General Approach to the Care of the Child With Pulmonary Hypertension

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Pulmonary hypertension (PH) is a complex pulmonary vascular disease of multiple etiologies, characterized by inappropriate elevation of pulmonary vascular pressure and resistance that can present at any age, including during childhood. The pharmacologic care of patients with PH has seen tremendous advances in the past 20 years, improving survival and overall quality of life for patients of all ages, although mortality remains high.[1] While the care of children with PH involves the same PH-specific medicines used for adults, PH-specific drugs are employed off-label due to a lack of Federal Drug Administration approval, which adds to the complexity of administration.[2] Furthermore, in addition to pharmacologic therapy, multiple other factors are involved in the care of the pediatric PH patient that require careful consideration, such as differences relating to growth and developmental stages and according to PH etiology. This review will discuss some of the highly relevant pediatric-related issues outside of traditional pharmacologic factors, with a focus on the importance of a collaborative approach to care, genetic testing, and palliative care.

CARE OF THE CHILD WITH PULMONARY HYPERTENSION IS COMPLICATED

The care of a child with pulmonary hypertension (PH) begins with the child and the child's family or caregivers. However, there is also an intricate network of programs and individuals joined in the common goal of optimizing current and future health. Ideally, a major partner for the child and family will be a specialty team of PH-focused clinicians with experience in the comprehensive management of children with PH.[2] Thus, a pediatric PH (or pediatric pulmonary vascular disease) program will be closely connected with the child's care until complete resolution of PH or transition to an adult program. However, pediatric PH is a broad specialty, encompassing children with an array of medical challenges from birth to young adulthood, crossing multiple medical disciplines in the outpatient and inpatient settings. As a result, successful PH programs benefit from thoughtful collaboration between the PH program and multiple inpatient and outpatient pediatric-focused subspecialties. This collective approach can be traced in part to the various etiologies associated with pediatric PH. For example, in the neonatal intensive care unit (NICU), patients with underlying pulmonary pathology may require a collaborative approach among NICU providers, pulmonologists, and PH specialists. In contrast, the young child with congenital heart disease in the cardiac care unit may require a cardiothoracic surgeon, specialty cardiologists, intensivists, and cardiac anesthesiologists in addition to the PH team. An older child with connective tissue disease and PH will require rheumatologic expertise. In this sense, clinical experts with a wide variety of medical expertise become involved in PH care to provide the range of expertise required to treat children with different underlying conditions associated with their PH.

The variety of proficiencies in a PH program extends beyond the physician-provider level to incorporate an array of individuals also crucial to the successful care of the pediatric PH patient. Often central to care is the contribution of nonphysician PH provider specialists. For example, many PH programs employ nurse practitioners (NPs) to support inpatient and outpatient care, providing continuity and knowledge across situations. Their combination of medical expertise and nursing background is extremely helpful for the navigation of clinical and complex logistical issues, such as chronic prostacyclin infusions. Similarly, involvement of consistent nurse management staff is ideal and can serve to facilitate administrative needs such as prior authorization approvals, medication refills, and immediate telephone support. Likewise, an administrative assistant can support a PH program by facilitating issues ranging from coordination of multiple appointments to reduce the travel burden on the patient to transfer of medical records to and from outside institutions.

However, the care of a child with PH extends well beyond the core members of a PH program and the child's family (**Figure 1**). Due to the various childhood growth and developmental stages, auxiliary hospital-based resources may aid in providing age-appropriate supportive care to the child and family. For example, dietitians with expertise in children with cardiopulmonary diseases offer valuable contributions

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since growth and nutrition are critical components of PH care in pediatrics. Meanwhile, child-life experts support the child and siblings in understanding the disease on a developmentally appropriate level. Individuals with expertise in palliative care approaches guide practitioners and families in complicated discussions pertinent to goals of care and end-of-life issues. Ideally, social work specialists also contribute, especially within the school system to help advocate for the child in receiving necessary resources.

However, despite these hospital-based services, care must extend beyond the walls of clinics and hospitals and into the child's community. This highlights the need for active communication and cooperation with other individuals involved in the child's life, including but not limited to the child's primary care provider (PCP), teachers, and extracurricular activity leaders. Active collaboration with the PCP team is vital. Patients often travel long distances to receive care at PH centers, but rely on continued management by their local PCP to support them through typical childhood illnesses that may require special considerations in the setting of PH. In addition to acute illnesses and routine primary care, PCPs may also provide resources such as serial laboratory monitoring or referral for psychosocial support as appropriate. Because some PH-specific medications have significant impacts on quality of life and complicated logistical issues related to delivery, education and involvement of PCPs, school nurses, and local emergency response teams offer support in proactively addressing problems. For example, aside from disease-specific complications such as syncope, therapeutic side effects may introduce challenges such as headache, nausea, vomiting, and diarrhea at home and at school.[3] As a result, the care of the child with PH is a complicated orchestra, typically coordinated by PH-focused clinicians, but requiring an integrated team approach.

