Published in final edited form as:

Contemp Clin Trials. 2008 March ; 29(2): 304–310.

Design of the Supervised Asthma Therapy Study: Implementing an adherence intervention in urban elementary schools

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Abstract

Background—Inhaled corticosteroids, when properly used, can offer considerable protection against asthma-related morbidity. However, adherence to prescribed inhaled steroids among children is low and rates differ markedly by population. The lowest rates of adherence and highest rates of morbidity are among inner-city and low income populations.

Purpose—To describe the design of a school-based clinical trial in a largely minority population that is examining the efficacy of a school-based intervention intended to increase adherence to daily inhaled corticosteroids.

Methods—The supervised asthma therapy study is a two-group randomized longitudinal trial. Children were randomly assigned to either school-based supervised asthma therapy or parent supervised asthma therapy. Children were followed longitudinally for 15 months. The primary outcome of the study is the time-averaged difference between the two groups in the percentage of children experiencing at least one asthma exacerbation each month.

Results—A web-based data collection system was designed to capture data at school. A total of 295 students, recruited from community and school sites, who attended one of 36 urban elementary schools enrolled in the study and 290 were randomized. The average age of the students was 10.0 years (sd=2.1), 91% were African American, 8% were white, and 1% were of other racial groups. 57% of students were male. The study has been recently completed and results are being analyzed.

Conclusions—Intervention studies requiring daily medication supervision and daily data collection can be successfully conducted within the elementary school environment.

Keywords

asthma; children; clinical trial; adherence

Background

Asthma is a common childhood disease with significant impact on morbidity and mortality [1]. Inhaled corticosteroids, when properly used, can offer considerable protection against asthma-related morbidity.[2] However, adherence to prescribed inhaled steroids among children is low with reported rates ranging from 22%–77%[3–10]. Adherence rates differ markedly by population with the lowest rates found among inner-city and low income

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populations[8,11–14]. Because morbidity is higher among inner-city, low-income, minority children with asthma[15] we designed a study to collaborate with urban school districts with largely minority populations to develop, implement, and test the efficacy of a school-based intervention designed to increase adherence to inhaled corticosteroids.

To accomplish the aims of this study, we had to implement a system that would allow for daily data collection and a system for supervising medication use at the school each day. In addition, unlike most school-based studies, children were recruited not only through the schools but also through the community. Previous experience has indicated that schools are not always aware of all children who have asthma[16,17]. This may be particularly true among those children who are not taking medications. Therefore, recruitment through the community allowed us to enroll children with asthma who were not known to the school.

Methods

Design overview

The supervised asthma therapy study was a two-group randomized longitudinal trial. Children were randomly assigned to one of two groups: either school-based supervised asthma therapy or parent-supervised asthma therapy (usual care). Children were followed longitudinally for 15 months.

Setting

The study was conducted in 36 urban schools in the Birmingham, Alabama area. The school population was predominantly African American. Inclusion criteria were: physician-diagnosed persistent asthma, need for daily controller medication, enrollment in one of the 36 participating schools, ability to use a breath-actuated inhaler, and ability to use a peak flow meter. As all children were going to be prescribed the same inhaled corticosteroid; children were excluded if their physician felt it was inappropriate to change their prescription to budesonide inhalation powder (Pulmicort). Children were recruited through multiple methods including local schools, physicians, and health department clinics. The University of Alabama at Birmingham's Institutional Review Board for Human Use approved and monitored the study.

Treatment Groups

Children who enrolled in the study were assessed by a physician (either their primary care provider or the study physician if no primary care provider was identified) and prescribed a daily inhaled corticosteroid (budesonide inhalation powder, Pulmicort Turbuhaler, provided by Astra Zeneca) in a dose specific to their needs. The dose, or number of inhaled puffs, was prescribed for each child based on asthma severity. This medication was chosen because it is breath activated and thus, minimizes the difficulty in drug delivery to the airways. Children were prescribed budesonide once daily because adherence to asthma medication among children is associated with the number of times a day the child has to take his/her inhaled corticosteroids and once daily dosing has been shown to be effective[18–20].

