Usefulness of Cellular Text Messaging for Improving Adherence Among Adolescents and Young Adults with Systemic Lupus Erythematosus

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ABSTRACT. ***Objective.*** In a cohort of 70 patients with childhood-onset systemic lupus erythematosus (cSLE): to determine the baseline adherence to medications and visits; to investigate the effects of cellular text messaging reminders (CTMR) on adherence to clinic visits; and to study the influence of CTMR on adherence to use of hydroxychloroquine (HCQ).

Methods. CTMR were sent to 70 patients prior to clinic visits for 14 months. A subgroup of patients were evaluated for medication adherence to HCQ: 19 patients receiving CTMR prior to each scheduled HCQ dose were compared to 22 patients randomized to standard of care education about HCQ. Visit adherence was measured using administrative databases. Pharmacy refill information, self-report of adherence, and HCQ blood levels were utilized to monitor medication adherence to HCQ. Sufficient adherence to visits or HCQ was defined as estimates > 80%. Disease activity was primarily monitored with the Systemic Lupus Erythematosus Disease Activity Index.

Results. At baseline, 32% of patients were sufficiently adherent to HCQ, and 81% to clinic visits. Visit adherence improved significantly by > 80% among those who were nonadherent to clinic visits at the baseline CTMR ($p = 0.01$). CTMR did not influence adherence to HCQ over time.

Conclusion. Patients with cSLE were only modestly adherent to HCQ and clinic visits. CTMR may be effective for improving visit adherence among adolescents and young adults with cSLE, but it does not improve adherence to HCQ. (First Release Nov 15 2011; J Rheumatol 2012;39:174–9; doi:10.3899/jrheum.110771)

Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS ADHERENCE COMPLIANCE
TEXT MESSAGING ADOLESCENTS

Adherence can be defined as the extent to which patients follow instructions given by their healthcare providers, especially with respect to intake of medication and clinic visits[1]. Difficulties with adherence are a ubiquitous problem in management of chronic diseases[1]. Nonadherence to medical recommendations is associated with poor disease control and increased mortality in patients with systemic lupus erythematosus (SLE)[2]. Children and adolescents with SLE appear to be adherent to medications 49%–61% of the time[2].

For this reason, effective interventions to improve adherence are urgently needed. Information and communication technology, particularly cellular telephones, continues to advance and is widely used by teenagers and young adults. During the first quarter of 2009, Nielsen ratings reported that teens were texting an average of 3339 messages per

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Supported by NIAMS P60 AR47784 and a Place Outcomes Award from the Anderson Center at Cincinnati Children's Hospital Medical Center.

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Accepted for publication August 19, 2011.

month[3]. Thus, cellular text messaging appears to be ideal for communicating with teenagers and young adults, as it is not only very popular but also portable. Further, it provides instant gratification with rapid, affordable distribution of information.

To our knowledge, promotion of adherence by text messaging has not been tested in adolescents and young adults with childhood-onset SLE (cSLE). The goals of our study were (1) to determine the adherence to hydroxychloroquine (HCQ) medication use and to clinic followup visits; (2) to investigate the effects of cellular text messaging reminders (CTMR) on adherence to clinic visits; and (3) to study the influence of CTMR on adherence to HCQ use in a cohort of adolescents and young adults with cSLE. We hypothesized that visit and medication adherence as well as disease outcomes would improve with the use of CTMR in patients with cSLE.

MATERIALS AND METHODS

Patient population. *Visit adherence population*. With approval of the institutional review board, all patients diagnosed with cSLE[4] and followed in a pediatric rheumatology clinic were identified using a lupus registry. For inclusion, patients had to be between the ages of 13 and 25 years and have unlimited access to cellular text messaging.

Medication adherence population. A subset of patients who were part of the visit adherence population were recruited for participation in a substudy to assess the benefits of CTMR on adherence to medication. To participate in the medication adherence substudy, patients had to be at least 15 years of age, be treated with HCQ for cSLE, and have a minimum disease duration of 6 months. Younger patients were excluded because they were unlikely to be responsible for taking their medications on their own. Patients with active neuropsychiatric SLE symptoms were excluded, as were those with other chronic diseases (e.g., diabetes mellitus) that might influence medication use.

