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Original Research

Implementing Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome management system by hospital pharmacists in Samutsakhon Hospital, Thailand

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Abstract

Objectives: To study the process of implementing the DRESS management system by pharmacists and its results, during 2016-2020. **Research method:** Operational Research, starting from the process of implementing the DRESS management system by the pharmacy department of Samutsakhon Hospital and reporting the results to the Pharmacy and Therapeutic Committee in patients diagnosed with DRESS according to the RegiSCAR criteria, collecting data from an electronic medical records database. **Study results:** The main DRESS management system implementation process is: 1) listing the High alert drugs which may cause an adverse reaction and preparation of pharmacists in DRESS; 2) Using RegiSCAR for patient assessment; 3) Suggesting a genotyping test before the patient receives the drug, starting with carbamazepine and allopurinol; 4) Using a Computerized Decision Support System (CDSS) to facilitate the screening alert. 5) Proposing to the Pharmacy and Therapeutic Committee for approval on gene testing. As a result, a total of 184 patients were sent for genotyping testing, and 92 of the drug allergy genes were identified, making the prevention or monitoring of patients more effectively. 31 patients were diagnosed with DRESS, and 54.84% were male. The 4 drug items with the highest incidence were phenytoin 28.95%, nevirapine 10.53%, rifampicin 7.89%, and pyrazinamide 7.89%. Clinical symptoms were rash 100.00%, fever 90.32%, lymphadenopathy 6.45%, at least one dysfunction in the internal organ system 74.19%, liver dysfunction 80.65%, and eosinophilia 58.65%. Phenytoin had a statistically significant induced eosinophil (p=0.044), which could be used as a factor in the CDSS drug surveillance. **Conclusion:** Even DRESS is a rare adverse drug reaction symptom but causes life-threatening. Continuous system management by pharmacists is significant with a huge effect. In the drug items, the highest incidence was phenytoin. Implementing a system to monitor patients' drug use, could reduce DRESS, and prevent the recurrence of drug allergies.

Keywords: DRESS; drug allergy; pharmacist; implementation; genotyping test; high alert drug

INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS) is an adverse drug reaction symptom which is a rare condition but life-threatening. The mortality rate can be up to 10%.[1] In Thailand, the prevalence rate of DRESS cases in hospitalised patients is around 9.63 cases per 100,000 patients.[2] The clinical symptoms of DRESS can be wide-ranging. The three main symptoms are fever, cutaneous eruption, and internal organ dysfunction such as blood disorders, hepatitis, kidney disorders, and neurological symptoms were found. The symptoms of DRESS commonly last longer than others. It can occur in the first 2-6 weeks after receiving the drug. However, if repeated receive such drugs the symptoms may occur rapidly and severely. Also, the symptoms will persist for a week even after stopping using the drug that caused it. Other symptoms, such as muscle pain and sore throat with swollen lymph nodes, can be found as well. Due to the beginning of DRESS's symptoms similar to an infection, therefore, the patient may get misdiagnosed the first time of treatment, and the patient will be sent to treatment again with more severe symptoms. About 10% of patients have died from internal organ system failure, especially liver failure. It includes the infection that leads to septic shock. At the time DRESS was found, the general accompanying diseases were: epilepsy, HIV, hypertension, diabetes, and hyperuricemia.[3]

Drugs that cause DRESS were antiepileptic in the class of the aromatic ring, such as phenytoin, carbamazepine, and phenobabital; drugs in the antibiotic class, such as cotrimoxazole, nevirapine, dapsone; and other drugs such as allopurinol. It can estimate the risk of DRESS in patients who receive such drugs is as high as 1:1,000 to 1:10,000 people.[1,2] Thus, when receiving high-risk drugs that DRESS can occur, surveillance systems should be in place to prevent the drug allergy in line with the duration of that symptom showing and

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clinical signs. So that patients can be treated and follow up on the complications promptly. For the said reasons, this study is purposed to examine the role of hospital pharmacists in monitoring and practising in order to minimize DRESS incidence in patients, as well as can be diagnosed on time when adverse reactions occur before it develops into more danger.

