SMGroup

Journal of General Medicine

Research Article

Using Technology to Improve Adherence to HIV Medications in Transitional Age Youth: Research Reviewed, Methods Tried, Lessons Learned

Spratt ES[1], Papa CE[1], Mueller M[2], Patel S[3], Killeen T[4], Maher E[5], Drayton C[1], Dixon TC[1], Fowler SL[1] and Treiber F[2]

[1]*Department of Pediatrics, Medical University of South Carolina, USA*
[2]*College of Nursing, Medical University of South Carolina, USA*
[3]*Technology Applications Center for Healthful Lifestyles, Medical University of South Carolina, USA*
[4]*Department of Psychiatry, Medical University of South Carolina, USA*
[5]*Department of Medicine, University of North Carolina, USA*

Article Information

Received date: Aug 31, 2017
Accepted date: Sep 18, 2017
Published date: Sep 21, 2017

***Corresponding author**

Spratt ES, Department of Pediatrics, Medical University of South Carolina, Charleston, South Carolina, USA,
Tel: (843) 876-0504;
Email: spratte@musc.edu

Keywords Human immunodeficiency virus; HIV; Non-adherence; Adherence; Adolescents

Abstract

In transitional age youth living with HIV or AIDS, non-adherence (<80%) to anti-retroviral medication is associated with viral resistance, disease progression, and an increased risk of death. This feasibility study investigated the Maya MedMinder electronic pillbox and cell phone texting with personalized motivational interviewing strategies to improve medication adherence in non-adherent youth. Twenty patients out of 30 identified as non-adherent by the Pediatric HIV team at the Medical University of South Carolina were approached, and 15 were recruited (Ages 12 to 20; 13.3% male, 86.7% female; 100% African-American). Following baseline MedMinder monitoring, subjects were randomized to intervention groups with reminder signals on or off. The time medications were taken was collected by the MedMinder, resulting in adherence scores. All were interviewed for readiness to change utilizing the Motivational Interviewing (MI) Stages of Change scores. Viral load and CD4 labs were scheduled every 6 weeks. Despite monetary incentives and personalized support, recruitment and adherence to the protocol was a challenge. Only 6/15 subjects completed the entire study scheduled for 6-months .Stages of change scores revealed that those that transitioned to making changes had higher CD4 percentages midway through the study. Challenges included missed appointments and labs despite efforts by text and phone to schedule convenient appointment times with participants. Device challenges included the large size of the MedMinder and faulty electronic signaling, especially from rural areas. The methodology was feasible with these patients. This small feasibility study highlights that technological tools to promote adherence and motivational enhancement strategies in teens and young adults who are non-adherent to HIV medication regimens can enhance biomarker outcomes associated with medication adherence.

Introduction

Medication adherence and successful retention in medical care are major treatment concerns for adolescents living with chronic illness, but are especially important with Human Immunodeficiency Virus (HIV) infection or acquired immune deficiency syndrome (AIDS) [1]. Non-adherence to HIV medications is defined as taking daily oral medication as directed less than 85% of the time and characterized by decreased CD4 cell counts and an increase in viral load count. It has been noted that even moderate non-adherence (<80%) is associated with the development of viral resistance, significant disease progression, and an increased risk of death [2]. This article reviews evidence-based literature on improving adherence to HIV medical regimens, describes a pilot project, and offers suggestions from the literature, as well as from an interdisciplinary Pediatric HIV health care team.

The most effective treatment approach to HIV infection is highly active antiretroviral therapy (HAART), but greater than 95% adherence is required for optimal viral suppression [3]. This can be challenging due to multiple medications, frequent dosing, and significant adverse side effects including acid reflux, upset bowel, skin rash, and metabolic changes [4]. In one study, 56% of patients with viral load increase had recent episodes of incomplete adherence or interrupted treatment [5]. Since HIV is an opportunistic virus, any non adherence can lead to decreased efficacy of medications, greatly increasing the risk of opportunistic infections. ETA-analysis of adolescent adherence to anti-retroviral therapy (ART) found North America to have the lowest rates in the world with 53% adherence [6]. This is a major public health problems as out of the 610,000 individuals aged 15-24 who were newly infected by HIV worldwide in 2016, 260,000 were adolescents aged 15-19 [7]. In 2014, South Carolina had the 13th highest AIDS case rate among all U.S. States [8], with Columbia and Charleston in the top 50 metropolitan areas in the country [9]. The 2015 incidence of HIV/AIDS cases in South Carolina was 40 cases per 100,000 youth between 13 and 19 years old with

a prevalence of 100 cases per 100,000 in the same population [10]. All health care providers working with individuals with HIV aim to avoid an early demise due to medication non adherence, yet guiding a successful behavior change takes careful patient engagement, time and effective treatment planning.

One of the challenges in caring for these youth in South Carolina is that some are living in rural areas, making access to regular follow up appointments challenging [11]. There are also many self-reported personal barriers to adherence among children with chronic diseases including fear of being stigmatized or rejected by peers, lack of parental support or a "bad home life", inadequate explanation of the importance of treatment by physicians, immature organizational and time management skills of the patient, and medication regimen complexity [11,12]. In a study investigating barriers to ART adherence in HIV positive adolescents, the most common barriers were simply forgetting to take the medication, not carrying the medication with them, and frequent changes in daily routine [13]. Similar challenges in adherence have been observed by this team.