Study questionnaires and disease measures. Patient demographic data including age, sex, race, insurance status, estimated socioeconomic status, and distance of residence to the medical center were noted. The latter was measured using Google Maps directions tool for each patient's postal code in relationship to the hospital address. Estimated median family incomes were identified using Geocoding (Federal Financial Institutions Examination Council, Fairfax, VA, USA; Website: http://www.ffiec.gov/Geocode/default.aspx) to provide an overall economic status for each patient. Information regarding disease damage was gathered at the time of each medication adherence visit and was measured by the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI)[5], the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), and the physician assessment of disease activity (by visual analog scale; range 0–10, 0 = inactive disease, 10 = very active disease)[6]. The number of emergency room (ER) visits and the number of hospital admissions were monitored among patients participating in clinic visit adherence.

Study interventions. Cellular phone number and cellular service carrier were obtained from patients at the beginning of the study and monitored periodically for changes throughout the intervention period. CTMR were sent over a free e-mail network system (e-mail to text).

Visit adherence intervention. A CTMR to the patient's cellular phone was sent 7 days, 3 days, and 1 day prior to each scheduled followup clinic appointment. CTMR were individualized for each patient by including the scheduled time of the upcoming clinic appointment (Table 1). Additionally, CTMR were sent in the event that a patient failed to schedule a followup appointment within the first 2–3 weeks after the preceding clinic visit. For each patient, clinic attendance data were compared with his/her visit adherence between January 1, 2006, and June 30, 2008, prior to the CTMR intervention, as well as his/her visit adherence after the CTMR was discontinued from November 15, 2009, through June 15, 2010.

Medication adherence intervention. Patients participating in the medication adherence substudy were randomized 1:1 to either standard of care (SOC group) or the CTMR intervention (CTMR group). Participants were followed for up to 6 study visits that occurred during regular clinic visits 2–4 months apart for up to 14 months. The SOC group received printed information about the benefits and side effects of HCQ as per current standards of clinical care. The CTMR group received a standardized daily CTMR for HCQ intake as prescribed (e.g., once or twice per day) in addition to the printed information sheet that was given to the SOC group. A CTMR was sent to all patients at a set time of day (e.g., morning or evening), according to self-report of HCQ intake (Table 1). Changes to dosing of HCQ were noted following each visit, and CTMR were altered accordingly.

Measurement of adherence. *Visit adherence*. Using electronic scheduling databases and information prospectively recorded in the electronic medical record, the following visit-specific information was collected for each patient in the visit adherence cohort: total number of rheumatology clinic visits attended, total number of "no-shows" (i.e., clinic appointment scheduled but never attended or canceled), total number of cancellations (i.e., clinic appointment scheduled and canceled by the patient in advance of the day of visit), and the suggested time interval between clinic visits as per the treating pediatric rheumatologist.

Adherence to clinic visits was measured as the percentage of clinic visits that occurred "on time" (i.e., within the timeframe recommended by healthcare providers). Visit attendance was deemed "on-time" when patients were seen in the rheumatology clinic within 1 week of a 1-month recommended followup time period, 2 weeks within a 2-month followup, 3 weeks for a 3-month followup, etc. Acceptable clinic visit attendance rates were defined as ≥ 80% adherence as per the healthcare provider visit recommendations[7].

Medication adherence. Due to its beneficial effects, most patients participating in the lupus registry are treated with HCQ for cSLE[8]. The half-life of HCQ is around 40 days, and drug levels can be measured in the blood, reflecting longer-term exposure to HCQ[9]. As there is no criterion standard for measuring medication adherence in a clinical setting, adherence to HCQ use was evaluated using 3 different approaches: (1) patient's self-report on the validated Medication Adherence Self-Report Inventory (MASRI)[10] at each study visit; (2) whole-blood levels of HCQ were measured by a commercial laboratory (NMS Labs Inc., Willow Grove, PA, USA) with methods as described[11]; and (3) pharmacy refill adherence, defined as the percentage of the number of HCQ doses dispensed (numerator) and the number of doses prescribed (denominator) for the period of time between study visits and pharmacy refill dates, with pharmacy refill information serving as primary measure of medication adherence[7]. These approaches were measured at baseline and at all followup visits (about every 2–4 months).

