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Application of mobile phone technology for managing chemotherapy-associated side-effects

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Background: Novel mobile phone technology linked to a server that communicates patients' symptoms to healthcare professionals has been adapted to register the side- effects of chemotherapy and provide advice on management of toxicity. We report a feasibility study to examine the utility of home monitoring of patients' symptoms via a mobile phone.

Methods: Six colon cancer patients receiving adjuvant chemotherapy, entered symptom data onto user friendly screens on a mobile phone twice daily. This 'real time' self assessment of nausea, vomiting, mucositis, diarrhoea and hand–foot syndrome and measurement of temperature was sent via a secured connection to a remote computer. In the event of moderate or severe symptoms (generating amber and red alerts respectively), the nurse was immediately alerted by the computer, via a pager. The nurse then contacted the patient to reinforce the automatic advice sent to the patient on their phone and to assess the patient using clinical algorithms.

Results: The patient used the mobile phones during the first two cycles of chemotherapy. The data were successfully analysed by the server software and alerts were generated alerting the study nurses to patients' symptoms at the appropriate time. There were 91 alerts—54 red and 37 amber; 54% (29/54) of the red alerts were data delay and transmission problems which were swiftly rectified. The remaining red alerts were managed appropriately by the study nurses. Both patients and staff felt confident in this approach to symptom management.

Conclusions: This study demonstrates that the technology for monitoring patients' symptoms worked well. The patients felt secure in the knowledge that their symptoms were being closely monitored and that they were participating effectively in their own care management.

Key words: managing side effects, mobile phone technology

introduction

In the last few years, the UK government has been highlighting the importance of self-responsibility and self-management in health and illness [1,2]. The mobile telecommunications industry offers one means of supporting patients in this endeavour [3–5].

It is widely recognized that the use of chemotherapy results in side-effects that adversely affect patients' quality of life [6]. Indeed, adjuvant regimens for colorectal cancer have toxic death rates (measured by 60-day all-cause mortality) that range from 0.8–2.2% and are driven by febrile neutropenia, diarrhoea, nausea and vomiting and mucositis, the most common life-threatening toxicities [7]. If side-effects can be reported early, e.g. via mobile phones, then, with prompt intervention, they may be minimized and ultimately lives saved.

The vast majority of patients receiving chemotherapy for colorectal cancer are treated in the out-patient setting and manage most side-effects at home. Side-effect 'risk management' is handled by a variety of measures including patient education with prechemotherapy discussion, information leaflets, patient-held diaries and targeted use of the internet. Good communication channels with the hospitals are essential, with clear contact procedures in place. Mobile phone technology has the potential to enhance these measures.

Telephone follow-up for monitoring, supporting and providing healthcare advice has been successfully utilized for many years [8], but tends to be non-targeted and therefore time consuming. Mobile phone systems, however, allow patients to alert healthcare professionals (HCPs) automatically, in real time and only when necessary and have been successfully piloted for diabetes [9] and asthma [10]. There are approximately 50 million mobile phones in use in the UK today and it should be possible for most patients to communicate their test results or symptoms to HCPs via the mobile phone if supported by robust, accessible programmes. Alerts can be generated for severe or potentially life-threatening toxicities,

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informing the HCP, who is then able to act appropriately, thus selecting and focusing on patients requiring intervention.

We report a feasibility study of utilizing mobile phone-based technology for symptom management during chemotherapy treatment as a component of a large, international adjuvant trial evaluating chemotherapy for patients with colon cancer, QUASAR 2, in which patients are randomized to capecitabine, with or without bevacizumab [11].

methods

A multidisciplinary steering committee comprising engineers, oncologists, senior nurses, a patient, a statistician and senior clinical trials staff executed the study. The study was approved by the study hospital's local research ethics committee, the local research and development committee and monitored by the Oncology Clinical Trials Office (OCTO) at Oxford University. Informal interviews were held with all participating patients and HCPs at the end of the on-study period to elicit their overall experience including their perceptions of the technology and training.

patient eligibility

Patients were randomized to QUASAR 2 (stage II or III colon cancer patients with complete resection of the primary tumour), able to understand, read and write English and willing and capable of entering their own symptoms and temperature on to the phone twice a day.

procedures

training

Six patients received a mobile phone (Motorola V600) with preloaded software. The research nurse instructed the patients on how to use the phone and the digital tympanic thermometer. Patients also received written instructions (a manual written by a patient in partnership with the technical team) and emergency contact numbers. Patients were asked to enter their temperature and symptoms related to nausea, vomiting, mucositis, diarrhoea/bowel movements and hand–foot syndrome onto the mobile phone, by answering specific questions displayed on the phone screen twice a day (Figure 1). These questions, derived from the Common Terminology Criteria for Adverse Events (CTCAE) grading system [12], were simplified for display on the mobile phone screen. Patients were able to select grade 1 (''mild'') or 2 (''moderate''), with grades 3 and 4 (where available) toxicities combined into a ''severe'' category. Patients were encouraged to contact the study nurse or doctor if they experienced any difficulties with any of the study procedures. All participating nurses were trained on how to access patients' individual data on the computer and to acknowledge and respond to alerts by using clinical algorithms for toxicity management in order to ensure quality and standardization.