The best methods for improving HIV care and medication adherence include multifaceted interventions, namely ones that incorporate innovation, monitoring approaches, patient support, and HAART regimens [14]. Motivational enhancement strategies are known to improve medication adherence among adolescents. Motivational Interviewing (MI) is a patient centered intervention to help patients resolve ambivalence about behavior change emphasizing self-efficacy. In an MI framework, the clinician works collaboratively with the patient to explore and resolve any ambivalence about change [15]. MI empowers patients to make decisions that are consistent with important life values and/or goals. The goal is for the patient to see a discrepancy between their current behavior and what they value leading to the patient deciding to make a healthy change leading to a healthy behavior change. The clinician uses specific skills to evoke change and commitment talk, which has been shown to be predictive of actual behavior change [16,17]. MI has been effective in changing behaviors when used in HIV positive adolescent populations [18]. The use of technology to monitor daily medication adherence has the potential to be useful in concert with a cognitive motivational enhancement program, as it provides automated real time positive supportive text delivery [19].

Adolescents with HIV are a vulnerable population and often difficult to engage and retain in treatment. As such, a consistent, autonomous, and collaborative approach of MI is more appealing for adolescents. Attitudinal (i.e. perceived risk, readiness) and behavioral (i.e., self-monitoring) changes have been reported in several studies. MI coupled with patient assessment feedback (Motivational Enhancement Therapy- MET) provides patients with objective information that can help guide decisions about change. For example, knowledge about viral loads and CD4 counts can inform adolescents with HIV about decisions regarding medication adherence. Compared to standard clinic treatment, targeting risk behaviors with MI in adolescents with HIV (substance abuse, antiretroviral drug non adherence, and sexual risk behavior) has been shown to reduce viral load at 6 but not 9 month follow up [20]. In one study of 94 HIV positive youth who participated in at least two motivational sessions, demonstrated significant improvements in their readiness to change compared to control youth not receiving the intervention [21]. Another study compared a two-session MI interactive computer intervention to a two-session interactive health intervention in 76 HIV positive adolescents' and changes in viral suppression and measures of adherence were better in the MI group [22]. In HIV positive youth ages 16-25, brief MI compared to wait-list controls showed greater reductions in unprotected sex acts and viral load [23]. These studies demonstrate that MI, whether delivered in person or via a computer, can be useful in an adolescent population who are at high risk for HIV treatment non adherence.

Rollnick [15] describes five main concepts for the clinician to remember when using MI: be empathetic, differentiate between the patient's goals and the desired change in behavior, avoid arguments, work with any resistance instead of against it, and be supportive and optimistic that change is possible. From a clinician's standpoint, one of the most difficult tasks to accomplish will be dedicating adequate time to the MI process, both immediately and long-term. In a single visit, interventions can take anywhere between five to thirty minutes, depending on the behavior being addressed and the needs of the patient involved. Additionally, in order to have the most effective change, MI is to be used as a continual process of communication with re-evaluation of the patient's behavior. Unfortunately, most clinical settings are not set-up for utilization of these strategies or to allow for such dedication of time, making this a difficult intervention to implement.

With that being said, MI has shown to be effective for behavioral changes, in a wide range of clinical settings [15]. Behavioral changes have been shown in use of Antiretroviral Therapy (ART), reduction of alcohol and drug abuse, asthma treatment using inhaled corticosteroids, nutrition and dietary intake, physical activity, and medication adherence [15,24,25]. In order for this method of encouraging adherence to be successful, the clinician needs to have a good understanding of who the patient is and have a good understanding of the patient's perceptions in order to cater the treatment to the specific needs of that patient.

Use of cell phone reminder calls to increase adherence in teens and young adults with HIV has been reported as acceptable and practical after some initial complaints [26]. The use of cell phone technology has the potential to have a global impact as a multisite randomized clinical trial of HIV-infected adults in Kenya, patients who received text messaging support had significantly improved ART adherence and rates of viral suppression compared with the control individuals [27]. Clinical research examining whether MI can be used over the telephone in addition to face-to-face encounters [28] found improvement in both access and availability of treatment, reaching those who might not otherwise have access and providing patients with more regular care (Table 1).

mHealth

In addition to telephone reminders, utilizing wireless technology may be a viable approach to improve medication adherence by allowing clinicians to identify non-adherent HIV patients in ways other than just self-report and interact with these patients in real-time. Real-time interactions could also improve the patient's general motivation and consistency towards overall health and well-being. Other advantages could be positively affecting biomarker levels and ultimately long-term clinical outcomes. Technology and electronic monitoring devices have been useful in increasing medication adherence among other patient populations [31]. A meta-analysis of adherence interventions

Table 1: Stages of change [29,30].