Patients with HCQ adherence > 80% were considered sufficiently adherent, while those with < 80% adherence were considered nonadherent to HCQ as per pharmacy refill information[7]. HCQ adherence was measured starting 9 months prior to CTMR and continued until 7 months after the CTMR for HCQ were discontinued.

Statistical analysis. Descriptive analysis included means and SD for numerical data and percentages for categorical data. Associations between patient demographics and visit adherence were determined in univariate analysis to identify confounders of nonadherence using contingency tables or logistic regression analysis for categorical data.

The effects of CTMR on visit adherence were assessed by comparing patient adherence behavior over time: preintervention (pre-CTMR), during intervention (CTMR period), and postintervention (post-CTMR). Similarly, HCQ adherence was assessed over time, with consideration of whether the patient received CTMR.

Table 1. Examples of text message reminders.

Visit Adherence	Days Before Scheduled Visit	Message
	7	"Don't 4get ur rheumatology appt in 1 wk! Call 513-636-4676 w/?s"
	3	"CU on Wed @1pm 4 ur rheumatology appt! Call 513-636-4676 w/?s"
	1	"CU 2moro @1pm in rheumatology!"

Medication Adherence	Dosing Schedule	Message	Time Sent
	Once daily	"Take ur HCQ now"	8 am
	Twice daily	"It's time 4ur meds"	8 am and 8 pm

Paired t tests (for visit adherence), 2-sample t tests with unequal variances (for HCQ adherence), and mixed models were carried out to assess the effects of CTMR on visit and HCQ, respectively. Effect sizes (Cohen's d) were calculated. By convention, t test effect size (d) values of 0.2, 0.5, and 0.8 are considered small, medium, and large, respectively. P values < 0.05 were considered statistically significant.

RESULTS

Demographics. Among the 108 patients in the lupus registry who were actively treated at the rheumatology clinic, 79 were eligible for study participation and agreed to receive CTMR for clinic visits. Excluded from the analysis were 9 (11%) patients due to loss of followup or inconsistent access to cellular text messaging. Among the remaining 70 participants included in the analysis, 65 (93%) were female and 36 (52%) were African American (Table 2).

The average age in the CTMR and SOC groups was similar, 18.6 (SD 2.5) years. At baseline, both groups were comparable with respect to disease activity (SLEDAI mean 5.5, SD 5.9), disease damage (SDI mean 0.8, SD 1.6), physician-rated disease activity, patient-reported well-being, and daily prednisone dose. In both groups, 80% were prescribed once-daily HCQ dosing, while the remaining patients were prescribed twice-daily intake.

Table 2. Visit adherence, patient demographics (n = 70).

Variable	Mean (SD)	No. Patients (%)
Female		65 (93)
Male		5 (7)
Age at the time of the study, yrs	18.4 (3.3)	
Age at diagnosis, yrs	13.9 (2.9)	
Disease duration, yrs	4.5 (3.1)	
Race		
White		33 (47)
Black		36 (51)
Other		1 (2)
Insurance status		
Public insurance (Medicaid, Medicare)		18 (27)
Private insurance		49 (73)
Uninsured/self-payer		—
Distance from clinic, miles		
< 10		23 (33)
10–20		18 (26)
21–40		12 (17)
41–60		9 (13)
> 60		8 (11)
Estimated median income, $	60,677 (22,532)	

At baseline, patients in the study were seen in the rheumatology clinic an average of 6.5 (SD 2) times per year, and about 85% of visits occurred within the physician-recommended timeframe, while 14% of all scheduled visits were no-shows, and rescheduling (visit cancellations) occurred for 18% of the clinic visits.