Many studies and research can help to understand the clinical symptoms of pathophysiology, comorbidity, drugs that increase the risk of DRESS occurring, and how to treat DRESS; as well as more understanding of relevant factors, such as race and human leukocyte antigen (HLA) alleles, which it found to be relevant with Cutaneous Adverse Drug Reaction (cADR). Even having such understanding, a proactive surveillance process that aims to prevent and screen, including through HLA alleles,[4] before the patient receives the drugs is still important to the safety of patients.

Samutsakhon Hospital is a public hospital under the Ministry of Public Health. It is a tertiary care centre hospital with a size of 602 beds. As an A-level hospital, it has specialised members of staff and advanced technology, and the number of outpatient cases is around 980,000- 1,100,00 a year. In an intention and consideration for the safety of patients, especially in drug use, the pharmacy department decided to conduct operational research[5] to study the hospital's problems regarding the risks of drug use that DRESS may occur. The study aims to find suitable measures for increasing the effectiveness of the safety of using drugs that are at high risk of drug allergy, which is in a class of high alert drugs, in order to coordinate, practice, and present the policy to Pharmacy and Therapeutic Committee (PTC) for further decision-making.

OBJECTIVE

To study the process of implementing the system of DRESS management by pharmacists of Samutsakhon Hospital and report the results of the implementation of such system from 2016 to 2020.

RESEARCH METHOD

This study was an Operational Research conducted by pharmacists of the Pharmacy Section for surveillance of ADRs and to improve the safety of patients who use drugs that are at risk of severe drug allergy. Since the DRESS management system in Samutsakhon Hospital became more concrete in 2015. Therefore, to study the tendency of the effectiveness of surveillance systems for high-risk drugs, the process of systematising the DRESS management used the concept of operational research[5] (see Figure 1) and planning to collect data on the surveillance results of ADRs in the patients who diagnosed with drug allergy as DRESS at Samutsakhon Hospital between 2016-2020. This research also collected data from the hospital's electronic medical index database. The collected data were lists of drugs found in patients diagnosed with drug allergy as DRESS, together with a study of clinical symptoms, laboratory examination results, and patient management. There are four pharmacists in the Pharmacy department of Samutsakhon Hospital, who are the main administrators of the DRESS management system. One of whom received a Board Certified of Pharmacotherapy, is a head of ADR monitoring center. One pharmacist received a certificate of general residency in pharmacotherapy and the remaining two of them are PharmD pharmacists.

Guidelines have been drawn up for diagnosis criteria, the criteria used in this study was the European Registry of Severe Cutaneous Adverse Reactions (RegiSCAR). The criteria included fever > 38.5°C, two or more swollen lymph nodes, skin rash, at least one internal organ dysfunction; blood disorders such as found leukopenia at the beginning or leukocytosis in the later stages; atypical lymphocyte, eosinophilia, thrombocytopenia, and past viral infections can be detected. Such information was evaluated with a RegiSCAR, and the score was divided into definite, probable, possible, and no case. It was used in this study only for patients evaluated as definite, probable, and possible. (Figure 2)

