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The role of mobile phones in improving vaccination rates in travelers

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Abstract

Rationale. Noncompliance with vaccination schedules undermines the potential benefits of immunization. The purpose of this study was to evaluate whether a reminder of the next vaccine dose sent by the Short Messaging Service (SMS) to the vaccinee's mobile phone increases compliance with hepatitis A + B and hepatitis A vaccination schedule.

Subjects and methods. In this experimental, controlled study, the study group comprised travelers who went to the Internacional-Clínic Vaccination Centre between the 1st June and 30th September of 2001 for the standard immunization schedule against hepatitis A + B and against hepatitis A. Trained health-care workers entered the data into a computer to generate text messages reminding vaccinees of their scheduled doses. Two control groups, one from the same period of the same year including travelers from the third office (Control 2001) and the second, all travelers seen in the same period of the previous year (Control 2000), were used.

Results. For the second hepatitis A + B dose, compliance in the study group (Message Groups) was 88.4% (83.3–92.2); in the Control 2001, 80.7% (76.3–84.4, relative risk [RR] 1.10 [1.02–1.17]); and in the Control 2000, 77.2% (73.3–80.5, RR 1.15 [1.07–1.22]). For the third hepatitis A + B vaccine dose, results were 47.1% (40.5–53.8); 26.9% (22.8–31.7, RR 1.75 [1.41–2.17]); and 23.6% (20.1–27.4, RR 2.00 [1.63–2.45]), respectively. As for the hepatitis A vaccine, compliance rates for the second dose were 27.7% (23.9–31.9); 16.4% (14.4–18.6, RR 1.69 [1.40–2.04]); and 13.2% (11.6–14.9, RR 2.10 [1.75–2.54]); respectively.

Conclusions. SMS seems to be an effective tool for increasing compliance with vaccination schedules.

Keywords: Mobile phones; Compliance; Vaccines; Vaccination schedules; Travelers

Introduction

Studies carried out with the hepatitis A vaccine have shown that a single dose is sufficient to achieve a seroconversion rate of at least 97%, while the rate increases to 99–100% after the second dose [1]. The commercially available combined hepatitis A + B vaccine requires three doses (at 0, 1, and 6 months) to confer a protection close to 100% [2]. Noncompliance with the recommended schedule limits the potential benefits of immunization.

It has been reported that noncompliance with therapeutic prescriptions in routine medical practice is around 50% [3]. The WHO's annual report for 2002 stated that global vaccination coverage in 2001 for the three doses of hepatitis B vaccine was only 30%, and around 75% for three doses of polio (Pol3) and for three doses of DTP (DTP3) [4].

Several factors contribute to the lack of compliance with the medical treatments, including the length of the treatment [5,6], the occurrence of adverse events [6,7], the healthcare providers' difficulties in transmitting information, costs, and the complexity of the administration schedule [8–10]. Other factors include those inherent in patients [11] and the long periods of time required between doses, as is the case for the hepatitis B vaccination schedule [12].

The use of new technologies (Internet, mobile phones) may help to reduce the impact of some of the factors mentioned because they improve the degree of compliance with the therapeutic or preventive actions. Areas where they can be used include the improved transmission of information, as they can be used as an easily accessible tool in monitoring treatments and facilitating access to medication. The new technologies are also of use simply to remind vaccinees when their next injections are due.

International travelers are a group that often requires several vaccination courses comprising more than a dose.

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Furthermore, some doses have to be administered some time after the traveler has returned home. It has been observed that compliance with therapeutic measures declines over time and that noncompliance is more frequent in preventive treatments due to their very nature; because of the circumstances surrounding their vaccination, travelers are a group of people in whom compliance with vaccination schedules is particularly low [13].

Access to new technologies by those who, for business or pleasure, travel abroad is high, mainly because of the age and cultural level of this group. For these reasons, it was hypothesized that new technologies, including text messaging by mobile phone, could be used as an intervention measure to improve compliance with the vaccination schedule.

