Improving self reporting of ADRs using socially-coupled Pharmacoinformatics in Al Ahsaa Area

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ABSTRACT

Healthcare organizations are focusing on the identification and management of Adverse drug reactions (ADRs) because of their linkages with medical problems, patient outcomes and drug discovery. The acquisition and processing of ADR-related information is challenged by the inefficiency of spontaneous reporting systems, the difficulty of promoting self-reporting by patients and the use of social media generated data. By focusing on ADR management information in Al Ahsaa area (Saudi Arabia), our study examined the way such information is being acquired, processed, presented and shared in some public hospitals of the city. The study revealed the limited application of Pharmacoinformatics for detecting, signaling and system-wide integration of ADR information. The paper proposes an agent-based information architecture to improve self-reporting of ADR information by patients and other stakeholders by emphasizing the use of user-generated ADR-related content on “guided” forums or social networks.

Keywords

Pharmacoinformatics, software agents, pharmaceutical care; adverse drug reactions; social networks.

INTRODUCTION

There has been a growing attention to use advanced information systems in healthcare for the automation of processes (such as pharmacy, surgery, pediatrics, diagnosis etc.) for two main reasons. Firstly, the standardization of medical management processes (through the use of professional manuals and automated standard operating procedures) has enabled complete or partial automation of processes. Secondly, technological developments (hardware capacity, software interface features and communication methods) are reshaping the context of information acquisition, processing, retrieval and sharing. However, the application of information systems and technologies for pharmaceutical care management continued to be marginal and restricted to monitoring drug issuance at hospital pharmacies (wards, outpatients and in-patient). Current Pharmacoinformatics applications in the sampled hospitals did not support the analysis of drug therapies, management of prescription inconsistencies and signaling and detection of ADR in accordance with the reporting requirements of Food and Drug Authority (FDA).

Agent-based Pharmacoinformatics can be used to manage drug interactions and allergies, clinical formulations, dose range check, drug indications and contra-indications, duplicate therapy monitoring, clinician and workflow management and anatomical therapeutic classification, among others. They enhance information availability and accessibility and contribute towards the reduction of occurrences of medical errors, patient safety problems and drug management inconsistencies. Their use enables decision makers to detect and manage ADRs, integrate information from heterogeneous distributed sources and extract information from social networks, instead of focusing on “stock control”. This paper examines the use of co-evolutionary concepts in multi-agent Pharmacoinformatics and crowd sourcing ADR-related management information from social networks to promote self-reporting of ADR information.
The paper falls into eight sections. Section 2 presents the methods of the study and section 3 describes the case study of Al Ahsaa area, Saudi Arabia. Section 4 presents the context of ADR-related management information with section 5 being devoted for related work. Section 6 presents an agent-based framework for the promotion of self-reporting using social media networks. Section 7 focuses on discussions and section 8 shows the conclusions of the paper.

METHODS

The methodology for this project is generally a descriptive analytical survey with both inductive and deductive methods being applied including empirically driven qualitative and quantitative theories. To account for the diversity of information across the different managerial levels of the pharmacy management landscape and to ensure the validity of the instruments of research, Anthony’s taxonomy of managerial levels, the technique of optimum allocation, the concepts of agents and the techniques of information modeling are used for the articulation of decision variables and process modeling. The majority of the project’s data was collected from electronic sources of many healthcare organizations (public and private hospitals, dispensaries and clinics) and pharmaceutical companies in Al Ahsaa city and the branches of regulatory agencies such as the National Pharmacovigilance Centers and their affiliated drug information centers operated by the Saudi Food and Drugs Authority (SFDA). Some data also availed through interviews with key pharmaceutical personnel. The study also benefited from the different tools and methods of data analysis provided by international organizations such as WHO. The tools include data matrix, tables, diagrams, models and output of computer programs.