Stages of Change	Goal of Intervention
Pre-contemplation: The individual has not yet begun to consider change as an option. No personal "ownership" of problem behavior	Raise doubts and increase awareness of risks and problems.
Contemplation: Initial recognition of problem. Ambivalence about change.	Acknowledgement of ambivalence, evoking reasons for change and tipping the balance in favor of change.
Determination: Mind is made up to change, but individual does not yet actually do it.	Recommendation of treatment options and arranging follow-up visits or referral.
Action: Behavior is actually changed, but individual does not yet feel comfortable.	Ongoing support
Maintenance: New behavior requires less conscious effort. Relapse is an ongoing possibility.	Positive reinforcement and strategies to prevent relapse.

in adults taking prescription medications showed increased adherence by 14%, and that electronically monitored feedback had the largest mean improvement (p=0.02) [32]. Another advantage to using technology is the ability to implement real-time monitoring of medication usage with signal transmission to the provider team, so as to engage in therapeutic encounters with the patient at the time of non-adherence, rather than weeks or potentially months later at a clinic appointment [33-37]. Real time cell phone reminders have shown to have a positive impact on adherence rates [38]. Martin, et al. [39] monitored adherence of HIV positive youth and found that compared to interviews, electronic monitoring devices offered the most detailed adherence information. The Maya MedMinder is one such electronic medication monitoring system (www.medminder.com) that features a series of reminder signals (blinking lights, chimes, phone call) set to a medication regimen schedule to alert the patient of medication times and to alert providers as well. The device records time stamps of each compartment opening and transmits the data via wireless cellular technology to the MedMinder central computer.

Purpose of this study

This pilot study was conducted to test the feasibility of a multi-faceted approach to improve chronic illness medication adherence in transitional age youth with HIV. The goal was to use technology and evidence based interventions to reduce psychosocial barriers that might affect treatment adherence and progression in a clinical population of non-adherent, HIV positive teenagers. As with most pilot studies, this study was not designed for hypothesis testing, therefore safety and efficacy are not evaluated, only feasibility. Findings are discussed on the feasibility and success of recruitment, retention, implementation of adherence technology using MedMinder pillbox and cell phone communication motivational interviewing intervention, and ongoing assessment procedures over a proposed 6-monthperiod with a 6 week follow up. Objectives of the study were to measure the impact of a) technologic support with the MedMinder and smart phone technology with motivational enhancement and measure changes in biomarker CD4 counts, CD4 percentages, viral load levels and changes in non adherent medication behavior.

Methods

Participants in this study were adolescents, ages 12-20 years, recruited from the Outpatient Pediatric AIDS Clinic (OPAC) at the Medical University of South Carolina (MUSC). Patients eligible for the study had a diagnosis of HIV for greater than one year, were prescribed 1-4 HIV medications, were identified by the OPAC clinic team as non-adherent with current medication regimens within the last year, had a detectable HIV viral load, and did not have other diagnoses which might prevent the ability to engage in the intervention. After OPAC staff identified non-adherent patients, a comprehensive EMR chart review was conducted. The PI, research coordinator, team nurse coordinator and peer advocate received motivational enhancement training from a certified trainer (TK).

The study protocol was reviewed and approved by the Institutional Review Board at MUSC. Participants and if applicable the caregiver received a full explanation of all aspects of the protocol and procedures. The patient and caregiver, if patient was under 18 years, were invited to participate voluntarily and written informed consent was obtained from each child's parent/guardian or from older participants who could self-consent. Written assent was obtained from children ≥12 years when appropriate. All participants were under the care of the MUSC OPAC clinic before and throughout the study. Caregivers and youth completed pre- and post-study behavioral questionnaires and each teen was interviewed to determine their score utilizing "Stages of Change" from the motivational enhancement literature [15]. Data obtained from the Maya MedMinder allowed Russel scores based on the timing of adherence to the prescribed medication regimen.

Medication adherence measures: The Maya MedMinder

The MedMinder (model: Maya, MedMinder Inc., Newton, MA, USA) (Figure 1) medication tray uses an 110 V power source, has 28 compartments (up to four doses daily × 7 days), and provides reminder signals through a cellular network to a Health Insurance Portability and Accountability Act compliant server. Alarm reminders were off in Group A and on in Group B. If the reminders were on when the medication was taken, a blinking light from a specific dose compartment activates. If the pill container is not opened, removed, and returned in 30 minutes, a loud chime activates for 30 minutes after which an automated personalized reminder message is sent via phone

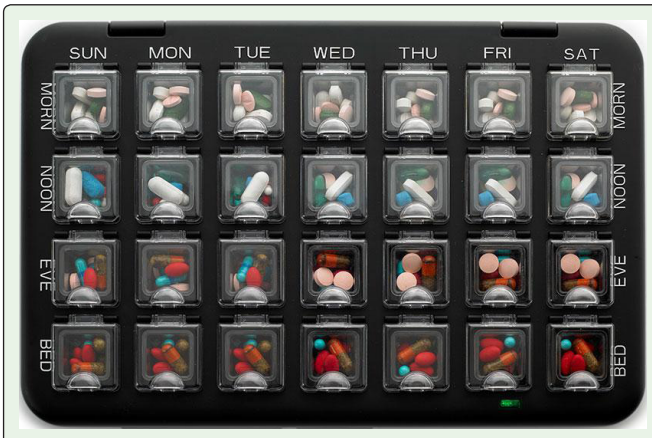

Figure 1: Model: Maya, MedMinder Inc., Newton, MA, USA.

call or text message. Group A did not have blinking light or chime reminders. For Group A and B, the medication tray dates and time stamps each sequence when one of the compartments is removed, and sends the information wirelessly to the cellular network in real time. Failure to open the compartment after 90 minutes triggered an automated email message to the study coordinator.