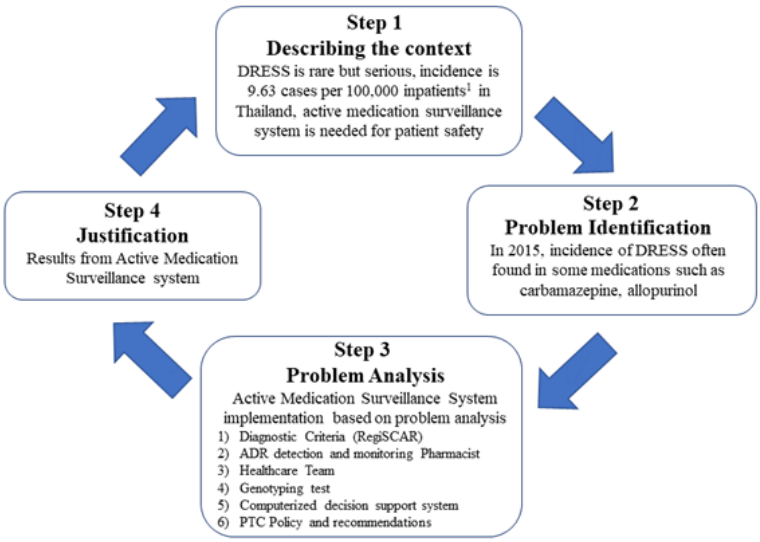

Figure 1. Operational Study of DRESS Surveillance System

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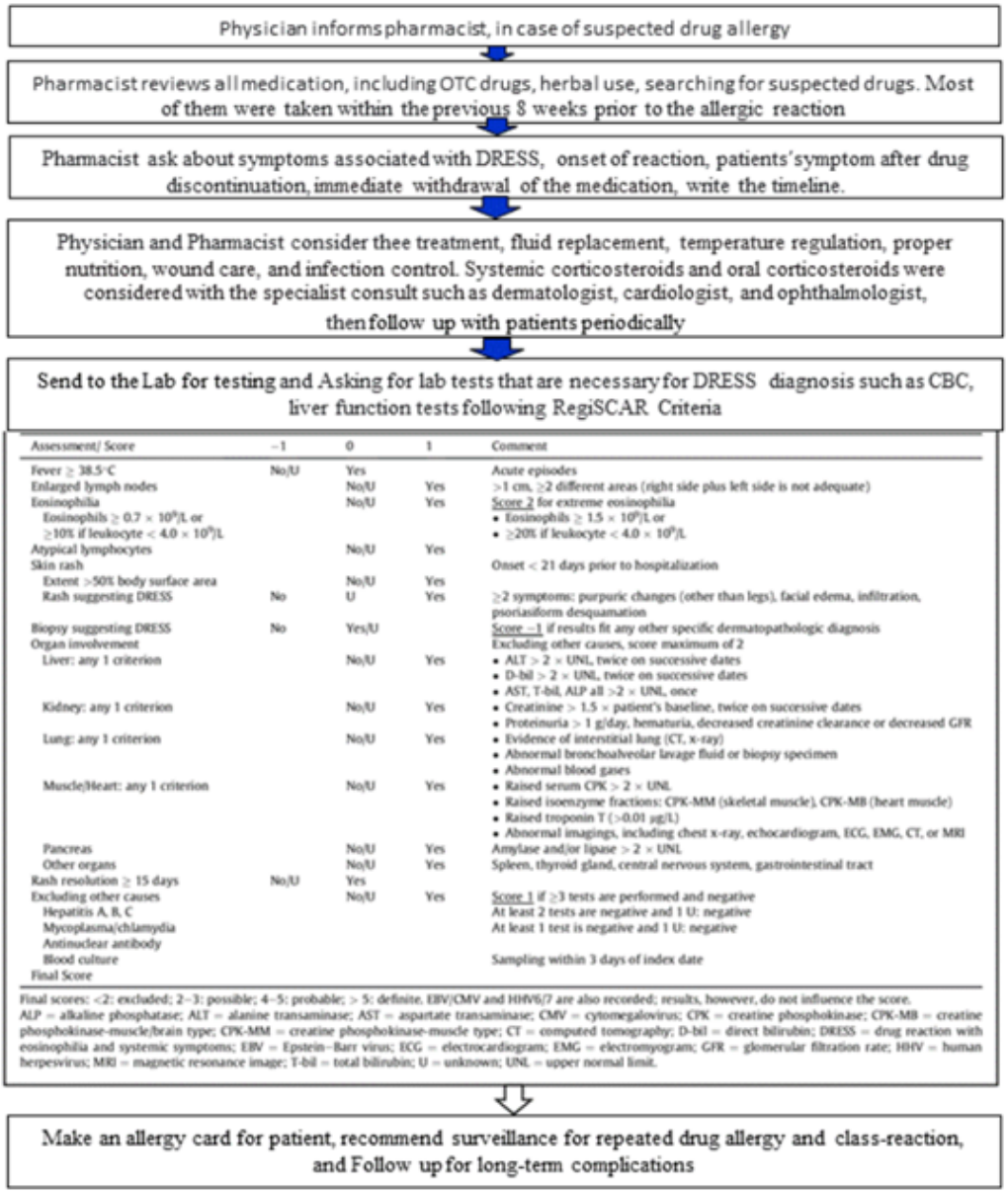