The purpose of this study was to assess whether text messaging by mobile phone with computer-generated reminders of the date of administration of the next vaccine dose would lead to increased compliance levels with the hepatitis A + B and hepatitis A vaccination schedules.

Subjects and methods

An experimental, controlled study in which the effectiveness of an intervention measure was evaluated, namely, text messaging to the mobile phone, with a view to obtaining stricter compliance with a medical prescription: the vaccination schedule.

The target population of the study comprised travelers who went to the International-Clínic Vaccination Centre during the period from 1st June 2001 to 30th September 2001, to start a vaccination course with the hepatitis A + B vaccine (*Twinrix*® GlaxoSmithKline) and the hepatitis A vaccine (*Havrix*® GlaxoSmithKline), who were 18 years and older. A substantial majority of subjects had a high educational level, were Caucasian, and were making a trip of less than 1 month in duration, a typical profile of patients attending Travel Clinics in our country.

In the center, vaccines are administered simultaneously and at random in three offices, where advice and vaccination are offered equally, with no differential due to the type of trip or traveler. The possibility of being included in the Message Group was offered only to travelers possessing a mobile phone who agreed to receive messages and was seen in two of the offices. This possibility was not available to travelers seen in the third office. Subjects included in the Message Group were recruited after they had signed an informed consent. The study protocol was approved by the Clinical Research Ethics Committee of the Hospital Clínic of Barcelona (Spain). The travelers received the vaccines in accordance with the standard immunization schedule: 0, 1, and 6 months for hepatitis A + B, and 0 and 6 months for hepatitis A.

The data regarding the mobile phone number and the date of the first dose of the selected vaccine (hepatitis A + B or hepatitis A) were entered in a web page by a trained healthcare professional who submitted the information by Internet. This information was processed by the system (mBusiness platform, developed by GlaxoSmithKline), which sent out pre-programmed messages at programmed times, so that at the appropriate time, the vaccinee first received a message of welcome to the program: ‘‘You have received your first dose of the hepatitis vaccine. We will remind you when you are due to receive the next one. Thank you. ’’ and then, at the appropriate time, the following message: ‘‘This is to remind you that you should go to the vaccination center to receive your hepatitis vaccine dose. Thank you.’’ The travelers received this message a few days before the date foreseen, that is, for the reminder of the second hepatitis A + B dose, within 30 days of the primary dose, and for the second hepatitis A dose and the third hepatitis A + B dose within 6 months of the primary dose. To evaluate the real impact of the message sent to the mobile phone, ‘‘correct compliance’’ was considered when the second hepatitis A + B dose was administered within 30 $\pm$ 10 days of first vaccine and when the third dose of hepatitis A + B and second dose of hepatitis A were administered within 6 months $\pm$ 30 days of the primary dose.

Two groups were used as controls: Control 2001 and Control 2000. Control 2001 comprised subjects who had received the same vaccines during the same period (1st June to 30th September 2001). Control 2000 included all subjects who had received the same type of vaccines during the same period of the previous year. This second control group was justified by the possibility of bias in Control 2001: given that most people do not travel alone, the subjects in this control group could have received information on the successive vaccine doses from family or friends who were members of the study group. Such information would undermine the real effectiveness of the text messages sent to the mobile phones.

The statistical analysis was carried out using the SPSS v. 10 and the Epiinfo 2000 programs. For comparison of qualitative variables, the chi-square test was used; for the comparisons of averages, the *t* test was used. To measure the impact of the intervention (mobile text messaging) the Relative Risk was calculated.

