Tuberculosis (TB) remains a major public health problem globally despite the fact that the causative organism has been known for more than 100 years, and highly effective drugs and vaccines have been available for decades [1,2]. The World Health Organization reported, a total of 1.5 million people died from TB in 2018 (including 251,000 people with HIV). Worldwide, TB is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS) [3,4]. Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat [5]. WHO estimates that there were 484,000 new cases with resistance to rifampicin – the most effective first-line drug, of which 78% had MDR-TB. Ending the TB epidemic by 2030 is among the health targets of the Sustainable Development Goals [6].

Directly Observed Therapy, Short-course (DOTS), has been the primary intervention strategy for Tuberculosis (TB) control worldwide and implemented by almost all WHO member countries [6,7].

**Abstract**

**Background:** Despite the implementation of effective preventive and therapeutic programs, the expected success in reducing and controlling tuberculosis (TB) cases, has not yet been achieved. Mobile phone text messaging (SMS) has the potential to increase medication adherence to tuberculosis.

**Purpose:** The aim of this study was to evaluate the effectiveness of Short Message Service-Based Intervention on Medication Adherence for Patients with Tuberculosis which accomplished in Masih Daneshvari hospital.

**Methods:** This comparative study, was conducted on TB patients in National Research Institute of Tuberculosis and Lung Disease, Masih Danesvari Hospital, Shahid Beheshti Medical University. According to the census method, 180 patients were entered to the study. Patients in the intervention group received SMS reminders reminding them to take their medication at specific times for 30 days beginning on the second day after discharging. We assessed adherence with the Combination of visual analog scale (10 points linear VAS), eight-item Morisky Medication Adherence Scale and Pills count. Data were analyzed by nonparametric chi square Mann-Whitney test and Kruskal-Wallis test using SPSS software. The significance level of the tests, was considered less than 0.05.

**Results:** Score of Morisky Medication Adherence Scale (MMAS) showed that there is a significant difference between the case and control groups (p=0.007). Averaged VAS score in case group was 8.50 while in control group was 8.20 but There was no significant difference between patient reports in case and control groups (p= 0.059).

**Conclusion:** In conclusion, we found that SMS reminders could be useful to combat forgetfulness and could increase patient motivation in keeping treatment.

**Keywords:** Medication Adherence; Tuberculosis; Text Message; Service-Based

**Introduction**

Tuberculosis (TB) remains a major public health problem globally despite the fact that the causative organism has been known for more than 100 years, and highly effective drugs and vaccines have been available for decades [1,2]. The World Health Organization reported, a total of 1.5 million people died from TB in 2018 (including 251,000 people with HIV). Worldwide, TB is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS) [3,4]. Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat [5]. WHO estimates that there were 484,000 new cases with resistance to rifampicin – the most effective first-line drug, of which 78% had MDR-TB. Ending the TB epidemic by 2030 is among the health targets of the Sustainable Development Goals [6].
Low level of adherence to medication is cited as one of the most important barriers to TB control [8,9]. Poor adherence to TB medication can be especially problematic because it can result in prolonged treatment, an increase in new cases, higher costs and the development of multidrug resistance. These consequences make treatment more complicated and more costly [4].

Medication adherence is defined by the World Health Organization as “the degree to which the person’s behavior corresponds with the agreed recommendations from a health care provider” [10].

Although, studies have shown that DOTS is highly effective in achieving high TB treatment adherence, DOTS can limit patient mobility and privacy, involves travel costs and may be especially difficult for patients who live far from health clinics [11,12].

Text messaging is comparatively simple to use, its use is extensive, and its cost is low for users. In addition, it is an appropriate intervention for a variety of health behavior changes [13]. Mobile phone facilitate communication between healthcare providers and patient with TB. This advantages of mobile phones bring the potential of overcoming the challenges associated with DOTS [14,15].

The aim of this study was to evaluate the effectiveness of Short Message Service-Based Intervention on Medication Adherence for Patients with Tuberculosis which accomplished in Masih Daneshvari hospital.

Methods

This was a Comparative study that was conducted at National Research Institute of Tuberculosis and Lung Disease, Masih Daneshvari Hospital, Shahid Beheshti Medical University, a hospital in Tehran, Iran. Patients admitted to the tuberculosis ward of Masih Daneshvari Hospital, who have been treated with medication for tuberculosis and are discharged in the winter of 2017, are divided to cases and control groups. Both groups were selected with equal proportions. Individual matching method was used to increase the accuracy of study and control of confounding. Assuming α: 0.05, level of confidence: 95%, power: 80% and a significant difference between the ratios of the two groups, a total of 196 patients were required for the study. Which were divided equally between the two groups of cases and control, 98 patients in case group and 98 patients in control group.