THE CASE STUDY

Al Ahsaa city is located in the eastern part of Saudi Arabia with an area of 430000 km² and a population of 1063112 inhabitants (Wikipedia). It includes nine specialist public hospitals, 33 (private and public) dispensaries and clinics, five private hospitals and a branch for the Saudi Red Crescent (Al Ahsaa website). Six of the public hospitals have websites. The link of the website of one of these hospitals is disconnected and for another one the content is still “under development”. Only one of these public hospitals (the psychiatric hospital) has a moderated forum including sections for consultation, clinical psychiatric, continuous education, psychiatric nursing, pharmacy and physiotherapy. Three of the public hospitals (with working web pages) have accounts on social media networks (mainly face book and Twitter) but such accounts are neither “interactive” nor “informative”. One of the public hospitals and one of the private hospitals are managing patient-related complaints through the Patients’ Relationship Office (PRO) which reports to the director of the hospital. Three of the public hospitals provides sections for “patients’ affairs” including sections such as “ask the specialist”, tele-care for managing diabetics, first aids, patient's rights, religious awareness and statistics”. Out of the 33 (private and public) dispensaries and clinics only six has web sites (including one website that cannot be opened, one without links to social media networks and one with content provided in English only). None of the dispensaries with web pages has a link to social media networks or moderated forums. Only four out of the five private hospitals have web sites but two of them are inaccessible. Only one private hospital has a link to social media networks without any support for the reporting of ADRs.

The Saudi Food and Drug Authority (SFDA) is responsible for regulating, overseeing, and control of food, drug, medical devices and setting mandatory standard specifications. It provides awareness information about food, drug and medical device matters. SFDA uses about 326 social media links to increase access of its website but not for the reporting of ADR information. It accepts web-based “comments” and “recommendations”. Its affiliated National Drug and Poison information Center and Pharmacovigilance Center are represented in some hospitals with noticeable concentration in the capital city. The information provided by SFDA about these centers includes email addresses (some of them are declared to be out of service) and phone numbers. As it the case of other FDAs who fear broadcasting of postings of (possibly inaccurate) patient complaints (including details on adverse events) (Leaman et al., 2010; Hochberg et al., 2007), SFDA discourages the reporting of non-serious drug events because of possible non-adherence with regulations and significant medical consequences. The majority of pharmaceutical companies in Saudi Arabia have web pages and some of them have social media links to promote access to their websites. Generally speaking, such companies use the internet for a one-way communication with customers due to their attitudes towards the scope of their obligations to report ADRs to FDAs (Shirazi and Soroor, 2007) and their inability to manage mass communications with patients and resolve discrepancies that may arise.

THE CONTEXT OF ADVERSE DRUG REACTIONS INFORMATION

An adverse drug event refers to incidents in which the use of a medication (drug or biologic) at any dose, a medical device, or a special nutritional product (e.g., dietary supplement, infant formula, medical food) may have resulted in an adverse outcome in a patient (Ceusters et al., 2008) that either compromises therapeutic efficacy, enhances toxicity, or both. Some adverse effects are limited but others are fatal and may lead to permanent organ damage or death. Acquiring ADR-related management information is important for the enhancement of the quality of pharmaceutical care services and the development of effective patient safety strategies. The main sources of drug safety and ADR-related management information are clinical trials and post-marketing surveillance instruments (Leaman et al., 2010). Because of their small
population sizes, short durations and limited generalizability of pre-approved clinical trials (Ahmad, 2003), clinical trials detect limited aspects of drug safety. A lot of additional adverse effects are observed after multiple drugs are made available to large population over long periods of time (Harsha et al, 2012) in patients with co-morbidities and in conjunction with other medications or when taken for off-label uses not previously evaluated (Brant, Richard and Bruce, 2011). Regulatory agencies such as FDAs use Adverse Event Reporting System (AERS) to conduct post-marketing surveillance programs and monitor ADRs. Input information is provided by hospitals, healthcare professionals, patients and companies. Due to the difficulty of using AERS and their voluntary nature, they grossly underestimate the prevalence of serious adverse events (Harpaz, 2010; Anon, 2009; Bates et al., 2003; Van der Hooft et al., 2006). Patients’ self-reporting detects less than 1% of ADRs (Jha, 1998) due to unwillingness of patients and their failure to associate ADRs with drugs. ADR-related management information that avails from clinical trials and post marketing surveillance programs can be recorded in public and open access databases such as drug labels (dailymed.com, n.d), the RXList database (rxlist.com, n.d), the Drug Information Portal (druginfo.nlm.nih.gov, n.d), the PharmaPendium (pharmapendium.com, n.d), the Side Effect Resource (SIDER) (Kuhn et al., 2010), and the drug side effect database (drugs.com, n.d), among others.