Participants in the intervention group were provided with budesonide for use at home when school was not in session or when the child otherwise did not attend school and rescue medication (albuterol) for home and school at no cost. Participants in the usual care group were provided with budesonide for daily use at home and with rescue medication (albuterol) for home and school at no cost. Refills were provided through the mail upon telephone request. Children were also provided with two peak flow meters (for home and school).

Randomization

Children were randomized to receive either the supervised therapy intervention or usual care. Allocation was concealed and randomization occurred at an individual student level within school system, in order to account for group-level and individual factors that may be similar among children in the same school system. Patients, their parents, and study staff were not blinded to intervention condition; however, physicians were blinded to their patient's intervention condition.

Intervention

For those students randomized to the intervention arm, daily use of inhaled corticosteroid medication was supervised by study staff at school each day. A standard daily time was arranged (preferably morning) with each school when students are called out of class to have study staff supervise their use of the inhaled corticosteroid.

Usual Care

Those randomized to usual care continued their usual parent- or self-supervised use of daily inhaled corticosteroids at home. Control group children did not have access to inhaled corticosteroids at school but did have access to rescue medication at school.

Primary Outcome Measure

The primary aim of this study was to compare children randomized to school-based supervised asthma therapy to children randomized to usual care with regard to time-averaged proportion having at least one asthma exacerbation per month. It was hypothesized that the supervised asthma therapy group would have fewer exacerbations compared to the usual care group.

The primary outcome measure for this study, asthma exacerbations, was defined by one or more of the following each month: 1) red or yellow peak flow meter reading; 2) rescue medication use more than two times per week (not including pre-exercise treatment); or 3) absence from school coded as respiratory illness/asthma. Data will be examined using graphical methods to display the frequency of exacerbations while incorporating the longitudinal aspect of the study. For each individual in the study, the time-averaged probability of experiencing at least one exacerbation per month will be computed as the number of months that at least one exacerbation occurred divided by the total number of months observed. This will provide a summary measure for which to compare the two treatment groups; however, this does not incorporate the longitudinal nature of the study and thus, may not be sensitive to seasonal variations in the frequency of asthma exacerbations.

The primary hypothesis of the study, that the frequency of asthma-related exacerbations differs between the school-based supervised and the usual care groups, will be tested in a number of ways using intent-to-treat analyses. A two-sample t-test will be used to examine the difference in the time-averaged probabilities of experiencing at least one exacerbation between the two groups. Because this summary measure does not incorporate the longitudinal nature of the data into the outcome, generalized estimating equations (GEEs) will be fit, in which the outcome will indicate if each individual experiences at least one exacerbation in each month of the study period. Use of GEEs allows examination of intervention effect change over time. Further, we will be able to incorporate correlations describing the relationships among an individual's outcomes, as well as correlations describing the relationships among individuals within a school.

Data Collection

To accomplish the primary aim of the study, it was necessary to collect daily data on peak flow meter (PFM) readings, rescue medication use, and school absences. Previous experience has indicated that such daily data collection is difficult to achieve without interrupting school schedules. Therefore, the investigators collaborated with Blue Cross and Blue Shield of Alabama to develop a web-based data collection system (*Asthma Agents System*) to collect this daily information with minimal interruption to the school day. A detailed description of this system has been published previously [21] and it has been shown to be associated with reduced missing data.

After enrollment into the study and prior to initiation of data collection, both children and school staff were trained to use the system correctly. Each school day, participating students logged into the *Asthma Agents System* through a school computer to submit the required data, after which school staff logged in to verify the child's data. Children were asked "How is your breathing today?" Answer choices included: fine, coughing, wheezing, or tightness in chest. Children could report more than one symptom. The system then prompted the child to blow into his/her peak flow meter and report whether the reading was red, yellow or green. Red and yellow peak flow meter readings were based on the values representing the child's "best" peak flow rates during healthy periods at the beginning of each school year. Red readings indicated peak flow rates less than or equal to 50% of the "best" value, while yellow readings indicated peak flow rates at 50–80% of the "best" value. Green readings indicated peak flow rates of greater than 80%. If a child reported a green reading, the system replied with the message, "Great! Go and play today"; if a child reported a yellow or red reading, the system instructed the child to "Stop and talk to an adult." Yellow and red readings generated automatic e-mails, with PFM results and symptoms, to the school nurse and study coordinator. Teachers were trained to permit children to log onto the system at the same time each day to prevent diurnal variation in PFM readings. Children and school staff earned prize-points for logging onto the system and completing their respective tasks.