The need for chronic continual infusion of parenteral therapies (prostacyclin and its derivatives) imparts an elevated level of complexity for patients, families, caregivers, and other individuals involved in the lives of children with PH. While the pumps used for infusion can be obtrusive and require the child to consider how best to carry with them at all times, other issues complicate daily lives. For example, intravenous infusions require an indwelling central line, which necessitates continued monitoring and maintenance, while subcutaneous infusions may be associated with significant pain at the insertion site (which can be successfully managed with certain judicious approaches).[4] Both delivery systems need close monitoring for safety and efficacy, as well as a focused understanding of how to prepare the medications and operate the devices.[2] Meanwhile, limitations on daily activities require vigilance, such as with swimming, participation in sports or physical education classes, and general bathing. All of these aspects of care not only require special training for the families and local care providers, but also highlight the importance of education for all individuals having routine contact with these children.

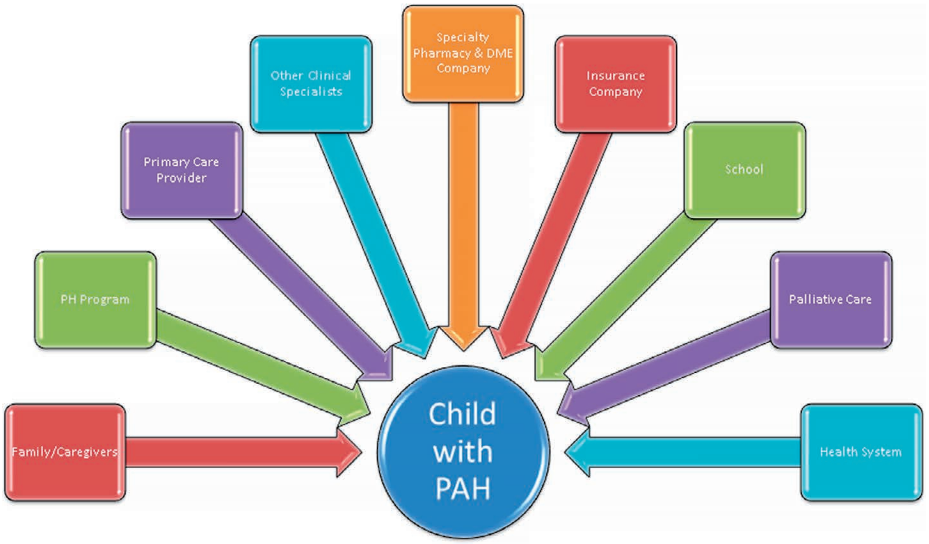

Figure 1: The care of a child with PH extends well beyond the core members of a PH program and the family, involving a wide spectrum of individuals with and without medical expertise. Thoughtful communication is imperative to support the health and wellness of a child with PH.

GENETIC TESTING FOR THE PEDIATRIC PH PATIENT

The period around the time of diagnosis is often characterized by the physical and emotional stress of a new illness and diagnosis, and the frantic nature of appointments, studies, and procedures. Pediatric PH program members work closely with the child and family/caregivers to explain the diagnostic workup, help describe pulmonary vascular disease conceptually, review medical approaches, etc. For the majority of individuals, PH is an entity not previously in their lexicon. This highlights the importance of education and support for potentially scared and confused children and families.

For the pediatric PH patient with precapillary pulmonary arterial hypertension (PAH), such as that associated with congenital heart disease or primary pulmonary hypertensive vascular disease, a discussion about the genetics of PAH should be considered.[2,5] A significant proportion of primary PAH cases, as well as congenital heart disease–associated PAH, correlate with mutations in one of several genes that may be considered PH-associated genes, such as bone morphogenetic protein receptor type 2 (*BMPR2*). Individuals with familial PH disease or mutations in a gene such as *BMRP2* have heritable disease, which may be present in other family members and/or progeny of the PH patient.[6] At the time of diagnosis, most cases of PAH do not have a known family history; however, a minority of cases will have occult heritable disease.[7] While clinical genetic testing does not currently contribute to the choice of therapeutic agents, it may hold value for a child and family/caregivers with PAH in a number of ways, including but not limited to: 1) contribute to understanding "why this child has PH"; 2) influence the selection of currently available therapies, as individuals with heritable PAH may have a more severe disease trajectory[8] (although this has not been confirmed in pediatric PAH); 3) assess the heritability of PH within a family to help guide screening of family members; and 4) contribute to reproductive considerations for the future. However, these discussions require detailed genetic counseling since there may be psychological effects related to genetic testing, cost-related issues, and concerns about future discrimination.[6]