Moreover, ADR-related management information can be extracted from social media networks. Such networks take the form of websites, social networking (Facebook, MySpace, LinkedIn, Goggle +), wikis, web blogs, customer forums, micro blogs (Twitter), social bookmarking (e.g. dig), location-based services ( foursquare), Virtual worlds (second life), and patient networking (e.g., PatientsLike Me) (Efraim, Sharda and Delen, 2010). According to Brant, Richard and Bruce (2011), online health forum data contains a wealth of information (including drug safety) that is not being utilized by the FDA to enrich the AERS database. Through such networks, patients create profiles and establish contacts to share drug-related information and ask for medical advice either explicitly (as it is the case of user-initiated and user-aware interlinking) or implicitly (based on similarity of user profiles). Research revealed the increase of the number of patients who use the internet for drug prescription information (Manhattan Research Press Release, 2009a), the use of social media for medical information (Manhattan Research Press Release, 2009b) and the engagement of healthcare professionals in social networks (Manhattan Research Press Release, 2009c). The emergence of location based social networks and the use of mobile communication systems have enabled many patients to share and incorporate spatial and location-embedded information into their social networks activities and services. Because personal data has been significantly tapped with online and hand-held “context-aware” applications, a large number of repositories of personal data are currently available on smart phones.

RELATED WORK

Software agents are regarded as computational entities that use different resources to achieve tasks on behalf of themselves, other agents or users. They play roles in understanding and managing large scale, complex and distributed systems. They assist in building independent components in heterogeneous, open and distributed systems, allocating resources and expertise and improving personalization, customization, interoperability and integration of complex systems. Software agents are characterized by some qualities that shape their capacity to provide relevant decision support and process-specific intelligence. The list of widely cited qualities includes autonomy, learning, mobility, social ability, reactivity and pro-activeness, benevolence, rationality, independence, adaptivity, cooperation, reasoning and intelligence (Lisa, Hogg and Jennings, 2001; Persson, Laaksolahti and Lönnqvist, 2001; Bonarini and Trianni, 2001; Hu and Weliman, 2001).

Software agents have been used for the automation of pharmaceutical workflows, information extraction and signal detection from local databases or social networks. Gasmelseid (2012a), developed a multi-agent Pharmacoinformatics reference model for the improvement of hospital management processes using functional “superior” and “subordinate” agents. Godo, et al, 2003, used multi-agent systems to monitor the prescription of restricted use antibiotics in hospitals by incorporating six functional agents, roles, dialogic framework, scenes, and performative structure. Yanqing et al., (2005) and Yanqing et al., (2010) used intelligent agents with a fuzzy recognition-primed decision model to develop a distributed ADR detection system by utilizing distributed electronic patient data. Multi-agent systems have also been used for the development of process centric methodologies for the management of pharmaceutical supply chains (Yanqing et al, 2007; Pathak S, Nordstrom G, Kurokawa, 2000; Fu Y, Pipiani, 2000; Frey et al., 2003; Davidsson and Wernstedt, 2004; Lu and Wang, 2008). (Shirazi and Soroor, 2007; Trappey, Lu and Fu, 2009; Seyed et al, 2010; Gottfried et al, 2011) examined coupling multi-agent systems with radio frequency identification (RFID), remote sensing, ontology-driven technologies and simulation concepts to automate and simulate procurement processes and track pharmaceuticals supplies. Harsha (n.d) proposed a machine learning-based system for the automatic identification of ADR assertive sentences in case reports by using dictionary-based named entity recognition for identifying the co-occurring drugs and conditions. Brant, Richard and Bruce (2011) focused on the extraction of less constrained textual data from social networks. Chee, Karahalios and Schatz, 2009 and Chee, Berlin and
Schatz, 2009 examined the use of manually generated lexicons to identify drugs and drug effects from online health forums. Azadeh and Graciela (2011) presented a system to automatically extract mentions of ADRs from user reviews about drugs in social network websites by mining a set of language patterns. Christian and Volkmar (2011) investigated the coupling of web services and mobile software agents to support the integration of users into social networks. Marko et al., (2009) presented an agent-based middleware for social networking (MAgNet) to enable the creation and management of groups of users and plan group events in social networks using mobile networks.