Results

During the study period (1st June 2001 to 30th September 2001), 2348 travelers started vaccination courses against hepatitis A + B and the hepatitis A. Messages were sent by mobile phone to a total of 738 travelers. Only one traveler to whom the study was proposed did not want to be reminded. The Control 2001 group comprised 1610 travelers who received the same vaccines during the same period, but not the computer-generated reminders. The Control 2000 group comprised 2247 travelers who had started the same

Table 1
Hepatitis A + B vaccine

	Message group	Control 2001 group	Control 2000 group
Men	126/225 (55.6%)	186/383 (48.6%)	264/547 (48.3%)
Women	100/225 (44.4%)	197/383 (51.4%)	283/547 (51.7%)
		$\chi^2 = 2.77$, $P < 0.096$	$\chi^2 = 3.39$, $P < 0.066$
Age (years ± SD)	28.6 ± 4.2	28.7 ± 5.2	27.1 ± 5.0

Descriptive characteristics of the study group and control groups.
χ^2 = chi square. SD: standard deviation.

type of vaccination course during the same period of the previous year. Tables 1 and 2 show the descriptive characteristics of those in the study groups and control groups who started the vaccination schedule against hepatitis A + B and hepatitis A, respectively. No statistically significant differences were found in the gender distributions between the message and control groups. For hepatitis A + B vaccine groups: chi square = 2.77, $P < 0.096$ (Control 2001) and chi square = 3.39, $P < 0.066$ (Control 2000). For hepatitis A vaccine groups: chi square = 0.88, $P < 0.348$ (Control 2001) and chi square = 2.44, $P < 0.119$ (Control 2000).

Hepatitis A + B

During the study period, 609 people started the hepatitis A + B vaccination course, of whom 226 received messages on their mobile phone (one was excluded from the analysis for not meeting the inclusion criteria regarding age). The 383 remaining people made up the Control 2001 group. In the Control 2000 group, 547 were included (Table 1).

Of the subjects who received the text message, 97.3% (219/225) went to the vaccination center for the administration of the second vaccine dose. Nearly the same percentage, 97.4% (373/383), was reported in Control 2001, whereas in the previous year, compliance of the Control 2000 group was 81.5% (446/547). When considering the proportion of subjects with "strict compliance" (second dose administered within 30 ± 10 days of the primary dose), the values obtained for the Message Group, Control 2001, and Control 2000 were the following: 88.4% (199/225), 80.7% (309/383), and 77.2% (422/547), respectively (Table 3).

Table 2
Hepatitis A vaccine

	Message group	Control 2001 group	Control 2000 group
Men	253/512 (49.4%)	576/1227 (46.9%)	771/1695 (45.5%)
Women	259/512 (50.6%)	651/1227 (53.1%)	924/1695 (54.5%)
		$\chi^2 = 0.88$, $P < 0.348$	$\chi^2 = 2.44$, $P < 0.119$
Age (years ± SD)	29.8 ± 5.4	29.6 ± 5.9	29.7 ± 5.6

Descriptive characteristics of the study group and control groups.
χ^2 = chi square. SD: standard deviation.

Table 3
Compliance with the vaccination schedule A + B hepatitis (second dose)

Any interval between the first and second dose

	Number [% (95% CI)]	RR 2001[a] (95% CI)	RR 2000[b] (95% CI)
Message group	219/225 [97.3 (94.0–98.9)]	1.00(0.97–1.03)	1.19(1.14–1.25)

Within 30 ± 10 days of the first dose

	Number [% (95% CI)]	RR 2001[c] (95% CI)	RR 2000[d] (95% CI)
Message group	199/225 [88.4 (83.3–92.2)]	1.10(1.02–1.17)	1.15(1.07–1.22)

[a] RR 2001: Relative Risk, reference 2001 group. 373/383 [97.4% (95.1–98.7)].
[b] RR 2000: Relative Risk, reference 2000 group. 446/547 [81.5% (78.0–84.6)].
[c] RR 2001: Relative Risk, reference 2001 group. 309/383 [80.7% (76.3–84.4)].
[d] RR 2000: Relative Risk, reference 2000 group. 422/547 [77.2% (73.3–80.5)].