On each day, if a student did not enter a report, a designated school staff member was prompted to enter a reason, with response choices of: absent, did not report (indicating that the child simply did not complete the report that day), or other. When "absent" was entered as the reason for no daily report being entered, upon the student's return, the staff was prompted to enter the reason for the absence. This information was obtained from a brief interview with the child. Response choices for reason absent included: asthma or respiratory illness, other illness, and other. Each school staff person had a designated back-up to perform these duties upon their absence.

At-school rescue medication utilization was monitored through the use of a DoserTM that was attached to the top of the inhaler and activated automatically to record each inhalation taken. Study staff read the child's DoserTM every two weeks to record usage.

No data were collected on rescue medication or inhaled steroid use at home. As children spend the majority of their time at school during the school year when exacerbations are most common [22–24], it was felt that the cost and effort of collecting data at home was excessive in relation to the return. Data on household smoking, quality of life and health care use were collected at the beginning of each school year and at the end of the study by telephone interviews with the primary caregiver.

Baseline data collection occurred from October 2005–December 2005. In January 2006, 290 children were randomized to either intervention or usual care. Follow-up data were collected from January 2006 – December 2006.

Safety issues

Adverse events were monitored by a Data Safety and Monitoring Board (DSMB) whose members defined two safety events to be considered: 1) a child reporting red peak flow meter readings with symptoms either three days in a row or more than five days in a calendar month, and 2) use of either 30 or 40 puffs of rescue medication in a two week period. The 30 puff limit applies to those children for whom rescue medication was kept in the school office while the 40 puff limit applied to children for whom medication was kept on their person. A child was able to carry rescue medication on his/her person at school if the parent and a physician had agreed that he or she had adequate maturity to recognize when the medication was needed, and the physician had completed an authorization form for the school.

In addition to monitoring safety events, investigators provided handouts to parents, teachers, and school staff about the side effects of the inhaled steroid and the appropriate response to take if a child showed signs of these side effects. This was to maintain the safest study environment possible.

DISCUSSION

This study was a randomized clinical trial involving 36 elementary schools and 290 elementary school children, recruited from the community as well as the schools. This unique intervention consisted of supervising a daily controller medication for asthma at school and daily data collection was necessary for analysis of the primary outcome variable. Below we discuss several issues that we encountered in attempting to implement this design which we feel may assist other investigators in implementing similar school-based programs.

Design issues

The use of an internet based system which allowed for daily collection of data was a unique feature of the design. Previous experience in the schools has indicated that these types of data are difficult to collect; therefore, we collaborated with Blue Cross and Blue Shield of Alabama to create such a system[21]. This system allowed us to collect daily peak flow meter readings as well as asthma symptoms and reasons for absence from school. Monitoring peak flow with a meter is a relatively simple and accurate way to assess children's airway obstruction as opposed to symptom monitoring which has been shown to underestimate the severity of disease [25]. Peak flow meters provide a reading of the air flow from the lungs, resulting in a value in liters per minute. Asthma interventions frequently train children to monitor their asthma through daily use of a peak flow meter. These data often are collected through daily diaries as part of the study outcomes or to monitor the child's health. However, children have been found to be poor record keepers of peak flow meter readings. In a study of the accuracy and completeness of peak flow diaries among 6–16 year old asthmatic children, Kamps and colleagues found that peak flow diaries were unreliable in that children did not actually utilize their peak flow meter as frequently as reported[26]. A study among African-American and Hispanic asthmatic children aged 5–9 years similarly found that the children involved had difficulty maintaining peak flow records, so that data recorded in diaries did not reflect data recorded electronically[27]. Poor compliance with adherence to monitoring translates to an inability to collect serial data of peak flow meter readings. To assess adherence with peak flow meter monitoring, Burkhart and colleagues utilized microchip technology, which is built in to the peak flow meter, and automatically tracks much of the data of interest[28]. However, devices such as these do not include assessment of symptoms, which was another aspect of interest in the current study.

