Randomized Clinical Trial to Test mHealth Interventions to Improve Adherence to a Once-daily Single-tablet Regimen in Patients with Chronic Hepatitis C Virus Infection

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Background

- Adherence to direct acting antivirals used to treat Hepatitis C Virus (HCV) infection has been found to be related to achieving sustained virologic response (SVR) [Akiyama et al. 2019, Annals of Int Med].
- Interventions to promote HCV medication adherence in challenging patient populations are needed. The HepCure toolkit is a software platform comprised of a mobile application for patients and a provider web dashboard developed to increase patient engagement in HCV treatment. To our knowledge, this is the first study in a real-world population utilizing an Internet of Things device to objectively measure HCV medication adherence
- The goal of this 3-arm randomized clinical trial was to investigate whether adherence to HCV medication is improved by the addition of E-health interventions (HepCure toolkit and medication reminders).

Methods

- Seventy-one patients initiating single-tablet treatment were recruited at an academic hospital from two primary care and one liver specialty practice.
- Patients used AdhereTech smart wireless pill bottles, which provided real-time data on bottle opening using cellular technology. 33 patients received no intervention (Arm 1). In the second phase, 38 patients were randomized to one of two interventions [Arm 2 -HepCure toolkit alone (n=19) or Arm 3 - HepCure toolkit + AdhereTech medication reminders (n=19)].
- Adherence was examined over the 84 days immediately following treatment initiation in terms of Dosing Adherence (DA = percentage of days that bottle was opened at least once) and Window Adherence (WA = percentage of days that bottle was opened +/- 4 hours from the scheduled dosing time)'.

Results

- 68 of the 71 patients (Arm 1= 32; Arm 2 = 18; Arm 3 =18) had usable adherence data (1 broke the bottle, 1 never began treatment, 1 began treatment with a pre-packaged medication). The baseline characteristics are presented in Table 1.
- 32 patients (47.1%) were on ledipasvir/sofosbuvir (with 1 also prescribed ribavirin), 35 (51.5%) were on sofosbuvir/ velpatasvir, and 1 (1.5%) was on sofosbuvir/ velpatasvir/ voxilaprevir; 66 (97.1%) were prescribed for 12 weeks, and 2 (2.9%) for 24 weeks.
- The adherence and treatment outcomes are presented in Table 2. Mean DA was 92.3% (±11.8%) and the mean WA was 80.6% (±26.0). 56 patients achieved SVR12; 2 relapsed (both in Arm 1, treatment-naïve, genotype 1b, noncirrhotic) and 10 had unknown statuses due to loss to follow-up).
- There was no significant difference in DA or WA across the study arms.
- DA was significantly lower in those who were lost to follow-up as compared to those with confirmed SVR statuses (DA Means = 82.9 vs. 93.9; p=0.005); whereas WA did not significantly differ (WA Means = 67.5 vs. 82.8, p=0.085).
- The DA was above 90% and the WA above 80% in both patients who had a virological relapse.

Table 1: Subject Baseline Characteristics

Study Condition	All subjects	No intervention	HepCure toolkit	HepCure toolkit + AdhereTech reminders	P value
Number of subjects	68	32	18	18	
Age, years, mean ± SD	51.4 ± 13.3	58.4 ± 9.4	44.8 ± 14.9	45.4 ± 11.7	**<0.001**
Male, n (%)	45(66.2)	20 (62.5)	10(55.6)	15(83.3)	0.177
Race, n (%) Black White	 24 (35.3) 44 (64.7)	 16 (50.0) 16 (50.0)	 5 (27.8) 13 (72.2)	 3 (16.7) 15 (83.3)	 **0.045**
Ethnicity, n (%) Hispanic non-Hispanic	 20 (29.4) 48 (70.6)	 8 (25.0) 24 (75.0)	 3 (16.7) 15 (83.3)	 9 (50.0) 9 (50,0)	 0.068
Monthly income, USD, mean ± SD	1482 ± 1643	1317 ± 772	1925 ± 2867	1331 ± 1007	0.438
Education, years, mean ± SD	12.6 ± 2.6	12. ± 2.3	12.6 ± 2.7	12.8 ± 2.9	0.844
HCV genotype, n (%) 1 2 3 4	 36 (52.9) 12 (17.6) 18 (26.5) 2 (2.9)	 27 (84.4) 2 (6.3) 2 (6.3) 1 (3.1)	 3 (16.7) 8 (44.4) 6 (33.3) 1 (5.6)	 6 (33.3) 2 (11.1) 10 (55.6) 0 (0.0)	**<0.001**
Treatment naïve, n (%)	61 (89.7)	28 (87.5)	16 (88.9)	17 (94.4)	0.734
On Medication Assisted Treatment, n (%)	45 (66.2)	15 (46.9)	15 (83.3)	15 (83.3)	**0.006**
HIV-co-infected, n (%)	2 (2.9)	2 (6.3)	0 (0.0)	0 (0.0)	0.314

Table 2: Adherence and Treatment Outcomes

Study Condition	All subjects	No intervention	HepCure toolkit	HepCure toolkit + AdhereTech reminders	P value
Number of subjects	68	32	18	18	
Dosing Adherence, mean ± SD	92.3 ± 11.8	94.7 ± 6.4	90.4 ± 15.9	89.9 ± 14.2	0.282
Window Adherence, mean ± SD	80.6 ± 26.0	81.3 ± 26.8	76.9 ± 25.7	82.9 ± 25.9	0.775
SVR (n, %) Achieved Relapse Unknown	 56 (82.4) 2 (2.9) 10 (14.7)	 28 (87.5) 2 (6.3) 2 (6.3)	 15 (83.3) 0 (0.0) 3 (16.7)	 13 (72.2) 0 (0.0) 5 (27.8)	0.134

Conclusions

- DA and WA were quite high in all arms of the study.
- There was no indication that these mHealth interventions improved adherence in this older age sample.
- The relatively small sample size as well as baseline differences across the 3 groups limited the power of these analyses.
- Interventions to improve retention to reach SVR12 monitoring are needed and should take into account the association between lower DA and failure to return for SVR12.

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