



Precision medicine: how to approach the adolescent asthmatic

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Abstract

It is well known that adolescent patients often have less than optimal outcomes. Adolescence is a time of much transition, physically, emotionally, and socially all of which have effects on asthma management and outcomes. Pubertal changes affect asthma, but mostly it is the move towards independence from the parents, peer pressures, stigma of illness, and adherence issues that cause the issue. It is thus important to learn to treat the patient directly, wherein currently often children are treated through the parent, to ensure success.

Keywords

Asthma, adherence, adolescents, stigma, peer

Introduction

Precision medicine, sometimes known as “personalized medicine” is an approach to tailor disease prevention and treatment by identifying specific factors such as age, lifestyle, environment, and phenotypes. The goal of precision medicine is to target the right treatments to the right patients at the right time [1]. Adolescence, due to these multiple factors happening at the same time, is the area to be explored in this article. Asthma is the most common chronic medical illness in adolescents, with 9% of US adolescents having an asthma diagnosis in 2023 [2] and this age group is notorious for poor control and less than optimal outcomes. In addition, ensuring adequate treatment beyond adolescence [3] is necessary to ensure optimal asthma management and prevent disease progression, exacerbations, and loss of lung function.

Adolescence is defined as a transitional stage of physical and psychological development that usually occurs from puberty to adulthood. While often considered in the teenage years, the physical, psychological, or cultural expressions can start earlier or end later [4]. The most common symptoms in this population include exertional dyspnea, wheezing in response to triggers, chest pain, chest tightness, and cough. They affect sleep, school, sports, and social engagements. Exercise-induced symptoms may be a more common presentation compared to younger children where viral triggers are more common. Exertional symptoms



may reflect how asthma actually presents in teens, but it may be due to sports and exercise becoming a more discreet activity for children of this age [5]. Over half of asthmatic adolescents will suffer from limitations in activity [6]. Also, 20–30% of all cases in adolescents may be undiagnosed [7].

Table 1. Issues and solutions for precision medicine in adolescent patients with asthma

Issue	Potential solutions
Lack of adherence	Understanding the reasons for such, which can include: <ul style="list-style-type: none"> (1) stigma of illness (2) locus of medication control taken from parent to patient (time of transition) (3) body image (4) social pressures, peer and family, need to give opportunity to discuss issues and not just try to solve them (5) simplify regimen and tie adherence to other activities (6) deal with concerns of dependence on the medication by explaining that inflammation is treated by ICS containing medication, and what one gets dependent on is the reliever (7) create relationship with pharmacy to keep you informed on adherence issues, such as lack of picking up prescriptions and overuse of rescue
Consistency of medical practitioner	May change from pediatric to adult clinician: <ul style="list-style-type: none"> (1) need to deal directly with the adolescent patient (2) need to empower the patient with education and perspective (3) keep primary care consistent even if a specialist is involved
Rebelliousness and risky behaviors	Consistent messaging about the dangers of inhaled products such as cigarettes, cannabis, and vaping Give them a non-judgmental space to discuss these issues
Pubertal changes	Along with other more obvious changes, asthma also changes, sometimes with poorer control and sometimes for the good (remission), but the same measurements of control are the basics of decision making
Lack of appreciation of how important control is for preventing bad outcomes	Education re control criteria and why it is important to them Technology such as Apps and digital inhalers
Inhaler technique	Digital technology Educators Watch the patient actually use their inhaler
Measuring control	Poor control is underestimated so need education SABA use needs to be watched carefully, do not be free with repeats, keep track and follow accordingly Do spirometry as you may get much poorer lung function than you expect based on the reported symptoms
Trigger avoidance	Evaluate for and discuss allergic triggers Review avoidance and preventative strategies Avoid substance inhalation
Inadequate use of action plan	Use digital technology to incorporate this into their world
Parental concerns	They can be your greatest ally to let you know how things are doing and to reinforce messaging They can also be a threat to your patient relationship by: <ul style="list-style-type: none"> (1) undermining recommendations (2) minimizing the importance of medication use (3) not providing resources such as financial barriers to access appropriate treatment (4) behaviors at home such as parenteral smoking and substances, finances leading to environmental issues

ICS: inhaled corticosteroids; Apps: applications; SABA: short-acting β_2 -agonists

There are several factors that lead this age group to have issues in asthma management that will be reviewed. For instance, the odds of a good outcome if the patient is adherent are almost three times higher

than the odds if the patient has poor adherence [8]. These include social and behavioral and/or biologic factors, all of which need to be explored and dealt with to ensure appropriate diagnosis and control. See [Table 1](#) for a summary of all of the factors discussed.

