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Assessment of "look-alike" packaging designs related to medication errors using information technology

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This study aimed to assess the similarity among press-through pack (PTP) sheets of pharmaceutical products in Japan. The appearance of PTPs was assessed using a pharmaceutical design database (PDD) of 2,750 pharmaceutical tablets comprising approximately 40 % of the 6,840 products marketed in Japan. Package sheet color (Sc), tablet color (Tc), character color (Cc), sheet line color (SLc), and upper color (Uc) were used to evaluate the uniformity of PTP sheet design. To assess the risk of misidentification, 1,000 prescriptions for 82,273 cancer patients were retrieved from 21,026,742 records in the claims database of the Japan Medical Data Center Co. Ltd., Tokyo, Japan. The most frequent PTP sheet colors for 143 drugs were Sc (silver), Tc (white), Cc (blue), SLc (none), and Uc (silver). The prescribing pattern of 1000 randomly chosen prescriptions was analyzed. Database records of prescriptions without tablets (n = 69), including only one PTP tablet (n = 292), and those with lack of PDD prescription data (n = 388) were excluded. Eventually, 236 prescriptions were evaluated. Fourteen prescriptions (5.9%) had PTP sheets with five matching elements and 29 had with four matching elements (12.3%). This novel PDD database for information technology concept easily identified similar PTP sheets involved in prescriptions dispensed in 18 % of evaluated cancer patients. The concept seems to be applicable for preventing look-alike dispensing errors.

1. Introduction

In the UK, dispensing errors occur in approximately 0.11-2.7 % prescriptions (James et al. 2009). Life threating medication errors were reported in 5.7% of all medication errors (Westbrook et al. 2010). Various pharmacy information technology strategies for preventing medication errors were tried such as bar code application (Young et al. 2010), robotic arms for dispensing of chemotherapy (Chen et al. 2013), tall man lettering (Chuang et al. 2012) and robotic systems to manage home-care medicines (Rantanen et al. 2017). In this decade, equipment for pharmacy practice has changed drastically. However, these technologies were not sufficiently widespread among pharmacies because of high initial costs, though these technologies are certainly able to prevent medication errors.

Contribution factors for medication errors include "work load", "similar drug name", "similar packaging" or "staff levels" etc. (James et al. 2009). Especially, medication errors caused by "look-alike" design was reported for approximately 7.6 % of dispensing errors (Ashcroft et al. 2005). Some cases caused by look-alike design were reported including label confusion and similar drug packaging design (Sawada 2015, Beverley et al. 1994, Shao et al. 2018). These look-alike designs were identified to cause a risk for medication errors (Thornton et al. 2016, Voelker et al. 2015) and some of these were regarded as the safety risk by the FDA (FDA Drug Safety Communication 2015). In 2007, the World Health Organization announced "look-alike, sound-alike medication names" that induced severe medication errors and suggested actions for preventing these errors (WHO Collaborating Centre for Patient Safety Solutions 2007). In this document, (1) continued production and marketing of look-alike, sound-alike drugs, (2) costs related to the introduction of prescribing technology applications are cited as potential barriers to prevent "look-alike" and , "sound-alike" errors.

In Japan, 6,840 tablet drugs are marketed in press through packs (PTPs) (National Health Insurance drug list 2017). Tsuchiya F (2002) has described the usefulness of a PTP sheet design database, but the concept has not been implemented as far as we know. This study involved the design and development of a database of the design elements of PTP sheets currently used in Japan for the marketing of tablet medications as a pharmacy information technology and analyzed the potential medication error risk assessment using a large claims data in Japan.

2. Investigations, results and discussion

2.1. The database and assessment of PTP sheet design

A pharmaceutical design database (PDD) was developed in Microsoft Access 2016 to assess the concordance of PTP sheet appearance (Fig. 1). The characteristics of 2,750 pharmaceutical tablets comprising approximately 40 % of the 6,840 products marketed in Japan were input. Pictures of the product PTPs were downloaded from the websites of 50 of the 67 members of Japan Pharmaceutical Manufacturers Association. The fields entered for each PTP record were sheet color (Sc), tablet color (Tc), character color (Cc), sheet line color (SLc), and upper color (Uc) (Fig. 2). The concordance of the five design elements was used to assess the similarity in appearance. A match of four or five elements was considered as an indication of a high risk of similar appearance.