Following enrollment, the Maya MedMinder pillboxes were programmed to fit with taking medications according to each participant's lifestyle and medication regimen. The set up was conducted in the clinic setting utilizing the online log in and settings at www.Medminder.com. The PI or the research coordinator gave instructions for how to use the MedMinder effectively and gave printed instructions to take home with a contact number to call should problems arise. Phone texting of time medications were taken was allowed in case the participant was not home or if a pill was removed early from the MedMinder to be taken on time at a location other than home. Each patient verbally acknowledged that he/she understood the information collected would be monitored weekly. Each machine was tested to ensure it worked properly before the participant could take it home. For medication adherence scoring, the time stamped data from the MedMinder and/ or phone texting data were collected. All usual team resources (Pediatric infectious disease physicians, Nurse Coordinator, social worker, child psychiatry) were available for support including adult and teenage peer advocates living with HIV. Medication adherence levels for the intervention group from the MedMinder device were assessed using a modification of the Russell et al algorithm [40]. Participants were instructed that in order to be fully adherent, all medications must be taken within 90 minutes on either side of the prescribed time (i.e., 3 hour window). Doses taken between 3 and 6 hours would receive a half score, and a missed dose was given a score of 0. The Russel daily scores can range from 0 to 1, with all daily scores averaged over the study length for adherence values [40].

All participants initially used the MedMinder for 4 weeks with the alert signals off to collect adherence baseline data. These 4 weeks allowed the study team to adjust the patients' medication schedules if needed. During week 5, participants were randomized into one of the two interventions Group-A or Group-B; Group-A continued to use the MedMinder with the alert signals turned off(no sound) and Group-B had the alert signal settings turned on for the duration of the study. In addition to the alert signals on the MedMinder, Group-B received weekly phone call motivational interviewing sessions or positive reinforcement text messages from a trained study team member. Participants were given a smart phone to use if needed for this study. Weekly motivational interviewing incorporated participant concerns, goals for maximal medication benefits, and identification of potential barriers for medication adherence. Stages of change scores were obtained based on personalized dialogue.

Following randomization, participants were scheduled to return to clinic every 6 weeks for blood work appointments. Blood draws were done at MUSC or at a standardized and approved laboratory and analyzed for HIV viral load count, and CD4 count. Protocol feasibility was tested using self-report, retention rates and recruitment rates. Compensation was provided for adherence to the appointment schedule, for study completion and for returning of equipment. Feasibility, acceptability, tolerance and adherence procedures data were collected from all participants. Data were collected from regularly scheduled OPAC appointments and via electronic medical records (Table 2).

Statistical data analysis

For this pilot study, we aimed to test feasibility of the Maya MedMinder pillbox and utilization of cell phone technology to improve adherence and to obtain pilot data on the efficacy of the intervention (i.e. trends toward improvement in adherence) rather than confirmation of a hypothesized differential treatment effect. The data were captured and managed in a REDCap online secure database [41] and data analysis was conducted using SAS v9.3.

For medication adherence analysis and scoring, we collected the time stamped data from the MedMinder and adjunct texting data. Analysis utilized Russell et al. adherence rate formula [42], which incorporates time of actual openings of the MedMinder and scheduled times for medications. Daily scores for each medication included a range from 0 to 1 (for example: 1=day dose: 0=didn't take it; 0.5 =taken within 6 hrs of scheduled time; 1=taken within 3 hours of scheduled time). Cumulative adherence rate across the month was calculated using this formula.

Primary statistical analyses were conducted for feasibility measures, including statistics involving medication adherence data, and results from the Stages of Change and Russel scores using averages and standard deviations. Recruitment and retention rates were also measured. Demographics were described using means

Table 2: Scheduled study protocol timeline.

Study Visit #: Week #	Procedures for Group A (MedMinder with signaling off)	Procedures for Group B (MedMinder with signaling on)
Study Visit 1: Week 1	IRB approved Informed Consent and HIPAA was reviewed and signed. Behavioral assessments given. Subjects assigned a Maya Medminder set-up according to individual medication requirements; all reminder signaling off to collect baseline measurement. Subjects had initial blood draw for labs.	IRB approved Informed Consent and HIPAA was reviewed and signed. Behavioral assessments given. Subjects assigned a Maya Medminder set-up according to individual medication requirements; all reminder signaling off to collect baseline measurement. Subjects had initial blood draw for labs.
Study Visit 2: Week 5	Subjects had 2nd blood draw. Subjects randomized to either Group A or Group B. Group A subjects continued to use the MedMinder with the reminder signaling off, and received regular clinical care.	Subjects had 2nd blood draw. Subjects randomized to either Group A or Group B. Group B subjects began the intervention: Medminder reminder signaling turned on (flashing light, alarm sound, reminder phone call) and received weekly motivational interviewing sessions.
Study Visit 3: Week 11	Subjects had 3rd blood draw. Subjects received regular clinical care.	Subjects had 3rd blood draw. Continued interventions.
Study Visit 4: Week17	Subjects had 4th blood draw. Subjects received regular clinical care.	Subjects had 4th blood draw. Continued interventions.
Study Visit 5: Week 23	Subjects had 5th (final) blood draw and final behavioral assessments given. Subjects returned Medminder to study staff.	Subjects had 5th (final) blood draw and final behavioral assessments given. Subjects returned Medminder to study staff.