data transmission and collection

The steering committee collaborated closely with e-San Ltd [13] on the development of the mobile phone technology. e-San Ltd (now t+ Medical Ltd) has a strong history of clinical and consumer-based e-health systems for monitoring medical conditions such as asthma, diabetes, hypertension and cystic fibrosis.

Data were collected during the first two cycles of chemotherapy each morning and evening. The patients were required to enter data using the phone keypad. These data were automatically transmitted to a dedicated server via a secure GPRS (General Packet Radio Service) connection. Each patient's cumulative toxicity chart was displayed both on individualized web pages (for review by the study nurse) and on the patient's phone (for information) (Figure 2).

If incoming readings gave rise to concern, amber or red alerts were generated according to criteria stored both on the phone and the server (Table 1) and the study nurse at the hospital site was automatically alerted by an alert generated by the server and sent to her pager. The nurses acknowledged all alerts on the patient's web page.

Figure 1. Examples of mobile phone symptom diary.

Amber alerts, sent by the server in batches to the study nurse's pager at 9.00 AM, 1.00 PM and 3.30 PM, 7 days a week, indicated that the patient was experiencing some difficulties at home but that these were not severe or life threatening. On receiving an alert, the study nurse accessed the patient's symptom history via their secure web page and, if appropriate, contacted the patient at home. Red alerts, however, indicated that the patient was pyrexial and/or experiencing symptoms at home that were severe or life threatening. If a patient failed to enter their data into the mobile phone for more than 24 hours, this also generated a red alert. If an amber alert was generated for four out of five consecutive 12-hour timeslots, it was automatically escalated to a red alert. Again, the nurse was able to view the patient's symptom history via their secure web page and contact the patient as soon as possible (but within a specified maximum period, originally set at 90 minutes) in order to initiate appropriate management. As the criteria for red alerts were also stored on the phone, patients were informed if a red alert had been generated and told that the nurse would contact them within the specified period (see phone screen on Figure 3). During out-of hours periods (evenings and at the weekends), the study pager was passed to an oncology nurse working on the ward and trained in the technology, in order to provide 24-hour cover for the patients.

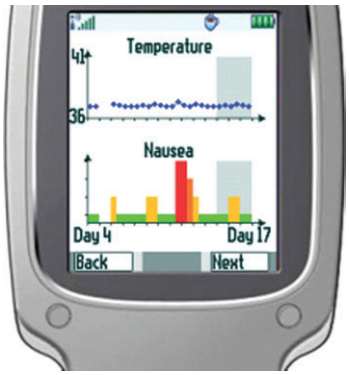

Figure 2. Example of time plots.

individualized self-care advice

After completing the twice daily questionnaire, patients also received self-care advice on their phone, directly related to their symptoms. Some examples are shown in Figure 4. Patients were strongly advised to complete their symptom and temperature data input prior to taking their capecitabine tablets in the morning and evening, as part of the advice may be to stop the capecitabine medication. A schematic diagram showing the complete system is shown in Figure 5.

results

Six patients consented and were entered into the study; four men and two women, aged 54 years to 76 years (median 64 years). Only one patient declined entry into the feasibility study indicating she had ''too much on''. All six patients were treated with capecitabine + bevacizumab. Data entry compliance was excellent (98% of the twice-daily input was