2.2. Prescribing patterns in cancer patients to analyze the potential medication error risk assessment

Prescription patterns likely to result in increased risk of PTP with a similar appearance were identified by evaluating claims data filed between January 2005 and January 2016 and were received

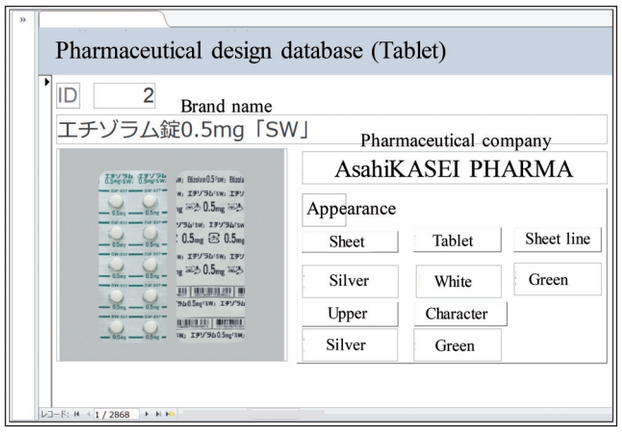

Fig. 1: The pharmaceutical design database.

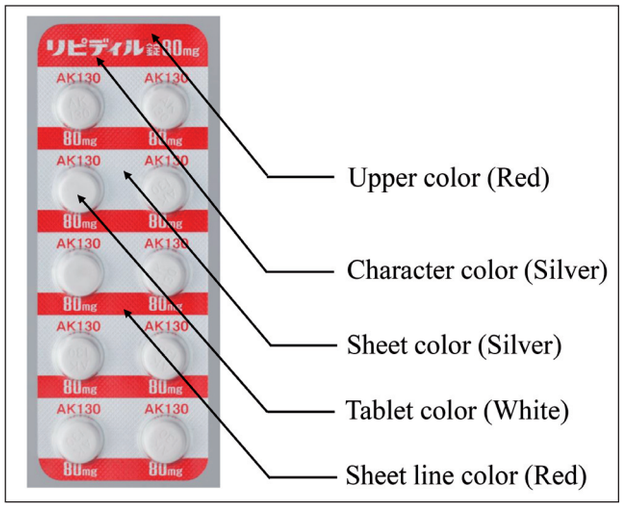

Fig. 2: Color example of five design elements.

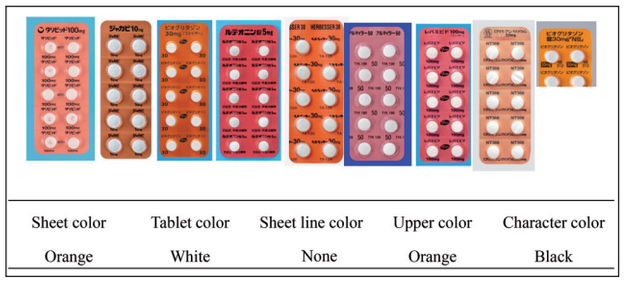

Fig. 3: Examples of five design elements used to match look-alike drug packaging (Orange sheet color, white tablet color, no sheet line color, orange upper color, black character color).

from a database maintained by the Japan Medical Data Center (JMDC) Co. Ltd., Tokyo, Japan. The JMDC collects medical and pharmacy claims from more than 50 occupation-based public health insurance agencies for corporate employees and their family members. In August 2016, the database included 3,600,000 recipients aged 0–74 years representing 2 % of the population in Japan. To assess the clinical risk, we randomly retrieved 1,000 prescriptions for 82,273 cancer patients from among 21,026,742 claims records. PTPs were assessed for concordance using data included in PDD. Data were expressed as medians with ranges or means±standard deviation.

2.3. *Pattern analysis for PTP sheet designs*

The most frequent PTP color variation pattern found in 143 of the drugs (5.2 %) was silver Sc, white Tc, blue Cc, none SLc, and silver Uc. The second most frequent was silver Sc, white Tc, green Cc, none SLc, and silver Uc found in in 120 drugs (4.4 %), followed by silver Sc, white Tc, blue Cc, blue SLc, and silver Uc in 81 drugs (2.9 %). The color variations identified in the five PTP elements included 606 patterns in 2,750 drugs. Of the 606 PTP patterns, there were 269 (44.4 %) PTP patterns that included 4 (2–143) of the same color variants PTP sheet drugs. The remaining 337 PTP patterns (55.6 %) had no look-alike drugs. For example, designs for five elements matching pattern for Orange Sc, White Tc, None Sc, Orange Uc, Black Cc was observed 9 drugs (Fig. 3).