Nineteen percent (13/70) of patients were nonadherent to clinic visits at baseline. Among them, there was a significant improvement of visit adherence during the CTMR intervention (p = 0.01), with only 10% of patients remaining nonadherent. However, post-CTMR, adherence rates declined (p = 0.02), but rates remained higher compared to baseline (p = 0.005; Figure 1).

As expected, those patients who were seen more frequently over time generally had more no-shows, had worse SLEDAI scores, had more ER visits and more frequent hospital admissions, and were treated with a higher number of medications. In contrast, patients who were adherent to visits had overall lower SLEDAI scores across all time periods. Among patients who were nonadherent, rescheduling (cancellation) rates also increased greatly during the CTMR intervention (effect size, d = 0.78).

The number of no-shows to clinic correlated with a greater number of ER visits across all time periods and similarly for hospital admissions. Lower estimated family median income was associated with a greater number of visit cancellations during the CTMR intervention (p = 0.04), a higher number of hospital admissions at followup (p = 0.01), and higher mean SLEDAI scores (p = 0.0008). There was no significant change in disease outcomes (ER visits, hospital admissions) over time among the visit-adherence group.

Risk factors of visit nonadherence. In a subanalysis assessing risk factors for adherence, certain demographic factors at baseline were associated with better adherence to clinic visits, including white race (p = 0.04), non-Medicaid status (p = 0.03), and greater distance from hospital (p = 0.008).

Adherence to HCQ. Among the 70 visit-adherence participants, 41 participated in the HCQ adherence study — 19 were randomized to receive CTMR and 22 received SOC. Of the subgroup, 38 (93%) were female and 26 (63%) were

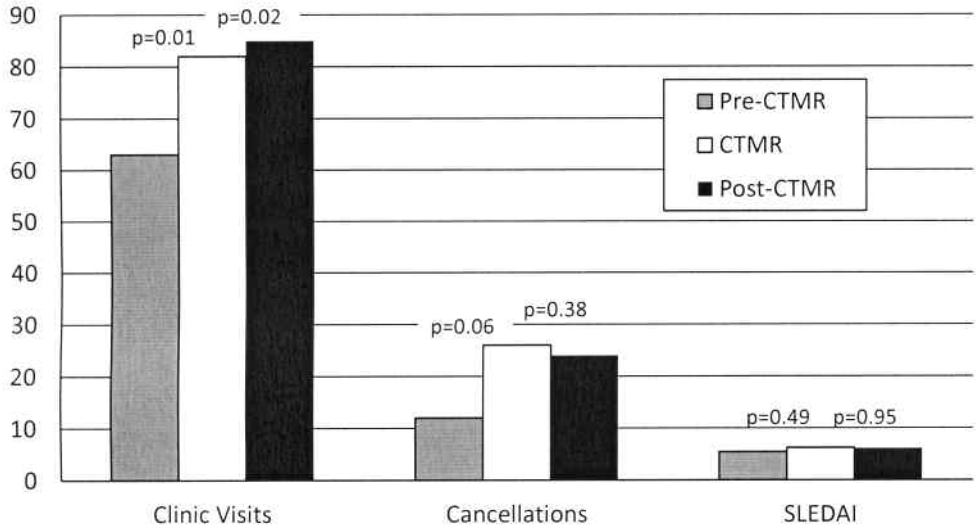

Figure 1. Percentage of clinic visit adherence, cancellation rates, and SLEDAI scores during the pre-CTMR, CTMR, and post-CTMR time periods (n = 70). SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; CTMR: cellular text messaging reminders.

African American (Table 3). Based on pharmacy refill information, only 32% of the patients were sufficiently adherent to HCQ at baseline. The mean HCQ adherence was 64% (SD 45%). If one accepts that blood levels of HCQ ≥ 900 ng/ml reflect adequate exposure to HCQ[9], then only 10 of 41 patients (25%) had sufficiently high levels, and 12

Table 3. Patient demographics, disease activity, and hydroxychloroquine (HCQ) medication adherence (at baseline) for the standard of care (SOC) and cellular text messaging reminder (CTMR) groups.