Table 3: Participant demographics (n=12).

	n	%
Gender		
Female	9	75%
Male	3	25%
Race		
African-American	12	100%
Reporting Caregiver		
Self	5	41.6%
Biologic parent	4	33.3%
Legal guardian (adopted)	3	25%
Infected		
Behaviorally	4	33.3%
Congenitally	8	66.6%

Results

Demographics

Thirty patients were identified under the age of 21 as being non-adherent. Twenty patients with a clinical history of non adherence were approached for enrollment in this study between 2011 and 2012; fifteen were successfully recruited (13.3% male; 100% African-American). Seven patients were lost to care and could not be recruited. For 3 participants, child protective services were involved and therefore not eligible for the study. At least two families had ongoing substance use concerns and it is suspected that this is why they refused the study. Three participants withdrew before randomization at least partially secondary to the size of the Medminder. For analysis, we considered only the 12 subjects, ages 12-20 years (mean age 17.1 +/- 2.6), who remained in the study past randomization. After randomization, six subjects went on to complete the entire protocol. (Table 3) shows pre-intervention demographics; anthropometrics were comparable between the MedMinder Group A reminder alarms off and Group B reminder alarms on.

Our protocol and IRB consent stated the study would last for 23 weeks (161 days from the time of receiving the MedMinder).

Table 4: Mean percent adherence by intervention.

Study Group	N	Adherence Variable	N	Mean Adherence	Std Dev	Minimum	Maximum
Group A (Control/signals off)	6	Adherence between Visit 1 to 2	6	39.10%	41.7	1.4	90
		Adherence between Visit 2 to 3	5	35.90%	43	2	98
		Adherence between Visit 3 to 4	3	43. during6%	40.5	7.1	87.2
		Adherence between Visit 4 to 5	2	55.30%	57.5	14.6	96
		Overall adherence during study	6	26.80%	35.5	2.3	93.4
Group B (Intervention/signals on)	6	Adherence between Visit 1 to 2	6	17.30%	17.4	0.9	44.6
		Adherence between Visit 2 to 3	6	30.00%	37.5	2.8	96.4
		Adherence between Visit 3 to 4	3	48.80%	30.6	27	83.8
		Adherence between Visit 4 to 5	3	52.70%	49.6	1	100
		Overall adherence during study	6	24.60%	25.8	2.9	69.3

Table 5: Mean CD4 count and % by intervention.

Study Group	CD4 Count at 3 time points	N	Mean	Std Dev	Minimum	Maximum
Group A (Control/signals off)	Before Enrollment	6	451.5	350.4	27	942
	During Study	6	561.2	474	19	1320
	Post-Study	6	480.5	401.6	28	1102
Group B (Intervention/signals on)	Before Enrollment	6	434.8	308.2	55	878
	During Study	6	384.3	248.5	47	768
	Post-Study	6	432.2	310.6	51	901
Study Group	**CD4 % at 3 time points**	**N**	**Mean**	**Std Dev**	**Minimum**	**Maximum**
Group A (Control/signals off)	Before Enrollment	6	22.20%	14.4	1	37
	During Study	6	23.80%	15.7	1	42
	Post-Study	6	22.70%	14.7	1	38
Group B (Intervention/signals on)	Before Enrollment	6	23.20%	15.4	2	40
	During Study	6	23.20%	15	2	41
	Post-Study	6	23.30%	15.7	2	42

and standard deviations. Secondary outcomes assessed longitudinal changes both within and between each group. These were examined at pre-intervention, and months 1, 2 and 3 using independent-samples Mann–Whitney U nonparametric tests to examine between-group differences. Wilcoxon signed-rank tests were used to compare changes between pre-intervention and successive intervention months. Statistical significance was set at p=0.05.

However, mean time from receiving the MedMinder to completion was 227.5 +/- 131.7 days, as all subjects changed appointments and did not arrive to confirmed appointments. Despite monetary incentives and personal support, some participants were not communicative for weeks. In addition, there were complications with scheduled medical transportation for some families. Follow up outcomes were measured 6 weeks after each subject's final appointment. For data analysis, observations were made regarding the collected data, though due to the small sample size we did not calculate statistical significance. Feasibility of the program was examined during all aspects of participation.

Adherence, viral load, and behavioral measures

As illustrated in (Table 4) using the Russell et al. algorithm [40], participants from both intervention groups Group a (alarm signals off) and Group B (alarm signals on) had improved medication adherence during the study. Although all participants showed some improvement, Group A participants demonstrated higher medication adherence (mean 40.1) percentages compared to Group B (34.7).

Group A showed a significant increase in CD4 number (Table 5) compared to Group B's decrease over the course of the study ($p<0.05$). One participant passed away during the study due to causes unrelated to study procedures but due to medication non adherence. When the participant who died is excluded from the data analysis, the remainder of the subjects had increased CD4 count means, increased CD4 percentage means, as well as decreased viral loads at the end of the study.

Discussion

The current work investigates the feasibility of using a Maya MedMinder electronic pillbox in conjunction with weekly motivational interviewing strategies to increase medication adherence in a population of adolescents with HIV infection with documented patterns of non adherence with their medications. The difficulty in recruitment and retention of this population illustrates challenges for the clinician to engage and intervene with patient's non adherent to HIV medications. Barriers include family challenges, psychosocial concerns, finances, denial, comorbid mental health concerns, secrecy associated with the illness as well as other personal factors. Goals are to always overcome barriers to non adherence while also conveying respect and joining with the patient. It was anticipated that these families would welcome additional supports to overcome a significant hurdle for maintaining health. There was the recognition that recruitment and retention was most successful when the clinic team endorsed support of the study and the family appeared to trust the study team members. Patients who were able to comply with more frequent follow-up and provide regular attention to their day-to-day adherence with medication had more success in improving their overall medication adherence.