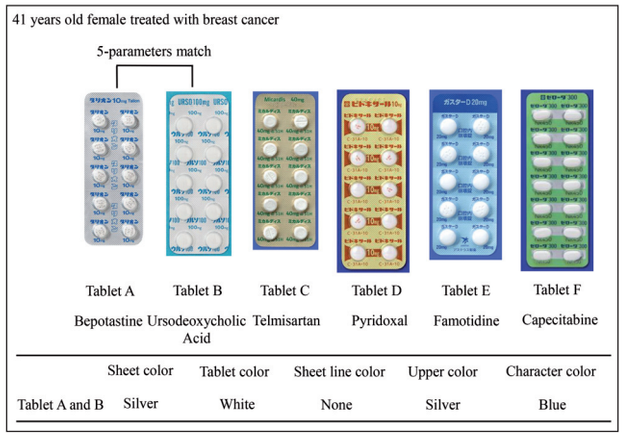

Fig. 4: A 41-year-old female cancer patient treated with six drugs that had PTPs with five parameters that matched concurrent prescriptions.

2.4. *Typical case of prescribed "look-alike" drugs prescribed for cancer patients*

A representative 41-year-old woman patient taking drugs to treat breast cancer was coadministered drugs for hypertension and rhinitis. A total of six drugs were prescribed to her: bepotastine, ursodeoxycholic acid, telmisartan, pyridoxal, famotidine, and capecitabine. The PDD database data indicated that all five PTP elements of bepotastine and ursodeoxycholic acid packaging matched (Fig. 4).

Table 1: Patient characteristics

Subjects	236
Age [mean (SD)]	55.8 (11.8)
Male [n (%)]	124 (52.5)
Female [n (%)]	112 (47.5)
Cancer type	
Gynecological cancer [n (%)]	57 (21.2)
Colonic cancer [n (%)]	43 (16.0)
Gastric cancer [n (%)]	31 (11.5)
Disease	
Metabolic disorders [n (%)]	150 (5.5)
Diabetes mellitus [n (%)]	110 (4.0)
Hypertension [n (%)]	108 (3.9)

2.5. *Frequency for "look-alike" drugs in cancer patients using a large claim data*

The drug-prescribing pattern was assessed in 236 cancer patients (124 men and 112 women) aged 55.8±11.8 years (Table 1). Fifty-seven patients had gynecological cancer, 43 had colon cancer, and

Table 2: Number of combinations of appearance-matching PTP parameters

Number of co-administration drugs [Median (range)]	3 (2–14)	
Number of sheet based tablet [Median (range)]	2 (2–11)	
Number of combinations of appearance-matching parameters of sheet-based tablet	Combination	Prescription
5 parameters match	16	14
4 parameters match	41	29
3 parameters match	87	59
2 parameters match	192	101

31 had gastric cancer. The median number of coadministered drugs was 3 (range 2–14). The median number of coadministered drugs that were tablets packaged in PTPs was 2 (2–11). Fourteen of the tablet formulations had PTPs with five matching elements (5.9 %), and 29 tablets had PTPs with four matching elements (12.3 %, Table 2).

3. Discussion

In this study, we built a novel concept for PDD database as a pharmacy information technology to find PTP sheets with matching elements and look-alike designs (Figs 1, 2 and 3). To analyze the potential medication error risk using the PDD database, PTP sheets with four or five matching design elements were identified in 18.2 % of cancer patients for simultaneously prescribed.

Medical error costs were estimated to approximately $17.1 billion annually (Van Den Boos et al. 2011). In this report, less than 4 % of all errors were medication errors. “Look-alike” design confusion has been considered because pharmaceutical industry continues marketing new products without sufficient research for packaging designs. Our concept for PDD database could easily pick up the look-alike package design drugs from numerous drugs. To identify drugs with potential for look-alike errors from PDD, and put the labels (drug storage shelf etc.) may potentially prevent harm.

The risk assessment using large claim data suggests that 18 % of cancer patients are exposed to potential look-alike medication errors (Table 2, Fig. 4). In general, some of cancer patients have low physical, mental or cognitive function. In these patients, if pharmacists dispensed wrong drugs caused by “look-alike” errors will leads to critical outcomes.

In pharmacy practice, easily updatable and low cost information technology for the prevention of medical errors is needed. So, information technology preventing package design related look-alike medication errors is applicable for most of pharmacies for making documents on the announcement for staffs on attention of “look-alike” designs from numerous drugs stored at the pharmacy, because 85 % of pharmacists experience potential “look alike” dispensing errors (Watanabe et al. 2012; Mohri et al. 2002). It may also be useful for making information leaflets for patients to prevent miss-taking, because 18.2 % of cancer patients are taking “look-alike” design drugs simultaneously (Tables 1 and 2, Fig. 4).

