team in Great Ormond Street is that the number of families choosing hospice care at the end of life, in preference to home, is increasing. This is likely to be due in part to improved local hospice provision and co-ordinated care provided jointly by the hospice and palliative care team.

9. Conclusion

Paediatric palliative care is now a defined specialty with distinct expertise. It has much to offer seriously ill children/ young people and their families. Although many advances have been made in the palliative care of children/ young people with incurable cancer, symptoms remain unrecognised and under treated, service provision is patchy and there is little evidence-based research. Access to skilled palliative care teams and specialists in palliative medicine remains geographically determined. Despite readiness and acceptance to incorporate palliative care into the management of children and young people with cancer, barriers still exist to prevent this from happening.

Paediatric palliative care is yet to come of age in paediatric oncology; perhaps it is in its infancy. With continued progress and growth all children and young people with cancer will have equitable access to skilled and informed professionals in this field.

Conflict of interest statement

None declared.

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