Table 1. Mobile phone toxicity alert criteria

Alert	Condition	Parameter
Amber	Borderline pyrexia with normal second reading	Reading in the range 37.5–37.9°C and 2nd reading (after 1 hour) is <37.5°C
	Mild or moderate diarrhoea lasting for 12 h	Total number of bowel movements over baseline in last two readings ≥4
	Severe mucositis lasting for 24 h	Severe mucositis in 2 or more of 3 readings
	Moderate mucositis lasting for 48 h	Moderate or severe mucositis in 3 or more of 5 readings
	Severe nausea lasting for 48 h	Severe nausea in 3 or more of 5 readings
	Moderate or severe vomiting lasting for 24 h	Moderate or severe vomiting in 2 or more of 3 readings
	Moderate hand–foot syndrome	Moderate hand–foot syndrome in current reading
Red	No readings for previous day	No readings received in the last 30 h
	Many sufficiently concerning amber alerts in previous 48 h	Any combination of ambers 2, 5 or 6, in 4 or more of 5 readings
	Pyrexia	Current temperature reading is 38.0°C or above
	Borderline pyrexia for 12 h	Borderline pyrexia where 2nd reading is also 37.5–37.9°C
	Borderline pyrexia and second reading not known	Borderline pyrexia where 2nd reading is not taken within 90 min
	Mild or moderate diarrhoea lasting for 36 h	Total number of bowel movements over baseline in last 4 readings ≥8
	Severe diarrhoea	Total number of bowel movements over baseline in current reading ≥4
	Moderate diarrhoea and severe nausea	Number of bowel movements over baseline ≥2 and severe nausea
	Moderate diarrhoea and moderate or severe vomiting	Number of bowel movements over baseline ≥2 and moderate or severe vomiting
	Moderate diarrhoea and severe mucositis	Number of bowel movements over baseline ≥2 and severe mucositis
	Severe mucositis and moderate or severe vomiting	Severe mucositis and moderate or severe vomiting in the current reading
	Severe mucositis and severe nausea	Severe mucositis and severe nausea in the current reading
	Severe vomiting for 12 h	Severe vomiting in 2 readings
	Severe hand-foot syndrome	Severe hand-foot syndrome in the current readings
	Moderate hand-foot syndrome lasting for 24 h	Moderate (not severe) hand-foot syndrome in all last 3 readings

complete) from all six patients with the exception of one question: the second temperature entry requested within 1 hour of a first borderline temperature entry (see Table 1) was not entered within the hour on 15 occasions, by two patients. One patient also found the tympanic thermometer was complicated to use and expressed preference for an oral thermometer which was duly provided.

connectivity and symptom profile

For the six patients, over their first two cycles of chemotherapy lasting 6 weeks in total for each patient, there were 91 alerts—54 red and 37 amber. However, 54% (29/54) of these red alerts were ''data'' alerts, occurring because the server detected missing data from the previous day and therefore automatically generated a red alert. Twenty-one of the 29 data alerts were due to poor network coverage at one of the patient's home and inconsistent data transmission. The technical team changed the Subscriber Identity Module (SIM) card to a different network provider covering the patient's area and there were no further transmission problems with that patient. Two additional alerts were generated due to isolated transmission problems resulting in data not being immediately sent to the server (two patients, once each). Five of the remaining ''data'' red alerts were generated as the server software wrongly interpreted the lack of data between the clinic visit and the patient's first data entry as missing data. The software was modified to deal with this issue. Only one instance of a patient not completing either of the morning or evening symptom diaries was observed.

The remaining 25 ''symptom-generated'' red alerts were divided into 15 (60%) for raised temperature (two patients), eight (32%) for diarrhoea (two patients), and two (8%) for hand–foot syndrome (two patients). No red alerts were generated for mucositis, nausea and vomiting. All 15 red alerts due to temperature readings were due to two patients with borderline temperatures (>37.4°C but <38.0°C) failing to re-enter their temperature after an hour as stipulated in the protocol. After discussion with the patients with borderline temperatures, the nurse decided no further intervention was deemed necessary in all cases. There were 37 amber alerts: 18 (49%) due to diarrhoea (four patients, two also experiencing red alerts); 14 (38%), hand–foot syndrome (two patients, including one red alert patient), four (11%) mucositis and one (3%) temperature. Nausea and vomiting did not generate any amber alerts.

None of the six patients stopped the capecitabine medication early or were hospitalized whilst on the study, although one patient was seen on the ward within 2 hours of data input due to severe hand–foot symptoms and was commenced on pyridoxine treatment.

Overall, all six patients found using the phones a very positive experience and simple to use. They all informed the nurse that they felt reassured their symptoms were being very closely monitored and that hospital staff could respond to their symptoms very quickly. Two patients commented that as it was the nurse contacting the patient to speak to them, and not vice versa, they felt that they were being less ''bothersome''. All six patients felt involved and responsible for their care management plan.

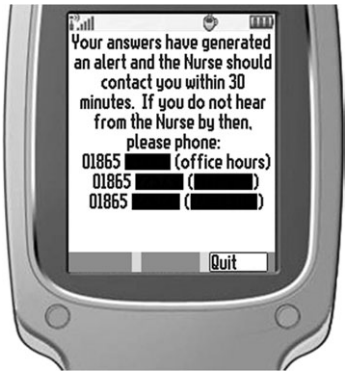

Figure 3. Example of phone screen for red alert.

staff

All alerts, except for one, were acknowledged within the specified times by the nurse holding the study pager. One acknowledgement of a red alert was not made on the computer within the specified maximum of 90 minutes but the patient had been phoned according to protocol. The computer acknowledgement was made 3 days later. After this, all clinical staff suggested that it was practical and may reduce patient anxiety if the response to red alerts were made within 30 (not 90) minutes. This timing was changed after the fourth patient.