Both case and control groups received all information required for a successful post-discharge period. The important points that explained to patients with face to face method includes:

- Information on diet
- Potential warning signs and symptoms that could arise
- Why, when, and how to take the medications
- Information on side effects of medications
- Days and times of the follow-up appointments

All instructions for care at home, including medications, diet, therapy, and follow-up appointments, explained in detail to all patients and then were presented in written form to take home upon discharge. Inclusion criteria for case group included the following: agreed to participate, no communication impairment (mental, visual, auditory, or speech), patient or family member able to use mobile phone to read SMS text messages, the patient should not be infected with HIV and should not be treated with other antivirals. Those who agreed to participate were directed to a researcher who provided information about the study and obtained written consent from each patient. During the introductory interview the researcher collected patients' demographic characteristics. The researcher counts the number of pills prescribed by the doctor for the patient and teaches the patient to count the remaining pills at the end of each week.

Intervention

Patients in the intervention group received SMS reminders reminding them to take their medication at specific times for 30 days beginning on the second day after discharging and could not choose the times the reminders were sent. SMS reminders also were contained Information on diet and times of the follow-up appointments.

At the end of the each week, we conducted a phone-based survey to assess patient medication compliance and demand for and satisfaction with the “text message medication reminder service.” And also we asked the number of remaining pills. If the patient did not respond to the phone call at the scheduled time, the phone call was repeated up to three times.

Measurements

At 1 months (visit 1) after the intervention, we assessed adherence with the help of an adherence assessment checklist using several methodologies:

1. visual analog scale (10 points liner VAS)
2. Eight-items Morisky Medication Adherence Scale
3. Pills count

The VAS was a 1-10 Likert scale enhanced with 3 pictograms (a thumb pointing downwards, horizontal, and upwards) for illiterate patients (Figure 1) and was used to assess self-reported adherence by asking: “How much of your medication have you taken in the last 4 weeks: Point with the finger on the line ranging from 0 to 10 to indicate where you think you are. 0 (thumb pointing downwards) means you have taken none of the pills, 5 (thumb is in a horizontal position) means you have taken half and 10 (or thumb is pointing upwards) means you have consistently taken every single pill”.

Interventions
Medication adherence also was assessed using the MMAS-8. The scale consists of eight questions, first seven items having a dichotomous answer (yes/no) that indicates adherent or non-adherent behavior. For item 8, a patient can choose an answer on a 5-point Likert scale, expressing how often happens that a patient does not take his medications. MMAS-8 scores can range from 0 to 8 points. Cut points were used to categorize high (sum score = 8), medium (sum score 6 to <8), and low (sum score < 6) adherence based on previously established categories [16]. The validity and reliability of the instrument have been calculated and confirmed in the research of Ebadi et al. The reliability of the questionnaire was based on Cronbach's alpha coefficient of 0.72 [17].

The pill counting information was done by phone call every week, and at the end of the month, the final count was done at the time of the first visit. According to the number of remaining pills, patients were divided into three groups. Group 1 was defined as admitting to have missed ≥ 1 dose, group 2 defined to have missed ≥ 2 dose and group 3 defined to have missed ≥ 3 dose.

At 3 months after the intervention, we compared the follow-up appointments for second visit in case and control groups.

**Data Analysis**

Collected data were coded and analyzed using descriptive statistics (e.g., frequency, mean, and standard deviation) and inferential statistics (including Chi-square test, Mann-Whitney test and Kruskal-Wallis test). All analyses were performed by SPSS version 16 at a significance level of 0.05. Normal distribution of data was determined using the Kolmogorov-Smirnov test.

**Compliance with ethical standards**

All stages of the study were carried out with the approval of the research ethics committee of Shahid Beheshti University of Medical Sciences. The objectives, study steps and right to withdraw from the study at any time were explained to the individuals.

**Role of funding source**

This research was financially supported by National Research Institute of Tuberculosis and Lung Disease, Masih Daneshvari Hospital, Shahid Beheshti Medical University Tehran, Iran.

**Ethical Approval**

The study was registered on the National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Science (IR.SBMU.NRITLD.REC.1396.396).

**Informed Consent**

Verbal consent was obtained from respondents.

**Conflict of interest statement**

Authors whose names are listed above certify that they have NO affiliations with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in this manuscript.

**Authors Contributions**

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [FS], [AZ], [ShE], [HE] and [ECh]. The first draft of the manuscript was written by [SD], [FB] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

**Results**

196 patients were included in this research but in 6 patient in case group and 6 patient in control groups were excluded from the study because of Willingness to leave the study. Finally, data analysis was performed for 90 patients in each group.