Variable	SOC, n = 22		CTMR, n = 19		Total No. Patients, n = 41	
	Mean (SD)	N (% of total)	Mean (SD)	N (% of total)	Mean (SD)	N (% of total)
Age at the time of the study, yrs	18.6 (2.6)		18.7 (2.5)		18.6 (2.5)	
Weight, kg	75 (18.2)		71 (18.7)		73 (18.4)	
Medications						
HCQ, mg/day	327 (93)		324 (75)		326 (84)	
HCQ, mg/kg/day	4.6 (1.6)		4.8 (1.2)		4.7 (1.4)	
HCQ dose frequency						
Every other day		1 (4)		1 (5)		2 (5)
1 time a day		18 (82)		15 (79)		23 (80)
2 times a day		3 (14)		3 (16)		6 (15)
Prednisone, mg/day	14 (17)		15 (19)		14 (17.5)	
Pulse methylprednisolone		—		3 (16)		3 (7)
Nonsteroidal antiinflammatory drugs		8 (36)		10 (53)		18 (44)
Immunosuppressive medications*		15 (68)		14 (74)		29 (71)
Antihypertensive medications		12 (55)		8 (42)		20 (49)
Disease activity indices						
Disease activity (SLEDAI)	3.7 (4.0)		7.9 (7.1)		5.5 (5.9)	
Disease damage (SDI)	0.8 (1.6)		0.7 (1.7)		0.8 (1.6)	
Physician global assessment of disease activity**	1.9 (1.6)		2.8 (2.3)		2.3 (2.0)	
Patient well-being†	7.6 (2.0)		7.2 (1.9)		7.4 (1.9)	
Medication adherence						
MASRI	80 (21)		83 (19)		81 (20)	
Pharmacy refill data	52 (32)		64 (45)		57 (33)	
No. patients with adherence > 80%		6 (27)		7 (37)		13 (32)
HCQ levels†† ($p < 0.03$)	0.46 (0.55)		0.64 (0.45)		0.54 (0.51)	

* E.g., mycophenolate mofetil, azathioprine. SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; 0 = inactive disease. SDI: Systemic Lupus International Collaboration Clinics Damage Index; 0 = no damage. ** Visual analog scale 0 to 10; 0 = inactive disease; 10 = very active disease. † Visual analog scale 0 to 10; 0 = very poor; 10 = very well. MASRI: Medication Adherence Self-Report Inventory (0 to 100); 0 = no medication taken; 100 = all doses taken as prescribed. †† Concentration measured in blood.

patients (29%) had undetectable HCQ levels (< 0.1 ng/ml). Mean self-report of adherence rates (by MASRI) were 80% (SD 20%) among both the SOC group and the CTMR group (Table 3). Medication adherence estimates using blood levels of HCQ correlated with adherence rates as measured using pharmacy refill information (Pearson correlation coefficient $r = 0.50$, $p < 0.0001$) and self-reported adherence ($r = 0.47$, $p < 0.0001$).

Patients in the CTMR group remained in the study for an average of 1 year (SD 5 months). During this period, CTMR had only a small effect ($d < 0.25$) on the adherence to HCQ, irrespective of the measure of adherence used (MASRI, pharmacy refill, HCQ blood levels). Further, there was no difference between patients who received once-daily versus twice-daily HCQ dosing/CTMR. Disease activity did not improve in the CTMR group. There was no Hawthorne effect[9]; i.e., the SOC group also had stable HCQ adherence during the study period.

DISCUSSION

CTMR is a practical and potentially ideal form of communication with adolescents and young adults with cSLE who regularly use cellular phones and text messaging. Our study suggests that CTMR can improve clinic visit attendance, but appears not to have an influence on adherence to medication (HCQ).