After training, the research nurse and ward nurses felt competent and confident to deal with the monitoring of patient data via the computer and the giving of advice, in line with set algorithms. They did not feel overwhelmed by the study alerts. The night ward staff decided not to discuss amber alerts with patients when the study nurse was on duty the next morning, thereby not disturbing the patients at night and

Figure 4. Examples of feedback screens.

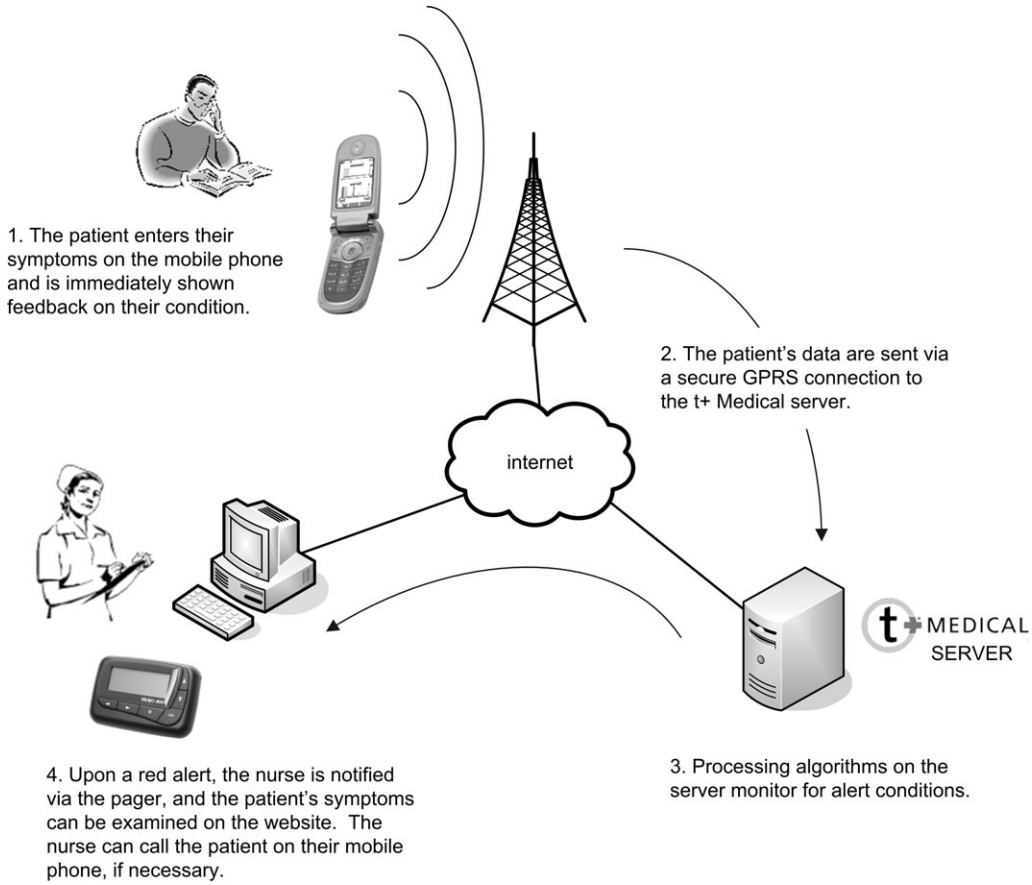

Figure 5. Overview of mobile phone-based system for symptom management during chemotherapy.

ensuring that they were contacted the next morning by a familiar HCP.

discussion

This ground breaking study used new technologies, first tested in patients with other conditions and now extended to the oncology setting, to measure and rapidly manage side-effects associated with chemotherapy. Overall, there were very few side-effects over the total of 12 cycles of capecitabine and bevacizumab monitored during the feasibility study. One patient who had grade 3 diarrhoea was treated immediately with loperamide and continued with grade 1 or no toxicity until the end of his two chemotherapy cycles. One patient who had grade 3 hand–foot syndrome was treated with pyridoxine which decreased the severity to grade 1. This patient's third cycle of chemotherapy was delayed 1 week and both patients had a capecitabine dose reduction of 25%. All toxicities were in keeping with the known side-effects of the two drugs [11].

This study demonstrated that the technology for monitoring patients' symptoms worked well; patients had no problems entering symptom data on to the mobile phone and the data were transferred automatically to the remote server. Age was not a barrier to use in this small sample. The data were successfully analysed by the server software and alerts were generated alerting the study nurses to patients' symptoms at the appropriate time. The technical glitches (non-symptom-related red alerts at patients' first entry and lack of signal reception) were quickly rectified. The research nurses and the ward staff were able to respond appropriately to all the alerts generated bar one within the time scales set out in the protocol. Most importantly, patients felt secure in the knowledge that their symptoms were being closely monitored and that they were participating more effectively in their own care management.

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