Assessment/ Score	−1	0	1	Comment
Fever ≥ 38.5°C	No/U	Yes		Acute episodes
Enlarged lymph nodes		No/U	Yes	>1 cm, ≥2 different areas (right side plus left side is not adequate)
Eosinophilia		No/U	Yes	Score 2 for extreme eosinophilia
Eosinophils ≥ 0.7 × 10^9/L or ≥10% if leukocyte < 4.0 × 10^9/L				• Eosinophils ≥ 1.5 × 10^9/L or • ≥20% if leukocyte < 4.0 × 10^9/L
Atypical lymphocytes		No/U	Yes	
Skin rash				Onset < 21 days prior to hospitalization
Extent >50% body surface area		No/U	Yes	
Rash suggesting DRESS	No	U	Yes	≥2 symptoms: purpuric changes (other than legs), facial edema, infiltration, psoriasiform desquamation
Biopsy suggesting DRESS	No	Yes/U		Score −1 if results fit any other specific dermatopathologic diagnosis
Organ involvement				Excluding other causes, score maximum of 2
Liver: any 1 criterion		No/U	Yes	• ALT > 2 × UNL, twice on successive dates • D-bil > 2 × UNL, twice on successive dates • AST, T-bil, ALP all >2 × UNL, once
Kidney: any 1 criterion		No/U	Yes	• Creatinine > 1.5 × patient's baseline, twice on successive dates • Proteinuria > 1 g/day, hematuria, decreased creatinine clearance or decreased GFR
Lung: any 1 criterion		No/U	Yes	• Evidence of interstitial lung (CT, x-ray) • Abnormal bronchoalveolar lavage fluid or biopsy specimen • Abnormal blood gases
Muscle/Heart: any 1 criterion		No/U	Yes	• Raised serum CPK > 2 × UNL • Raised isoenzyme fractions: CPK-MM (skeletal muscle), CPK-MB (heart muscle) • Raised troponin T (>0.01 μg/L) • Abnormal imagings, including chest x-ray, echocardiogram, ECG, EMG, CT, or MRI
Pancreas		No/U	Yes	Amylase and/or lipase > 2 × UNL
Other organs		No/U	Yes	Spleen, thyroid gland, central nervous system, gastrointestinal tract
Rash resolution ≥ 15 days	No/U	Yes		
Excluding other causes		No/U	Yes	Score 1 if ≥3 tests are performed and negative
Hepatitis A, B, C				At least 2 tests are negative and 1 U: negative
Mycoplasma/chlamydia				At least 1 test is negative and 1 U: negative
Antinuclear antibody				
Blood culture				Sampling within 3 days of index date
Final Score				

Final scores: <2: excluded; 2–3: possible; 4–5: probable; > 5: definite. EBV/CMV and HHV6/7 are also recorded; results, however, do not influence the score.
ALP = alkaline phosphatase; ALT = alanine transaminase; AST = aspartate transaminase; CMV = cytomegalovirus; CPK = creatine phosphokinase; CPK-MB = creatine phosphokinase-muscle/brain type; CPK-MM = creatine phosphokinase-muscle type; CT = computed tomography; D-bil = direct bilirubin; DRESS = drug reaction with eosinophilia and systemic symptoms; EBV = Epstein–Barr virus; ECG = electrocardiogram; EMG = electromyogram; GFR = glomerular filtration rate; HHV = human herpesvirus; MRI = magnetic resonance image; T-bil = total bilirubin; U = unknown; UNL = upper normal limit.