Social and behavioral factors

Adolescence is a time of transition for the patient and their family. It is important, therefore, to empower the young person with self-efficacy and the educational skills needed to implement such. All of this by involving parents to allow balancing parental fears and concerns of “letting go”. To do this, it is first required to assess the knowledge and attitudes of both the patient and caregiver [9], looking for conceptual errors that are common such as fears of medication, lack of recognition of this being a chronic illness, and utilization of controllers compared with rescue therapy. Attitudes between parents and child often begin to diverge in the two groups leading to conflict. These occur due to multiple issues which include adolescent factors such as developing independence and not infrequent episodes of rebelliousness, preoccupation with self-image, peer pressure, stigma of chronic illness, and trials of substances including smoking. In addition, there will be differences in behaviors of adolescents between early to mid to late adolescents [10–12] each showing different barriers and behaviors regarding their experience with asthma, parental involvement and supervision, and communication with providers.

Multiple factors need to be identified and assessed including the patient and family’s emotional reaction to their disease and treatment responsibilities, the need for knowledge about asthma triggers and control, taking control of medication use and procurement, parental dependence vs. the desire to become an adult and independent, dealing with the family, and most importantly dealing directly with the adolescent as the patient.

Medical practitioner availability may be a factor in discontinuity of asthma care, lapses in prescription medication use [13], and no follow-up for issues such as comorbidities and inhaler technique. Communication strategies need to evolve from giving recommendations to the family unit to giving them directly to the patient instead (or also). If transitioning from a pediatrician to adult physician, there may be changes in recommendations or patient and family comfort. If the disease is severe enough to involve a respiratory specialist, a change from a pediatric specialist to an adult one may lead to availability issues, change in comfort level, or familiarity with even medication indications by local formularies. A level of trust in the new clinician is paramount to outcomes and for the clinician; it is important for the clinician to set aside time to meet with the adolescent on their own during an appointment and utilize good communication skills such as listening and empathizing. Time concerns for the clinicians and attention spans of adolescents may require other health care system resources such as educators and case managers but follow-up messages by using social media and Apps can sometimes better help reach these patients.

There are some unique issues in these age groups as puberty and body changes are occurring. Social forces such as peer pressure and the stigma [14] of having a chronic illness can lead to fears of medication side effects and medication avoidance.

The lack of appreciation of the consequences of medication nonadherence can also be a result of the cognitive changes that are occurring. The transition from concrete thinking to more abstract thinking will factor in here, as beliefs may result from what they have seen and experienced compared to expert and parenteral advice. Hypothetical thinking to analyze multiple types of evidence may be lacking, especially when stressed, such as being ill; problem solving skills may deteriorate. While outwardly maturing, they often remain self-centered and feel invulnerable to consequences, leading to risk-taking behavior such as sexuality, sports, driving, and drug experimentation. Low adherence to treatment can be another way of testing limits. Rebellious behavior can also lead to further family strife complicating relationships required for adherence encouragement.

Adherence issues particular to adolescents

Having to deal with a medical issue can derail the development of self-concept and identity during these formative years. As they are developing a sense of self, the frustration and confusion of having to deal with

an illness may lead to apathy regarding how severe the illness can be and even outright denial of their condition. Teens want to take control of their own lives and make their own choices as they are trying to develop some independence from their family, and having a chronic illness may lead them to deal with the loss of this control by confronting parents and professional authority with making poor choices such as being non-adherent to their therapy, not avoiding triggers, not following instructions, and missing vital consultations. Parental concern can lead to over-protective parents which can further lead to adolescent frustration, but also to the teen not taking responsibility for their own condition. It is important to encourage the adolescent to become more autonomous and take responsibility for their health, but this degree of autonomy will be quite variable between individuals [15]. They need to understand their regimens, follow-up responsibilities, making their appointments, inhaler techniques, understand action plans/self-management skills [16], and understand how to assess asthma control.

The adolescent, their family, and the entire health care system will suffer from the effects of this deficit in adherence. Poor adherence increases morbidity and medical complications (exacerbations, hospitalization, and oral corticosteroid use), leads to poorer quality of life (fatigue and absenteeism from school or their part-time occupations), and an overuse/misuse of the health care system (unnecessary medical assessments and treatments) [17]. Adolescent adherence in chronic illness can vary from 10% to 89% [18]. An asthma study showed adherence of only 50% to 60% adherence to their prescribed doses of inhaled medications [19]. Different types of non-adherence require different solutions. Non-adherence can be divided into three timelines: failure to initiate, implement, or persist with treatment [20]. Non-adherence may either be intentional or non-intentional [21]. Intentional non-adherence examples are not attending their appointments, not taking or inappropriately adjusting their advised treatments [22]. Intentional nonadherence requires strategies such as delving into the reasons for this attitude and motivational interviewing. Non-intentional non-adherence examples include lack of organizational skills, memory issues with respect to times to take medications, or inhaler device technique errors. This requires teaching devices with intense follow-up or linking the timing of medications to other activities such as meals or brushing teeth.