In this study, the control group and intervention group's opinion and adherence aspects and procedures were tested for feasibility, consistency, and acceptability and there was self-reported tolerance of all procedures. Both intervention groups used a MedMinder (Group A with signals off and Group B with signals on) to measure the opening of the pill container. Participant experiences throughout the study were varied. The protocol worked best when participants arrived to scheduled appointments and participated in the regularly scheduled motivational interviewing phone calls. Behavioral questionnaires did not predict success in improving CD4 counts, CD4 percentages or viral load, but the higher the motivational enhancement Stage of Change was to maintenance level, the more likely the behavior changes led to improved adherence scores.

Motivational enhancement approaches can support those adolescents with non adherence to HIV medication use and enhance motivation to change. The Pre-contemplation stagea"1" on the Stages of Change indicates the individual has not begun to think about change as an option and a "2"the Contemplation stage on the Stages of Change indicates recognition of the problem with ambivalence about change. The Determination stage "3" on the Stages of Change indicates the individual has decided to change their behavior, but has not actually made any changes. None of the subjects started above a 3) determination stages. The participant with 4) Action stage made a change in behavior but was not yet comfortable with the change, or 5) Maintenance stage, indicating behavior had changed and requires less conscious effort, on the Stages of Change. Subjects who transitioned to the 4) Action or 5) Maintenance stages had higher CD4 percentages midway through the study than subjects who rated at the 1) Pre-contemplation or 2) Contemplation stages. Subjects who were ranked in the 4) Action or 5) Maintenance stage on the Stages of Change had much lower viral loads than those verbalized scores consistent withthe1) Pre-contemplation, 2) Contemplation, or 3) Determination stages.

When the participant who died is excluded from the data analysis, all subjects that completed the protocol had increased CD4 count means, increased CD4 percentage means, as well as decreased viral loads at the end of the study.

The most significant outcome of improved adherence came from observations of Stages of Change attitudes being at 4) Action or 5) Maintenance level. If the participant was able to verbalize the discrepancy between behavior and desired result of improved biologic markers of CD4 count and viral load then this led to the most favorable outcomes. This project was consistent with research that has demonstrated that MI is successful in motivating patients to change across a variety of problem domains, including adherence to prescribed treatment and HIV risk reduction [43]. A study examining group MI for HIV infected women found those with higher group attendance demonstrated better medication adherence outcomes [44]. Our findings were similar in that active engagement is recognized as being helpful in promoting adherence and verbal commitment to an action plan led to the most favorable outcomes.

The MedMinder technology allowed for this aspect of the research to be conducted. The use of technology for this protocol had distinct advantages and disadvantages. It was evident that knowing a provider was "watching" daily adherence (Group A) was enough for some patients to improve their adherence. Given the small size of the study, it is not clear if the alarm chime reminders (Group B) were useful as there was less improvement noted with this group. One participant verbalized that she was very annoyed with these sounds and with time really came to resent hearing it. The technology also provided disadvantages, as it was not always functional in rural communities where cellular service was minimal and there was cellular signal interference. In these situations, the MedMinder was not able to accurately transfer adherence data. This led to frequent texting

patients often to determine time of dosages and this may not have been reliable. A phone call to one participant found the grandmother was using the iPhone that was provided for the study participant.

This feasibility project provided a chance to develop consistent practices to enhance data integrity and protection of human subjects including refinement of source documentation, informed consent procedures, data collection tools, regulatory reporting procedures, and monitoring/oversight procedures. Although the study was small and the degree of success expected was not realized, the feasibility of the procedures was established. Even when advanced technology is not available, MI strategies including being empathetic, differentiating between the patient's goals and the desired change in behavior, avoiding arguments, working with any resistance instead of against it, and being supportive and optimistic that change is possible [15] can be useful. This small study highlights that technological tools and motivational enhancement strategies in teens and young adults who are non-adherent to HIV medication regimens can be useful approaches to use to improve health outcomes.

Limitations

A potential problem of any pilot study is recruitment of eligible participants, and results were disappointing for this pilot, which is a reflection that often those with non-adherence have other proprieties rather than promoting positive health care maintenance. The goal of recruiting 20 participants was not met and this may be due to the secrecy or embarrassment associated with the illness. A potential issue may be subject "technophobia". However, the majority of teenagers and adults, irrespective of ethnicity or SES status, own or have operated a cell phone. The only requirement to operate the Maya MedMinder device is to open the pill container and have the transmitter plugged into an 110V wall outlet. Overall, the current methodology was successful with adolescents; however the protocol might be more effective in a different chronic illness with less stigma and secrecy. This is a small study that illustrated important challenges and potential solutions for working with youth or adults with a history of HIV medication non adherence feasibility.