Figure 2. Protocol of DRESS Management by hospital pharmacists in Samutsakhon Hospital

For the part of drug allergy, Naranjo's algorithm was used to evaluate, and it was divided into certain, probable, possible, and unlikely. Similar to the RegiSCAR evaluation, only patients evaluated as certain, probable, and possible were used in this study.

Mann-Whitney U test was used for quantitative data analysis and Chi-square for qualitative data, and $p < 0.05$.

STUDY RESULTS

When starting the DRESS surveillance process, which was carried out by the hospital pharmacists and using an Operational Study continuously, it was found that the number of DRESS in patients was reduced, especially when consulting and asking the physician to conduct the genotyping test in patients who began using carbamazepine, and gradually reduce when asking the doctor to conduct allergy gene testing in patients who receiving allopurinol. Finally, the DRESS evaluation report was presented to PTC in order to approve the hospital's policy for the genotyping test in patients who start to receive three types of drugs, namely carbamazepine, allopurinol and abacavir, as shown in Table 1 and Figure 3.

Results of DRESS management in 2016-2020

The total number of patients admitted to Samutsakhon Hospital during 2016-2020 was 36 diagnosed with DRESS, among which patients met the criteria of RegiSCAR 31 cases and were divided into 2 definite (6.45%), 11 probable (35.48%), and 18 possible (58.07%).

For patients' general information, there were 17 males and

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Table 1. Genotyping test for high alert drugs in Samutsakhon Hospital during 2017-2020

Genotyping test in hospital	Drugs	Number of Genotyping test (n)	% Positive Genotyping	Prevalence of drug-induced DRESS in Thailand
HLA-B*1502	Carbamazepine	34	9 (26.47%)	1.4-10.2% carbamazepine-induced DRESS[7,19,2]
HLA-B*5801	Allopurinol	95	19 (20.0%)	14.8-15.4% Allopurinol-induced DRESS[6,7,19]
HLA-B*5701	Abacavir	55	3 (5.45%)	1-9% Abacavir-induced hypersensitivity reaction[21]
-	Phenytoin	-	-	20.8% phenytoin-induced DRESS[22]

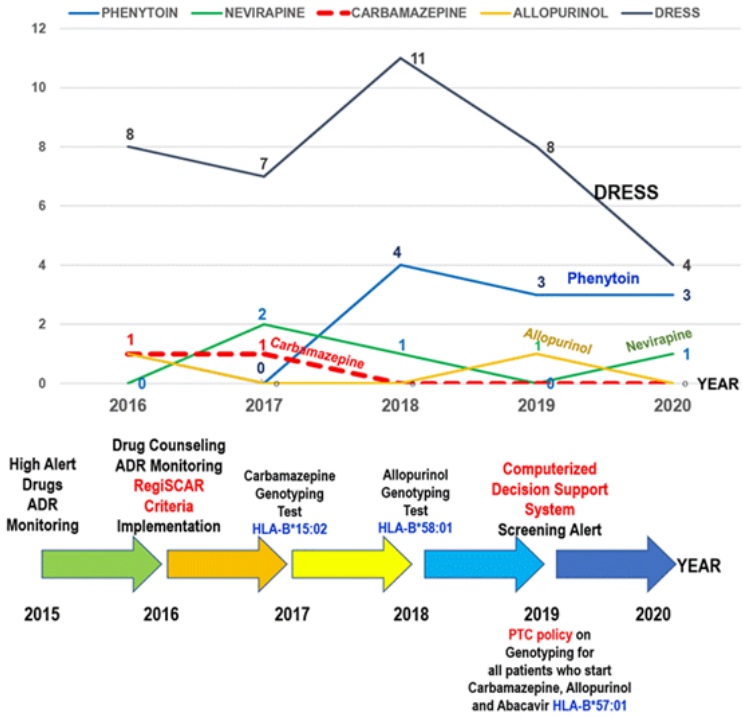

Figure 3. DRESS Management System and DRESS trends in Samutsakhon Hospital: 2015-2020

14 females, with a 1.2:1 ratio of males to females, and the median age was 49. It is found that phenytoin was associated with DRESS in middle-aged patients, and nevirapine in late adolescence, with statistically significant (p=0.048 and 0.054). The median range for the number of days patients received the drug to the day of diagnosis was 18 days (IQR 10 - 30 days). The number of days in which a patient was hospitalised, starting from 1 to 101 days, the median of hospital stay days was 10 days (IQR 3.5 - 23.5 days).