When assessing compliance with the complete vaccination schedule, that is, the proportion of subjects who received the third dose of hepatitis A + B vaccine, we observed, for any time interval between first and the third dose, a compliance rate of 56.4% (127/225) in the Message Group and of 39.2% (150/383) and of 38.6% (211/547) in the Control 2001 and Control 2000, respectively (Table 4). No statistically significant differences regarding compliance and sex were found in any of the groups.

When taking into account strict compliance (within 180 ± 30 days of the administration of the primary dose), the analysis showed the following results: 47.1% (106/225) of the subjects of the Message Group received the vaccine within the strictly correct period, compared

Table 4
Compliance with the hepatitis A + B vaccination schedule (third dose)

Any interval between first and third dose

	Number [% (95% CI)]	RR 2001[a] (95% CI)	RR 2000[b] (95% CI)
Message group	127/225 [56.4 (49.7–63.0)]	1.44(1.22–1.71)	1.46(1.25–1.71)

Within 180 ± 30 days of the first dose

	Number [% (95%CI)]	RR 2001[c] (95%CI)	RR 2000[d] (95%CI)
Message group	106/225 [47.1 (40.5–53.8)]	1.75(1.41–2.17)	2.00(1.63–2.45)

[a] RR 2001: Relative Risk, reference 2001 group. 150/383 [39.2% (34.3–44.7)].
[b] RR 2000: Relative Risk, reference 2000 group. 211/547 [38.6% (34.5–42.8)].
[c] RR 2001: Relative Risk, reference 2001 group. 103/383 [26.9% (22.8–31.7)].
[d] RR 2000: Relative Risk, reference 2000 group. 129/547 [23.6% (20.1–27.4)].

with 26.9% (103/383) in the Control 2001 group and 23.6% (129/547) in the Control 2000 group. As shown in Table 4, differences in the Message Group with respect to the control groups were significant, both for "correct" and "incorrect" compliance.

Hepatitis A

A total of 1739 travelers started the hepatitis A vaccination course in 2001, of whom 512 received messages on their mobiles, while the remaining 1227 made up the Control 2001 group. Control 2000 was composed of 1695 travelers who started the hepatitis A vaccination course in the same period of the previous year. Table 2 shows the characteristics of the different groups.

When analyzing the data without regard to the time passing between the first and second dose, the following results were obtained. In the Message Group, compliance was 36.7% (188/512), whereas in the Control 2001 and Control 2000 groups, compliance was 23% (282/1227) and 30.9% (523/1695), respectively.

When the interval of time passing between the doses (strict compliance) was taken into account, the results were as follows: compliance of 27.7% (142/512) in the Message Group, 16.4% (201/1227) in Control 2001, and 13.2% (223/1695) in Control 2001. Table 5 provides data on compliance and the statistical associations are described. The differences between the Message Group and the control groups were statistically significant both for "correct" and "incorrect" compliance.

Table 5
Compliance with the hepatitis A vaccination schedule (second dose)

Any interval between first and second dose			
	Number [% (95% CI)]	RR 2001[a] (95% CI)	RR 2000[b] (95% CI)
Message group	188/512 [36.7 (32.7–41.1)]	1.60(1.37–1.86)	1.19(1.04–1.36)
Control 2001 group			
Control 2000 group			
Within 180 ± 30 days of the first dose			
	Number [% (95% CI)]	RR 2001[c] (95% CI)	RR 2000[d] (95% CI)
Message group	142/512 [27.7 (23.4–31.9)]	1.69(1.40–2.04)	2.10(1.75–2.54)

[a] RR 2001: Relative Risk, reference 2001 group. 282/1227 [23.0% (20.7–25.5)].
[b] RR 2000: Relative Risk, reference 2000 group. 523/1695 [30.9% (28.7–33.1)].
[c] RR 2001: Relative Risk, reference 2001 group. 201/1227 [16.4% (14.4–18.6)].
[d] RR 2000: Relative Risk, reference 2000 group. 223/1695 [13.2% (11.6–14.9)].