Acknowledgments

This study was supported by the South Carolina Clinical & Translational Research Institute (SCTR) at the Medical University of South Carolina (MUSC) grant number UL1RR029882, by the MUSC Office of Biomedical Informatics Services grant NIH/NCATS UL1TR000062. The MUSC SCTR is supported by the National Institutes of Health (NIH) Clinical and Translational Science Award (CTSA) program, grant UL1TR00062 and the CTSA program is led by NIH's National Center for Advancing Translational Sciences (NCATS). Study data were collected and managed using RED Cap electronic data capture tools hosted at the Medical University of South Carolina, grant UL1 TR001450. Special thanks to the team peer advocate.

SCTR retreat related novel methods pilot project - using technology to improve adherence to pediatric HIV medications

1. Project Title/s and each Project Begin/End Dates.

   Using Technology to Improve Adherence to Pediatric HIV Medications; 10/10/2011-10/10/2012.

2. Funding Mechanism (i.e., pilot award, KL2 award, and/or Community Engaged Scholars).

   SCTR Retreat Related Novel Methods Pilot Project.

   Grant Number: 1204 UL1RR029882.

References

1. Young B. The Importance of Retention in HIV Care. Medscape 2014.
2. Gifford AL, Bormann JE, Shively MJ, Wright BC, Richman DD, Bozzette SA. Predictors of self-reported adherence and plasma HIV concentrations in patients on multidrug antiretroviral regimens. J Acquir Immune Defic Syndr. 2000; 23: 386-395.
3. Viswanathan S, Justice AC, Alexander GC, Brown TT, Gandhi NR, McNicholl IR, et al. Adherence and HIV RNA Suppression in the Current Era of Highly Active Antiretroviral Therapy. J Acquir Immune Defic Syndr. 2015; 69: 493-498.
4. Brogly S, Williams P, Seage GR 3rd, Oleske JM, Van Dyke R, McIntosh K. Antiretroviral treatment in pediatric HIV infection in the United Stastes: from clinical trials to clinical practice. JAMA. 2005; 293: 2213-2220.
5. Paris D, Ledergerber B, Weber R, Jost J, Flepp M, Opravil M, et al. Incidence and predictors of virologic failure of antiretroviral triple-drug therapy in a community-based cohort. AIDS Res Hum Retroviruses. 1999; 15: 1631-1638.
6. Kim SH, Gerver SM, Fidler S, Ward H. Adherence to antiretroviral therapy in adolescents living with HIV: systematic review and meta-analysis. AIDS. 2014; 28: 1945-1956.
7. UNICEF Data: HIV/AIDS. Turning the tide against AIDS will require more concentrated focus on adolescents and young people. 2017.
8. South Carolina Department of Health and Environmental Control. Diagnoses of HIV Infection and AIDS in the United States and Dependent Areas, 2013. HIV Surveillance Report. 2013; 26: Tables 23 and 25.
9. South Carolina Department of Health and Environmental Control. Diagnoses of HIV Infection and AIDS in the United States and Dependent Areas, 2014. HIV Surveillance Report. 2014; 26: Table 27.
10. South Carolina Department of Health and Environmental Control. HIV Surveillance Report. 2015; Table 10.
11. Hudelson C, Cluver L. Factors associated with adherence to antiretroviral therapy among adolescents living with HIV/AIDS in low- and middle-income countries: a systematic review. AIDS Care. 2015; 27: 805-816.
12. Hanghøj S, Boisen KA. Self-reported barriers to medication adherence among chronically ill adolescents: a systematic review. J Adolesc Health. 2014; 54: 121-138.
13. Murphy DA, Sarr M, Durako SJ, Moscicki AB, Wilson CM, Muenz LR. Barriers to HAART adherence among human immunodeficiency virus-infected adolescents. Arch Pediatr Adolesc Med. 2003; 157: 249-255.
14. Dieckhaus KD, Odesina V. Outcomes of a multifaceted medication adherence intervention for HIV-positive patients. AIDS Patient Care and STDS. 2007; 21: 81-91.
15. Rollnick S, Miller WR, Butler CC. Motivational Interviewing in Health Care. The Guilford Press. New York, NY, USA. 2008.
16. Moyers TB, Miller WR, Hendrickson SML. How does motivational interviewing work? Therapist interpersonal skill predicts client involvement within motivational interviewing sessions. J Consult Clin Psychol. 2005; 73: 590-598.
17. Amrhein PC, Miller WR, Yahne CE, Palmer M, Fulcher L. Client commitment language during motivational interviewing predicts drug use outcomes. J Consult Clin Psychol. 2003; 71: 862-878.
18. Naar-King S, Suarez M. Motivational Interviewing with Adolescents and Youth Adults. The Guilford Press. New York, NY, USA. 2011.

19. Pop-Eleches C, Thirumurthy H, Habyarimana JP, Zivin JG, Goldstein MP, de Walque D, et al. Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders. AIDS. 2011; 25: 825-834.

20. Naar-King S, Parsons JT, Murphy DA, Chen X, Harris DR, Belzer ME. Improving health outcomes for youth living with the human immunodeficiency virus: a multisite randomized trial of a motivational intervention targeting multiple risk behaviors. Arch Pediatr Adolesc Med. 2009; 163: 1092-1098.

21. Naar-King S, Parsons JT, Murphy D, Kolmodin K, Harris DR. A multisite randomized trial of a motivational intervention targeting multiple risks in youth living with HIV: initial effects on motivation, self-efficacy, and depression. J Adolesc Health. 2010; 46: 422-428.