QUALITY OF LIFE AND PALLIATIVE CARE ISSUES

It is plausible that with the rapid emergence of new PH therapies, medical management overshadows quality of life in children with PH. Children do not escape the psychosocial burden of living with a terminal illness. In fact, there are unique quality-of-life issues for children, and managing these challenges is especially difficult due to the limitation of childhood activities in the setting of PH. Complicating this factor is the possible reduction in parental coping skills in the setting of a chronic childhood illness such as PH.[9] Therefore, quality of life must receive special attention.

A promising strategy to address the unique needs of the pediatric patient with moderate to severe PH is the integration of palliative care early in the disease process. Pediatric palliative care aims to promote the quality of life in children diagnosed with a terminal illness by addressing the physical, psychosocial, and spiritual needs of the patient.[10] The palliative care model encourages providers to use a holistic approach that can help address the issues that may be surpassed by the focus on curative efforts in children with PH. For example, palliative care can help navigate aspects of care other than medical management such as dealing with anxiety, evaluating overall goals of care, and adjusting to changes in lifestyle associated with PH and its therapies. For adults with lung cancer, palliative care proved to increase quality of life, delay premature death as appropriate, and assist patients and families with reaching end-of-life goals.[11] Caregiver functioning in the postmortem period is also improved by palliative care involvement. In the years following the death of a child, caregivers reported better coping skills when palliative care services were utilized prior to death; parents reportedly experienced less anxiety if the psychosocial needs of their child were met during the last phases of life.[12,13] Therefore, integrating a pediatric palliative care program can have benefits that remain beyond the life of the child.

The American Academy of Pediatrics recommends that children with terminal illnesses start receiving palliative care on the day of diagnosis as part of their disease management to promote well-being for the patient and their families. Delayed access to palliative care can result in suboptimal symptom control, increased psychosocial and emotional symptoms in patients and families, and lack of preparedness for end of life.[10] Traditionally, palliative care programs were accessed once life-prolonging treatments were exhausted or electively ceased. However, new integrative palliative care models coexist with curative medical models of care to help evaluate the patient's goals of care throughout the disease process. Early integration of palliative care has been shown to affect pediatric outcomes positively even in areas such as cost reduction, and may be an important component of care in children with PH.[14] Death from severe PH can be gradual due to right-sided heart failure or sudden due to acute pulmonary hypertensive crisis or acute pulmonary hemorrhage.[3] Therefore, early integration of palliative care in PH management is especially important since death can be sudden or drawn-out, making prognosis hard to determine.

CONCLUSION

The facets of childhood combined with the complexity of pediatric PH yield a complicated disease state to manage. In order to effectively improve quality of life and prolong survival, a team approach must be engaged. Close attention to multiple issues is necessary, including but not limited to the care team, general medical care issues, and the consideration of issues related to activities of daily living (**Table 1**). Utilization of nonpharmacologic resources to augment the currently available PH therapies will enhance the efforts of the medical and local communities in providing the optimal care for the child with PH. Care collaboration, genetic counseling, and

Table 1. General Recommendations for Care of the Child With PH

Recommendation	Example
Successful evaluation and treatment of children with PH often involves a specialized pediatric PH program, which integrates multiple medical specialists relevant to the care of the child as needed.	1. PH director and program colleagues 2. Collaborative medical specialties • Nutrition • Cardiac anesthesiology • Interventional cardiology • Critical care • Genetics • Palliative care • Rheumatology
General health maintenance is a crucial component of care, including continued involvement and access to a PCP.	• Routine health maintenance visits • Routine child care sick visits • Routine vaccinations • Specialty vaccinations (eg, RSV)
Expertise in the discussion and evaluation of the contribution of genetic variations to PH is important for patients and families.	• Clinical genetic testing • Genetic counseling • Family planning • Screening of family members as appropriate
Appropriate review and counseling with patients and families on the risks and benefits of physical activity and exercise.	Due to the risk of syncope and other concerns, caution is needed. However, growing data suggest the importance of physical fitness.

involvement of palliative care are key aspects that may profoundly affect the child with PH.

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