Discussion

The results of this study suggest that text messages sent to a mobile phone can be an effective intervention measure for adherence to vaccination schedules because compliance greatly improved for the third dose of hepatitis A + B and for the second dose of hepatitis A. The results confirm that these new technologies can be used to increase compliance with vaccination schedules and, very probably, with other preventive or therapeutic measures.

Compliance with medical prescriptions is particularly poor in chronic treatments and in the follow-up of preventive measures. Factors such as the complexity of the treatments, the occurrence of adverse effects, high costs, or multiple doses diminish adherence to therapeutic measures. Our study seems to indicate that the absence of the perception of risk and the sensation of "feeling well" both contribute to noncompliance with preventive measures because many travelers who started the vaccination course did not go for the administration of the third dose. Without the intervention, just under 40% of the subjects completed the hepatitis A + B vaccination and only 25% (23.6–26.9%) followed the recommended schedule within the foreseen terms. In the case of the hepatitis A vaccine, compliance was 23% in Control 2001 and 30.9% in Control 2000; however, these rates dropped to 16.4% and 13.2% if only the intervals considered as strict compliance were taken into account.

One possible limitation of the study could be that travelers receiving messages could have traveled to higher risk countries or been exposed to high risk populations for longer periods, thus giving them a greater incentive to finish the vaccination series. However, the study selection method, selecting patients from only two of the three offices, the comparison with Control Group 2000, which included all candidates for vaccination against hepatitis (A + B and A), and the fact that the sociodemographic profile and journey duration were similar in all three groups, we think, is sufficient to mitigate any possible bias.

There might also be objections to the definition of strict compliance as "within 30 ± 10 days of the administration of the primary dose", and we agree that the standard schedule which we recommend is 0, 1, and 6 months. However, for many travelers, this schedule is impracticable for logistic reasons, and recent publications have indicated that an accelerated vaccine schedule provides satisfactory results [14–16].

The clear differences in the compliance rates of Control 2001 and Control 2000, when the interval of time between doses is not considered, are explained by the fact that many subjects in the Control 2000 group made further trips during the following year, thus having additional opportunities to receive the doses pending. Nonetheless, the impact of messaging to mobiles significantly improved compliance with the established schedules a priori. On the other hand, the relatively good compliance with the second hepatitis A + B dose in the control groups (although lower than compli-

ance in the Message Group) can probably be explained by the short period of time between doses and by the fact that the second dose is administered before starting the trip, without overlooking the healthcare providers' role in stressing the importance of the correct administration of the two vaccine doses before departure. The impact of health education—a very important measure in improving adherence to therapeutic or preventive measures—is difficult to assess, but would have been similar in all groups. In any event, it was not an aim of this study. Despite the expectations generated by health education in the application of preventive measures, some studies have shown that health professionals are often too concerned with direct and objective actions at the expense of health education activities [17].

Different methods for improving health interventions, such as advice given in the medical visit itself, direct supervision (tuberculosis treatment) [18], reminders by letters or telephone to improve tetanus, flu, and measles vaccination rates, have been studied both in adults [17,19] and in children [20,21]. A combination of several methods has proved to be most effective in increasing immunization rates in children (36% without intervention, 44% when reminded by telephone or letter, 58% for both methods) [22]. A similar study reported a 20% increase in vaccination coverage of children when the intervention was applied [23,24], and another an increase in vaccination rates of 2.3 times in children who had received a call or a letter compared with those who had not [25]. Nevertheless, errors in addresses or telephone numbers can undercut the effectiveness of these methods [26]. In any event, a well-established vaccination program can increase vaccination coverage [27].

A recent meta-analysis [28] and a Cochrane revision [29] of interventions designed to improve immunization programs of adults and cancer screening emphasize the role in routine care of structural organizational changes based on the use of postal and telephoned reminders to boost the use of these services; also considering the possibility of using economic incentives. These studies indicate that the routine incorporation of new technologies into the follow-up of vaccination or therapeutic schedules will also increase the effectiveness and the efficiency of interventions because it will have a minimum impact on costs.