The use of the agent paradigm for the improvement of the quality of pharmaceutical care processes, as shown in previous studies, is characterized by some considerations.

1. The majority of the studies focus on using available ADR information that avails through the use of spontaneous reporting systems without trying to relax their associated data-related limitations. Despite the emphasis on standardizing, automating ADR-related processes and specifying agent-specific functionalities, little has been done to trace ADR-related information to their origin by analyzing hospital-based clinical and pharmaceutical care processes to understand the way such information is being acquired, processed, represented and used in a wider organizational context.

2. The emphasis on using agent-based applications in certain ADR-related aspects such as the examining the impact of using certain drug (e.g. antibiotics), communication between departments and ADR detection processes without adopting an integrated approach.

3. The limited focus on coupling "paradigms" rather than "technologies" and machines. Paradigm coupling is a prerequisite for improving the capacity of healthcare organizations to benefit from the unprecedented developments exhibited in social networks and their useful ADR-related user-created contents. Together with locally-acquired information, social networks constitute the backbone for promoting self-reporting ADR information by patients, healthcare professionals and other stakeholders.

AN AGENT-BASED ADR SELF REPORTING FRAMEWORK

In his work on Pharmacoinformatics (Gasmelseid, 2012b) proposed the focus on the “co-evolution of systems” rather than “information exchange” to improve the detection of ADRs by adopting functional (exchange of inputs and outputs) and structural (sharing the elements of sociotechnical configurations) couplings. At the hospital level, as shown in figure (1) below, the detection of medication-specific ADRs is based on comparing prescriptions against general lab and microbiological tests. Post-discharge ADRs are detected only in case of re-admission.
As shown in figure (2), Pharmacovigilance centers use AERS to signal, validate and manage ADRs to take actions.

![Figure 2: PV-based ADR detection](image)

Using agent-oriented co-evolutionary measures, ADR-related processes can be assigned to superior (e.g., Hospital, Patient, Physician, Pharmacist and Pharmacovigilance) and subordinate (interface and information) agents as shown in figure (3) below.

![Figure 3: agent-based hospital-centered co-evolutionary detection of ADRs](image)