In conclusion, our PTP database can be easily pick up the “look-alike” drugs and update information following new drugs approved or changes in the packaging elements by the pharmaceutical industry. The database will be of use to pharmacists when dispensing drugs, to the drug industry for PTP sheet design, and to patients. Pharmacists should pay attention to the PTP design and instruct patients who are prescribed similar drugs. Our concept for pharmacy information technology of packaging design provides a tool to prevent design related medication errors, not only for PTP tablet but also injections, topical agents, vials etc.

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Conflict of interest: None declared.

References

Ashcroft DM, Quinlan Blenkinsopp A (2005) Prospective study of the incidence, nature and causes of dispensing errors in community pharmacies. Pharmacoepidemiol Drug Saf 14: 327-332.

Orser BA, Oxorn DC (1994) An anaesthetic drug error: minimizing the risk. Can J Anaesth 41: 120-124.

Chen WH, Shen LJ, Guan RJ, Wu FL (2013) Assessment of an automatic robotic arm for dispensing of chemotherapy in a 2500-bed medical center. J Formos Med Assoc 112: 193-200.

Chuang MH, Wang YF, Chen M, Cham TM (2012) Effectiveness of implementation of a new drug storage label and error-reducing process on the accuracy of drug dispensing. J Med Syst 36: 1469-1474.

FDA Drug Safety Communication FDA cautions about dose confusion and medication errors for antibacterial drug Zerbaxa, [05-20-2015].

James KL, Barlow D, McArtney R, Hiom S, Roberts D, Whittlesea C (2009) Incidence, type and causes of dispensing errors: a review of the literature. Int J Pharm Pract 17: 9-30.

Mohri R, Katoh H, Terasawa K, Mizutani K, Kondoh K, Matsuzaki N (2002) Touin niokeru Tyouzaikago no Jittai ni tsuite (Analysis for the dispensing error in our hospital). J Muroran City Gen Hosp 27: 64-66 [Published in Japanese].

National Health Insurance drug list from Medical Professions Division, Health Insurance Bureau Ministry of Health and Welfare. Ver. 1/Apr/2016. http://www.mhlw.go.jp/topics/2014/03/tp0305-01.html (assessed 2017 Dec 14).

Rantanen P, Parkkari T, Leikola S, Airaksinen M, Lyles A (2017) An in-home advanced robotic system to manage elderly home-care patients’ medications: a pilot safety and usability study. Clin Ther 39: 1054-1061.

Sawada Y (2015) Housouruijki no Kusuri wo Maikai Mushimegane de Kakunin shite Shikuhakku shiteita Kanja (A case with similar design drugs depending troubles). Tyouzai to Jouhou. 21: 91-97 [Published in Japanese].

Shao SC, Lai EC, Owang KL, Chen HY, Chan YY (2018) Look-alike medication packages and patient safety. J Patient Saf 14: e47-e48.

Thornton P (2016) Medication safety. J Pharm Pract Res 46: 52-56, 156-168, 269-276.

Tsuchiya F (25 Dec 2002) Med safe.Net. “Ebidensu ni Motozuita Iryoujiko no Boushisaku ga Kanounnaru!?” (Prevention for the medical error based on the evidence) http://www.medsafe.net/recent/16ikashika.html (assessed 2017 Dec 12) [Published in Japanese].

Van Den Bos J, Rustagi K, Gray T, Halford M, Ziemkiewicz E, Shreve J (2011) The $17.1 billion problem: the annual cost of measurable medical errors. Health Aff. (Millwood) 30: 596-603.

Voelker R (2015) Label confusion leads to errors. JAMA 314: 17.

Watanabe Y, Sato H, Minagawa T, Tsukioka R, Sugiyama Y, Okayama Y, Ishima Y, Watanabe H, Kadowaki D, Anraku M, Maruyama T (2012) Effect of the similarity in appearance of PTP packaging between original and generic drug products on safety management for medication. Jpn J Pharmaceut Health Care Sci 38: 18-24 [Published in Japanese].

Westbrook JI, Woods A, Rob MI, Dunsmuir WT, Day RO (2010) Association of interruptions with an increased risk and severity of medication administration errors. Arch Intern Med 170: 683-690.

WHO Collaborating Centre for Patient Safety Solutions (May 2007) look-alike, Sound-alike medication names, Patient Safety Solutions, 1 (1).

Young J, Slebodnik M, Sands L (2010) Bar code technology and medication administration error. J Patient Saf 6: 115-120.