Factors that affect adherence include demographic, familial, socioeconomic, personal, type of illness, low awareness of asthma risks, their own and their parents' anxiety [23], somatization, hostility, therapeutic regimens, and the relationship with health care professionals [24]. Adherence is positively affected [25] by positive family functioning, close friends, internal locus of control, treatment with immediate benefits, parent's beliefs in the seriousness of illness and efficacy of treatment [26], and physician empathy. Conversely, adherence is negatively affected by being an older adolescent, family conflicts, complex therapy, medication with side effects, mental health issues in the patient and/or caregiver, and illness denial. It is not surprising that adolescents who have to try to cope with emotional, social, family, or mental health problems will struggle more adherence to their treatments. Patient and parental beliefs and attitudes are clearly important predictors of adherence [27].

There is also the potential that low adherence can be a marker for more serious family dysfunction (such as parental mental health problems, family violence, substance use, or child abuse or neglect). This brings up other concerns for the child beyond just the asthma management of course and as such, needs to be considered.

Peer acceptance and their social milieu are tremendous drivers for most teens, and having a chronic condition is a challenge for this. For example, in adolescents with diabetes, negative relationships with peers are related to poor outcomes [28]. Understandably, adolescents do not want to be seen as disparate from their peers. This can lead to further adherence issues due to them hiding their illness and their treatments from their peers and even outright denial. Also, the teen may feel that lower adherence can be helpful, by reducing medication side effects (including possible cosmetic concerns such as acne, weight gain, and hirsutism), financial concerns about paying for medications, concerns re medication taste, fear of addiction or dependence [29], increased flexibility in their personal schedules, avoidance of responsibilities such as school, homework, and household chores, attention seeking behaviors, and the temporary freedom from thinking about their disease.

The use of technology with smartphone and tablet Apps for asthma is particularly promising for both self-management and education in the adolescent age group [30]. Adolescents love to use technology, have access to smartphones and tablets, and use the internet regularly. A 2018 survey of US teenagers between 13 years and 17 years of age, showed that 95% either had or could have a smartphone, just under half of them reported use of the internet in an almost constant fashion [31]. They are, however, often early adapters of technology. Their internet usage had almost doubled since the 2015 survey [31]. With those factors in mind, health interventions perhaps need to use these modalities to provide a generation-appropriate and accessible platform [32], to assist in disease self-management. As strong long-term beliefs about medications, and relationships with their medications are made, these innovative solutions for education and self-management solutions are required. In addition, devices can remind patients of appointments with text messages, create reminders to refill prescriptions and even to take their medications, invoke personalized asthma action plans [33], include peak flow measurements and include air quality [34]. Clearly, it would also be advantageous to involve adolescents with asthma in the design process of these Apps, which is only rarely done [35]!

Physiological issues

Males have a higher risk of asthma pre puberty, the risk is equal between sexes at puberty and the risk is higher in females post puberty. These known sex differences in asthma may also be due to multiple other factors [36] including hormonal effects, fetal and childhood lung development, airway caliber, genetic susceptibility, immunologic response, differences in consultation practices, and health-seeking behaviors [37].

Asthmatic children may hide or not recognize significant airway obstruction and may deal with it by avoiding exertional behaviors such as sports which can again lead to social isolation. Children with chronic airway obstruction may suffer from less breathlessness than children with acute obstruction [38]. Adolescent asthmatics are often poor perceivers, which can lead to a greater risk of respiratory function decline and acute exacerbations [39]. Objective assessment of asthma in adolescents is similar to other age groups and includes measurements of control, spirometry, oscillometry, and fractional exhaled nitric oxide (FENO). Symptoms, however, are poorly correlated to the forced expiratory volume in 1 s (FEV1) and the FEV1/forced vital capacity (FVC) ratio, so asthma management should not be based solely on patient symptoms [40]. Forced expiratory flow (FEF; 25–75%) could be a better correlate with symptoms in children to help decide treatment [41, 42].

Treatment issues particular to adolescents

Proper inhaler device use is critical to medication reaching the site of action for inhaled medications. The most common options include pressurized metered dose inhalers (pMDIs) and dry powder inhalers (DPIs). The most used class of drugs are the pMDIs which require coordination of breathing with actuating as well as a long slow deep breath and a subsequent breath hold. Concerns about greenhouse gas emissions by metered dose inhalers (MDIs) have led to some suggesting that medications be given by DPIs instead as they do not have any propellants. Choosing the best DPI is still a real challenge [43]. It requires a rapid inhalation of sufficient force followed by a proper breath hold.