The layered architecture of superior and subordinate agents enables healthcare organizations to investigate the context of ADRs at the bottom level and orchestrate all necessary processes. As for medication-specific ADRs, the Physician’s agent (FA) exchanges information with the Patient’s agent (PA) and uses the information agent (IA) to access information. The FA compares information, detects ADRs and recommends scenarios such as drug withdrawal, change of labels, dosage, route and duration. The detection of post-discharge ADRs through self-reporting, requires hospitals to establish “guided” patient forums and/or presence on social network websites. Guidance is required because “analytical errors”, “misspellings”, “misuse of words”, and “ambiguous abbreviations” can lead to poor information retrieval results (Kuhn et al., 2010; Manhattan Research Press Release, 2009d; Kogan et al., 2001; McCray, et al., 1999; Zeng et al., 2001). Therefore, case dictionaries describing pain levels and symptoms, for example, can be used to bridge vocabulary gaps, enhance self-
reporting and classify ADRs. Because social networks are subject to information overload (Vandenbroucke, 2001) human mediated processes are required to associates detected ADRs with structured patient-specific information included in EMRs, hospital exit logs, discharge summaries and medical reports. The entire agent infrastructure then classifies detected ADRs into type (A), (B) or (C). Type (A) events are dosage-based and related to the pharmacokinetic properties of drugs. Type (B) events are related to the patient’s reactions and tend to be allergic, idiosyncratic, immunological, or non-immunological. Type (C) events tend to be serious and may result in significant implications on public health. They originate from the impacts of drugs used for improving the quality of life of patients with serious chronic diseases (Meyboom et al., 2000). Accordingly, the hospital agent can communicate reported ADRs to the Pharmacovigilance agent, undertake simulations and define intervention scenarios.

DISCUSSION

The use of software agents for the detection of ADR information and mainstreaming mentions on social networks plays a significant role in the improvement of self-reporting of ADRs in Al Ahsaa area. However, some issues need to be re-visited. Firstly, priority should be given to the development of innovative methodology for the acquisition and analysis of data acquired from social networks. The growing number of prescription drugs, over the counter drugs and herbal remedies to be examined and the diversity of diseases and food types and the ADRs associated with them are sources of complexity. Therefore, it is not suitable to articulate ADRs by comparing drugs and “symptoms” against their peers and the similarity of the expressions of patients. The perception of drugs is different from their actual effects and many people may like their drug despite low efficacy or serious side effects (Silver, 2002). Because of the lack of “guidance”, the reliance on aggregating ADR mentions across all disease groups and ignoring the prescription backgrounds (microbiology and general lab tests, re-admission complians, and the degree of patient-specific risks, among others) and also ignoring drug safety challenges the normal distribution of data and the generalizability of results. Secondly, the emergence of location-based social networks demands the focus of the “context awareness” features of the agent infrastructure. The resulting new social structure generated by such networks generates new processes that significantly affect co-evolutionary processes and patient-centric interactions. Thirdly, relaxing ontological limitations is becoming essential. According to (Campbell and Shapiro, 1995), an ontology is a data model that “consists of a representational vocabulary with precise definitions of the meanings of the terms of this vocabulary plus a set of formal axioms that constrain interpretation and well-formed use of these terms“. Despite the existence of web-based ontologies such as Yahoo™, VerticalNet™ (Aseem et al., 2001) and common-sense ontologies (Lenat, 2001), the lack of data about diseases and their geographic dynamics on social networks complicates analysis. The optimization of classification trees (Campbell and Shapiro, 1995), semantic interoperability, schema integration and enhancement of information retrieval patterns can assist in the development of globally-aware intelligent Pharmacoinformatics applications. Fourthly, because co-evolutionary paradigms incorporate massive communication processes, attention should be paid to security concerns and the impact of sociomaterial representation of problems into “agent” formats.

CONCLUSION

The identification of ADRs in the public hospitals is still challenged by different internal and external challenges which are expected to continue. Despite the efforts exerted to use Pharmacoinformatics, internal hospital functionalities are able to detect a limited percentage of ADRs in a fragmented pattern. Even for ADR-concerned hospitals, the detection of ADRs does not include an assessment of drug’s safety and interactions. But, observations show that the focus on detecting and analyzing ADRs will continue to grow and gather momentum attention of policy makers and the community at large. While the diversity of intervention mechanisms will continue to shape the responsiveness of healthcare organizations, deploying intelligent information systems in healthcare organizations is also expected to grow as a result of the foreseen technological developments. Addressing situation-specific and agent-based issues are the main critical success factors especially in resource limited situations and complex organizational and institutional domains. The change of “mind sets” rather than "programs” enhances the effectiveness of co-evolutionary processes and allows for the incorporation of radical innovations into the niches of the pharmaceutical care systems.

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