The importance of preventing hepatitis A and B in travelers falls outside this discussion. The risk of hepatitis A is related to the endemicity of the disease in the geographic area to be visited [30–35]. A study conducted in the United Kingdom identified travel to endemic zones as an important risk factor, with an OR of 19.8 (4.87–80.6) [33]. Infected travelers (sometimes asymptomatic) can represent a source of infection for their households and other contacts when they return home [31,32]. On the other hand, infection due to the hepatitis A virus can have a significant mortality rate [36], which increases with age. In the US, mortality rates are less than 5/1000 in people under 49 years, but they rise to 17/1000 cases in those who are older [37]. In the UK, hepatitis A causes 10–20% of cases of impaired liver function [38] and in France it is responsible for 10% of liver transplants [39]. A single dose of vaccine confers 97–100% protection, while cover is 100% after the second dose at 6 months [1]. It has been indicated that the booster effect also occurs when the period from the primary dose is much longer than that routinely recommended, even a few years [40–42]; this is probably also the case with hepatitis B [43]. In any event, our aim was not to evaluate the immunogenicity of vaccine [44], but the effectiveness of an intervention measure.

Hepatitis B can also represent a risk for travelers who go to countries with high endemicity [45]. The administration of three doses of vaccine is necessary to confer optimal, long-lasting protection [46]. The hepatitis B vaccine has a seroconversion rate of 70–95% after the administration of two doses and of almost 100% after the third dose [47]. Many travelers are at risk of contracting both types of hepatitis, and so the combined hepatitis A + B vaccination represents an important added value, as they protect the vaccinee beyond the risks strictly related to the trip in question [48–50].

Travelers are typically healthy people who usually make a trip a short time after starting the vaccination schedule. Their main reason for immunization is to travel as safely as possible, so that this incentive and the recommendations of the healthcare provider should have a positive effect on compliance rates with the successive doses.

In our study, we observed excellent compliance as regards to the administration of the second hepatitis A + B dose (1 month after the first shot). Nevertheless, adherence to "distant" doses, that is, those that must be administered 6 months after the primary dose, is far lower. When the time comes round, the reasons the vaccination schedule was started are almost forgotten (both in those receiving Short Messaging Service (SMS) text messages and those who did not). It is difficult to compare the compliance rates found in the present study with those of other vaccination schedules recommended in travel clinics, as these often require only a single dose (yellow fever, typhoid fever, meningococcal disease, MMR). In other cases, where more than one dose is required (rabies, Japanese encephalitis, Central European encephalitis), the schedule allows administration of all the doses before the beginning of the trip (less than 1 month). According to unpublished data from our vaccination center, compliance with these pre-trip schedules is satisfactory.

There are few studies published on the compliance of vaccination schedules in travelers [51,52]. However, there is some information on the inadequate compliance of malaria prophylaxis, where the principal motives seem to be the appearance (real or imagined) of adverse events and forgetfulness. If travelers frequently forget to take malaria drugs during the trip, when the motivation should be high, forgetting about vaccination doses scheduled for some months after the trip seems more reasonable [53,54].

The upgrading and application of new technologies in travelers, other population groups, and the general population to encourage development and improvement of preventive strategies (vaccination and others) and therapeutic strategies in chronic patients should open up great opportunities. The latest technical information indicates that, in October 2001, according to market studies conducted by Fimestic, mobile phones had a 68% penetration rate in Spain, a percentage estimated to reach 90% by 2005 [55,56]. In 2001, mobile phone penetration in most Western European countries was between 60% and 85% [57]. By text messaging to mobiles, vaccinees receive reminders in accordance with the day on which the vaccination course was started. Our study has shown the effectiveness of SMS technology in this area, as compliance with two different vaccination schedules considerably increased. The use of new technologies will probably permit direct intervention in the improvement of compliance rates for chronic treatments as well as in the implementation of new preventive measures.

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