**Patient characteristics**

Differences between groups were tested using the Chi-square test, case group and control group was the same at all the variables. One hundred and eighty TB-patients were included in the study. Median age was 50 years ranging from 27 to 90 years, and 60%
were male. 30% of patients had formal education and were graduates, only 2% had a bachelor degree and 68% had not finished school (Tables 1 and 2).

<table>
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Table 1: Patient characteristics

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Table 2: Patient characteristics

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<td>14</td>
<td></td>
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<tr>
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<td>85</td>
<td>100%</td>
</tr>
<tr>
<td>no</td>
<td>0</td>
<td>2</td>
<td>0%</td>
</tr>
<tr>
<td>Expire</td>
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<td>3</td>
<td>0%</td>
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</table>

Table 3: Morisky and Clinic follow up

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<tbody>
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<td>Mean</td>
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<td>Pill count</td>
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<tr>
<td>Standard deviation</td>
<td>.61</td>
<td>.48</td>
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Table 4: VAS and Pill count

Assessment of Medication Adherence

Morisky Medication Adherence Scale (MMAS) Score: Highly adherent patients were identified with the score of 8 on the scale, medium adherers with a score of 6 to < 8, and low adherers with a score of <6. Using these cut points, this study population in case group had 8.9% low adherers, 32.5% medium adherers, and 55.6% high adherers, while the population in control group had 16.1% low adherers, 51.7% medium adherers, and 32.2% high adherers. According to these results, there was a significant difference between the case and control groups (p=0.007).

Pills count: There were no significant difference between patient reports in case and control groups (p=0.059), although the mean was different in case and control groups. The low mean at the number of remaining pills in case group indicated the higher drug adherence for these patients.

Visual analog scale (10 points linear VAS): Averaged VAS score in case group was 8.50 while in control group was 8.20. There was a significant difference between the case and control groups (p=0.002).

Clinic visits and follow-up treatment

There were no significant difference in rate of clinic visits and follow-up treatment in case and control groups. The follow-up rate and came to the clinic in the case group was 100% while three patients died in the control group and the follow-up rate was 94.4%.

Discussion

This intervention aimed to investigate the impact of short message service-based intervention on medication adherence for patients with tuberculosis. We found significant impact of SMS medication reminders on self-reported adherence. Medication Adherence was measured by VAS and MMAS scores and patient pills count report.
We found significant difference between the case and control groups in MMAS and VAS scores. Although there were no significant difference between the case and control groups in pills count, the number of remaining pills in case group indicated the higher drug adherence for these patients. Some patients reported that they had used drugs with time delay, although the number of remaining pills in both group was almost equivalent, the mean at the number of remaining pills in case group was lower than control. The MMAS and VAS scores were reported different.

This finding mirrors that of Sadoughi, et al., which carried out a systematic literature search and examined the benefits and effects of short-message service (SMS) interventions on medication adherence. The results of this systematic review indicated that text messaging interventions have improved patients' medication adherence rate (85% studies) [18]. As well as Musiimenta, et al., indicated that mobile telephones could provide alternative approaches to providing social support for TB medication adherence especially where patients do not stay close to their social supporters [19].

The results of this study are not in line with the finding of Bediang, et al., who through a simple blinded randomized controlled with 279 participants, found that SMS reminders do not increase treatment success and cure proportions. But their results obtained at 5 months, showed that the proportion of patients with treatment success is higher (approximately 6% difference) in the intervention group compared to the control group [20].

On the other hand, there were no significant difference in rate of clinic visits and follow-up treatment in case and control groups. As we discussed above one of the limitation of our study was study time. We think that there is a possibility to decrease the amount of clinic follow up during 6 months.

We evaluated patient satisfaction with the "text message medication reminder service." some of them reported that during receiving the SMS reminder they feel cared for, which can play an important role to increase motivation in keeping treatment. Evidence suggests that patients more likely to gain adherence goals when they realize their providers care about them [21,22].

Conclusion

In conclusion, we found that SMS reminders could be useful to combat forgetfulness and could increase patient motivation in keeping treatment.

The studies also have several limitations. Firstly, main limitation of our study was the lack of an objective adherence measure. Adherence was self-reported. Which is a possibility to overestimate in reporting? Using of objective measurement like sputum smear-negative could be more reliable. Secondly, in accordance with WHO guidelines, patients require at least 6 months treatment regimens while our study time was three months. There is a possibility to decrease the medication adherence during 6 months. Thirdly, we did not capability to use interactive SMS reminders; using "one-way" communication was inevitable. Finally, there was a possibility of recall bias in reporting the amount of adherence. To reduce this bias, we used several measurement tools simultaneously.

References