22. Naar-King S, Outlaw AY, Sarr M, Parsons JT, Belzer M, Macdonell K, et al. Motivational Enhancement System for Adherence (MESA): pilot randomized trial of a brief computer-delivered prevention intervention for youth initiating antiretroviral treatment. J Pediatr Psychol. 2013; 38: 638-648.

23. Naar-King S, Wright K, Parsons JT, Frey M, Templin T, Lam P, et al. Healthy choices: motivational enhancement therapy for health risk behaviors in HIV-positive youth. AIDS Educ Prev. 2006; 18: 1-11.

24. Lavoie KL, Moullec G, Lemiere C, Blais L, Labrecque M, Beauchesne MF, et al. Efficacy of brief motivational interviewing to improve adherence to inhaled corticosteroids among adult asthmatics: results from a randomized controlled pilot feasibility trial. Patient Prefer Adherence. 2014; 8: 1555-1569.

25. Golin CE, Earp J, Tien HC, Stewart P, Porter C, Howie L. A 2-arm, randomized, controlled trial of a motivational interviewing-based intervention to improve adherence to antiretroviral therapy (ART) among patients failing or initiating ART. J Acquir Immune Defic Syndr. 2006; 42: 42-51.

26. Puccio JA, Belzer M, Olson J, Martinez M, Salata C, Tucker D, et al. The use of cell phone reminder calls for assisting HIV-infected adolescents and young adults to adhere to highly active antiretroviral therapy: a pilot study. AIDS Patient Care STDS. 2006; 20: 438-444.

27. Lester RT, Ritvo P, Mills EJ, Kariri A, Karanja S, Chung MH, et al. Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. The Lancet. 376: 1838-1845.

28. Mohr DC, Ho J, Duffecy J, Reifler D, Sokol L, Burns MN, et al. Effect of telephone-administered vs face-to-face cognitive behavioral therapy on adherence to therapy and depression outcomes among primary care patients: a randomized trial. JAMA. 2012; 307: 2278-2285.

29. Knight JR. Adolescent substance use: Screening, assessment, and intervention. Contemporary Pediatrics-Montvale. 1997; 14: 45-73.

30. Prochaska JO, DiClemente CC. Transtheoretical therapy: Toward a more integrative model of change. Psychotherapy. 1982; 19: 276-288.

31. Bangsberg DR, Hecht FM, Charlebois ED, Chesney M, Moss A. Comparing Objective Measures of Adherence to HIV Antiretroviral Therapy: Electronic Medication Monitors and Unannounced Pill Counts. AIDS and Behavior. 2001; 5: 275-281.

32. Demonceau J, Ruppar T, Kristanto P, Hughes DA, Fargher E, Kardas P, et al. Identification and assessment of adherence-enhancing interventions in studies assessing medication adherence through electronically compiled drug dosing histories: a systematic literature review and meta-analysis. Drugs. 2013; 73: 545-562.

33. Krishnan A, Ferro EG, Weikum D, Vagenas P, Lama JR, Sanchez J, et al. Communication technology use and mHealth acceptance among HIV-infected men who have sex with men in Peru: implications for HIV prevention and treatment. AIDS Care. 2015; 27: 273-282.

34. Perera AI, Thomas MG, Moore JO, Faasse K, Petrie KJ. Effect of a smartphone application incorporating personalized health-related imagery on adherence to antiretroviral therapy: a randomized clinical trial. AIDS Patient Care STDS. 2014; 28: 579-586.

35. Thurston IB, Bogart LM, Wachman M, Closson EF, Skeer MR, Mimiaga MJ. Adaptation of an HIV Medication Adherence Intervention for Adolescents and Young Adults. Cogn Behav Pract. 2014; 21: 191-205.

36. Tufts KA, Johnson KF, Shepherd JG, Lee JY, Bait Ajzoon MS, Mahan LB, et al. Novel interventions for HIV self-management in African American women: a systematic review of mHealth interventions. J Assoc Nurses AIDS Care. 2015; 26: 139-150.

37. Ofmmayo NO. Telephone reminders fail to improve adherence to HIV medication regimens. Nursing Standard. 2014; 29: 16.

38. Harrison P. Text Reminders Improve Adherence to Antiretroviral Therapy. Medscape. 2014.

39. Martin S, Elliott-DeSorbo DK, Calabrese S, Wolters PL, Roby G, Brennan T, et al. A comparison of adherence assessment methods utilized in the United States: perspectives of researchers, HIV-infected children, and their caregivers. AIDS Patient Care STDS. 2009; 23: 593-601.

40. Russell CL, Conn VS, Ashbaugh C, Madsen R, Hayes K, Ross G. Medication adherence patterns in adult renal transplant recipients. Res Nurs Health. 2006; 29: 521-532.

41. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009; 42: 377-381.

42. Russell C, Conn V, Ashbaugh C, Madsen R, Wakefield M, Webb A, et al. Taking immunosuppressive medications effectively (TIMELink): a pilot randomized controlled trial in adult kidney transplant recipients. Clin Transplant. 2011; 25: 864-870.

43. Hettema J, Steele J, Miller WR. Motivational interviewing. Annu Rev Clin Psychol. 2005; 1: 91-111.

44. Holstad MM, DiIorio C, Kelley ME, Resnicow K, Sharma S. Group motivational interviewing to promote adherence to antiretroviral medications and risk reduction behaviors in HIV infected women. AIDS Behav. 2011; 15: 885-896.