The internet-based system also allowed us to collect precise information on reasons for absences among the children. School records often do not indicate the reason for absence and

among inner-city populations reasons for absence can be highly varied. In fact, previous data indicated that only 24% of absences among children with asthma were due to asthma or respiratory illness[21]. Therefore, this system allowed us to assess absences for respiratory illness which gives us a precise measure of the type of absence the intervention was expected to effect.

This design had limitations, many of which were due to feasibility constraints. One limitation is that we provided supervised medications to our intervention group only five days per week during the school year. In addition, due to the feasibility and cost of acquiring data on non-school days, we did not collect data during summer break and school holidays. Others have reported that summer is a time period with few asthma exacerbations.[29–32], so collecting data during this period was less important for our evaluation. Our previous experience indicated that parental involvement in school-based interventions is low and attempts to collect data from parents have proven to be ineffective. Therefore, in order to obtain high quality data for analyses, data were collected only from the child and school personnel directly. We chose not to collect any measures of school absences from school records because our previous experience has indicated these data are unreliable[33] and are not specific regarding the reasons for absences.

Another limitation is the lack of a true control group. Both groups were provided medications, experienced the educational component of the *Asthma Agent System*, and were required to provide data by reporting asthma symptoms and PFM readings. Medication provision was necessary to remove access to medications as a reason for non-adherence. Therefore, it is conceivable there may be an intervention effect on both groups in the same direction, thus biasing results toward the null hypothesis of no difference in exacerbations between conditions. Using a daily diary system of data collection has been found to sensitize participants to the phenomenon they are being asked about that can result in changes in behavior[34]. In this study, the daily logging of asthma symptoms and PFM reading may serve to increase students' awareness of their asthma and provides feedback which could cue students in the control group to use their daily controller medication.

Investigators chose to randomize by child as randomization by school would inflate the variance of our outcome measure due to intra-class correlation among students within the same school. By randomizing children within the same school to different treatment groups, we recognize the potential for contamination if intervention children or their parents discuss taking asthma medications with someone in the control group, thereby serving as a “cue” for taking daily medication. Having study personnel, not school personnel, supervise treatment should reduce the potential contamination from having both conditions in the same school.

Intervention issues

One of the major issues that had to be addressed in the design of this study was how to accomplish the supervision of the inhaled steroid medication use at school. This needed to be done by study staff for several reasons. First, not every participating school has a nurse and those available already have a substantial work load. As well, it would have been difficult to monitor intervention fidelity. Second, to reduce the potential for contamination, study staff were required to supervise medication administration. To accomplish this goal we had to communicate the rationale behind this decision to the school districts and work with our State and local school boards to understand the policies on medications given at school. Due to state laws requiring that medical personnel administer medication, non-medical study staff could not assist the children with taking inhaled corticosteroids as this crossed the line from supervision to administration. Physician orders for student self-administration of medication were obtained for all children and filed at school. Medication was stored at school each day in a secure, locked location determined by the school medication team. As it was considered

important that intervention group children use proper technique when taking their medication, study staff were supplied with placebo inhalers to demonstrate correct technique when necessary.

Study status

A total of 295 students who attended one of 36 urban elementary schools enrolled in the study and 290 were randomized (5 transferred to a non-participating school during the baseline data collection period). Two hundred and forty children completed the study (49 transferred to a non-participating school and 1 was expelled from school). Parents provided consent for the child's participation and children gave assent. The average age of the students was 10.0 years (sd=2.1), 91% were African American, 8% were white, and 1% were of other racial groups. Fifty seven percent of students were male. The study was recently completed and results will be available in the near future.

Acknowledgements

Funded provided by: NHLBI 5 R01 HL075043, Blue Cross and Blue Shield of Alabama, Astra Zeneca Pharmaceuticals

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