Asthmatic adolescents could be affected by the subjects' pattern of airflow limitation. Peak inspiratory flow rate is known to be an issue potentially in people with significant chronic obstructive pulmonary disease (COPD) and hyperinflation. De-aggregation and the aerosolization of dry powders to be inhaled through DPIs require a pressure drop occurring during maximal inspiratory maneuvers. Adolescents obviously can vary significantly in body type, but at least one study suggested that mid-resistance devices have the most consistent response in this group [44] compared to a low resistance device. DPIs also must be discarded, leading to concerns about plastics in our oceans and doing harm other than to the atmosphere.

Another issue that will affect adherence and success of treatment is the treatment regimen. Simple beats complicated. The clear need for the use of ICS to treat the underlying inflammation drives treatment. Overuse of SABA even along with ICS increases the risk of both asthma exacerbations and mortality [45, 46]. Evidence has shown that a once daily ICS/long-acting β_2 -agonist (LABA) for a patient with mild to moderate disease can be very successful [23]. Many patients, especially adolescents, have trouble taking medication regularly. The SYmbicort Given as needed in Mild Asthma (SYGMA) trials have shown that using ICS/formoterol as required has outcomes equally as good as regular ICS for the reduction of exacerbations [47, 48]. As such, using ICS/formoterol as needed for very mild and mild asthma might be more attractive than regular ICS which will often not be taken regularly.

It is well known that triggers of asthma should be avoided. Adherence to this step is likely also decreased [49] for adolescents. Lack of attention to allergic triggers and avoidance strategies leads to continued allergic inflammation. Rebellious behavior can lead to inhalation of substances such as cigarette smoke, cannabis smoke, or vaping. Cannabis has mixed effects on asthma [50]. Cigarette smoking is clearly associated with a higher risk of developing asthma symptoms [51], poorer lung function, and asthma exacerbations. Vaping, or the use of electronic cigarettes can lead to the inhalation of toxic components such as propylene glycol (PG) and vegetable glycerin (VG), and other components such as color, flavoring, and nicotine can further induce respiratory morbidity and lung function changes. Teens are difficult to get into smoking cessation programs and even if they do enroll, they have high dropout rates [52].

Asthma remission

Remission is more common in adolescents than in adults, with remission rates reported at 16–60% [53]. An increased probability of asthma remission has been associated with having mild disease and minor airway inflammation before adolescence, male sex, and the absence of allergic sensitization. While disease remission is of course a good thing, it subsequently requires an appropriate subsequent organized tapering of medications can lead to patient and parent confusion and lead to discord with the physician and doubting that the disease actually ever did exist. It is also not uncommon for the disease to “recur” in young adulthood, which should be communicated. Predicting who will remit is an inexact science, but persistent asthma can be predicted by socioeconomic factors such as insufficient perinatal care, maternal health behaviors, breast-feeding, and breast-feeding duration, environmental risk factors such as family housing conditions, potential exposure to infections through childcare type and sibling number, and neighborhood characteristics [54].

The corollary is that conditions that predict against remission [55] include the presence of type 2 (T2) inflammation as represented by allergic sensitization or elevated FENO, comorbid illnesses such as eczema and rhinoconjunctivitis, obesity, and maternal history of allergy and asthma.

Transition

Adolescence is a time of transition. Early adolescence is the transition from childhood and as such requires the child understanding more about their illness and asthma control, taking responsibility for taking their doses, and using their inhalers correctly. Parents are still often very involved in care with assessment, making appointments, reminding to take medications, and day-to-day management.

Late adolescents are transitioning to adulthood. More rebellious activity and risk-taking is likely here, potentially leading to further trigger exposure as mentioned with inhaled substances such as smoking or vaping of tobacco or cannabis. In attempts to derive further independence from the parents, issues can occur regarding medication adherence, appointments, and follow-up.

Both the patient and their parents thus require education about their disease, an understanding of their medications and inhaler technique, and an understanding of how inadequate control puts them at risk. Clinicians must learn to ensure that they are communicating directly to the adolescent patient, even if parents are still involved, to give them some feeling of control over their condition. Clearly, it is necessary to support each adolescent personally as per the individual need for that individual and the entire family unit.

Conclusions

Adolescent asthmatic patients have needs and requirements that require quite precise attention. Attention to adherence issues and behavioral issues that are somewhat unique have been discussed. Sensitivity is required to the needs of both the parental caregivers and the individual patient. Basics like diagnosis, inhaler technique, removal of triggers, and attention to comorbidities continue to require attention. Let's help these young people grow up into healthy, happy well controlled adults.

Abbreviations

Apps: applications

DPIs: dry powder inhalers

ICS: inhaled corticosteroids

Declarations

Author contributions

AK: Conceptualization, Investigation, Writing—original draft, Writing—review & editing.

Conflicts of interest

Alan Kaplan is a member of advisory board or speaker's bureau for Astra Zeneca, Boehringer Ingelheim, Covis, GSK, Merck Frosst, Sanofi, Teva, Trudel, Valeo.

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