While previous studies have shown cellular phone reminders to be effective in improving diabetic blood sugar control[12], smoking cessation[13], and asthma symptoms[14], none have attempted to improve adherence in patients with cSLE. In our study, more patients were adherent to clinic visits at baseline than expected. The use of CTMR had a positive effect on clinic visit adherence among our adolescents with cSLE. Our results were in accord with findings of improved clinic attendance following CTMR in a Chinese primary care clinic[15] and a British ophthalmology clinic[16].

The consequences of nonattendance to scheduled clinic visits or no-shows have a large effect on both patients and the healthcare system[17]. Suboptimal use of both clinic space and personnel results in financial losses, and waiting times for patients to get a clinic appointment are longer due to "no-shows" blocking other patients from scheduling visits. Although cancellations of clinic appointments are not ideal, they offer the opportunity to use the newly vacant clinic times for sick visits and patients in line for a clinic appointment. In our study, cancellation rates appeared to be increasing during the CTMR time period, indicating the potential effectiveness of CTMR to remind families about their appointments and to take appropriate action if they could not attend.

In contrast to visit adherence, rates of adequate medication adherence were poor in our study, but were similar to findings of our previous study[2]. Nearly one-third of our patients had undetectable blood levels of HCQ. As seen in other pediatric chronic illnesses (inflammatory bowel disease, oncology)[16,17], patients with cSLE are historically poorly adherent to medications[2]. Our study suggests poor adherence in more than two-thirds of our cohort based upon HCQ blood levels, self-reports, and pharmacy refill data. While similar daily text messaging reminder studies of liver transplant medication use and sunscreen have reported CTMR to be effective in improving medication adherence[2,18,19], our study indicated otherwise. Our data do not support any consistent effect of CTMR on HCQ adherence. Exploratory analysis also did not show that the effects of CTMR changed over time, nor were they related to any of the baseline characteristics. We hypothesized that the effects of HCQ may not be instantaneous enough to entice teenagers to take the medication regularly. And differently from others' results, another reason why CTMR appeared to have no effect on medication adherence may be that others used somewhat different methods of providing text messaging than we did, allowing for more patient-tailored message delivery as well as varying the prompts/messages to maintain interest. However, our results were similar to the limited efficacy reported for text messaging for oral contraceptive use among adolescent girls[20,21]. We speculate that over time the constant reminders became repetitive, and as the novelty wore off, they were eventually ignored by the recipients.

There was no apparent effect on disease outcomes among visit adherence participants in our study. The number of unplanned ER visits and hospitalizations did not change significantly, nor did the mean SLEDAI scores between groups. There were indications that those who were seen more frequently and who had a greater number of no-shows tended to have worse disease activity and required more ER visits and/or hospitalizations. These findings were not unexpected, as typically those with active disease are monitored more frequently. However, generally, the relatively small population, short followup period, and lack of power may have contributed to the lack of observed changes.

While our patients informally provided positive feedback regarding CTMR for clinic visits and initially with medication reminders, there were limitations and challenges to sending CTMR. CTMR did not allow the opportunity to explore barriers or provide an optimal method for addressing necessary behavior changes. An interactive dialogue could not be supported with an e-mail-to-text message format. Patterns of cellular phone use (prepay cards, multiple carriers) were varied among a few select patients. Further, our small study population and potential selection bias may have contributed to a lack of statistical power. We attempted to limit bias by randomizing patients to both SOC and CTMR groups. Additionally, confounders of inherent changes in SLE disease activity and outside economic influences could not be controlled.

Adherence to routine clinic visits and medication use is

crucial for monitoring and maintenance of chronic diseases such as cSLE. Unfortunately, poor medication adherence is a significant problem among the majority of patients with cSLE. Advances in communication technology, including cellular text messaging, are regularly used by adolescents and young adults with cSLE. CTMR, an inexpensive and rapidly receivable method of individualized communication, could be a potentially useful method of improving clinic visit adherence. In contrast, CTMR did not appear to be effective for improving medication adherence. It is possible that effects on disease outcomes may be seen with a longer, sustained CTMR intervention time period. In addition, CTMR may prove to be a cost-effective quality initiative for improving adherence and ultimately outcomes in the care of chronic conditions such as cSLE.

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