A medical history of drug allergy was found in 5 cases (16.13%), with 1 patient having allergy to dicloxacillin. The symptoms were pruritic rash on the back and abdomen, no chest tightness or unable to breathe, and being DRESS drug allergy type.

The four drugs with the highest incidence were phenytoin 11 (28.95%), nevirapine 4 (10.53%), rifampicin 3 (7.89%), and pyrazinamide 3 (7.89%).

The clinical symptoms are shown in Table 2. Most of the patients (28 people or 90.32%) had a fever higher than 38.5 °C. 24 patients (77.42%) had a rash greater than 50% of their body surface. All patients (100%) had cutaneous manifestations. The most common skin rashes were Maculopapular (MP) rash (90.32%), and other cutaneous manifestations included angioedema, facial edema, mouth ulcer, genital ulcers, and eye inflammation.

23 patients (74.19%) had one internal organ disorder, and 4 had two or more. Found 3 cases with both liver and kidney dysfunctions. The liver was the most common visceral organ at 80.65%, with a median alanine aminotransferase level (ALT) of 225 IU/L (IQR 149 - 273 IU/L). The second most common organ dysfunction was kidney in 5 cases (16.13%). It was found that receiving phenytoin resulted in more kidney dysfunction than other drugs. 2 heart abnormalities were found (6.45%).

For blood system disorders, eosinophilia was reported in 18 patients (58.06%), and those who received phenytoin had a statistically significantly higher rate of eosinophilia (p=0.044) (Table 3). The % eosinophil was 15% (IQR 9.30 - 18.90%), and the eosinophil cell count was 1,066 cell/µL (IQR 847 - 1711.50 cell/µL). Among 13 patients (41.94%), atypical lymphocyte was reported with a % atypical lymphocyte (IQR) of 2% (2 - 4%), and thrombocytopenia was reported in 6 patients (19.35%) with platelet count (IQR) 122,000 cell/µL (100,750 - 134,250 cell/µL). Most of the patients (28 or 90.32%) had lymphocytosis with a lymphocyte count (IQR) of 8,000 cell/µL (5,900 - 10,875 cell/µL).

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Table 2. Characteristics of patients with DRESS (n=31)	
General information of the patient	Number (percentage)
Gender: Male:Female	17 (54. 84):14 (45.16)
Age (The median of years, IQR Median)	49 (33.00 - 59.00)
Number of days that hospitalised (The median number of days, IQR median)	10 (3.50 - 23.50)
Number of days that the patient received the drug until the diagnosis	18 (10.00 - 30.00)
Initial assessment	
Drug reaction with eosinophilia and systemic symptoms (DRESS)	18 (58.06)
Drug allergy	8 (25.81)
Drug hypersensitivity	3 (9.68)
Other	2 (6.45)
Evaluation level according to RegiSCAR score	
Definite (score > 5)	2 (6.45)
Probable (score 4-5)	11 (25.48)
Possible (score 2-3)	18 (58.07)
Medical history of drug allergy	5 (16.13)
Underlying disease/Medical condition	
Hypertension	13 (41.94)
Human Immunodeficiency Virus (HIV) infection	8 (25.81)
Dyslipidemia	7 (22.58)
Ischemic stroke	6 (19.35)
Tuberculosis	5 (16.13)
Convulsion disorder	4 (12.90)
Diabetes mellitus	3 (9.68)
Chronic kidney disease	3 (9.68)
Hyperuricemia	2 (6.45)
Other	9 (29.03)
Treatment	
Systemic steroid	19 (61.29)
No treatment/Only anti-histamine	26 (83.87)

Table 3. Clinical symptoms and features of DRESS syndrome	
Clinical Symptom	Number (percentage)
Fever (temperature)≥38.5 degree Celsius	28 (90.32)
Lymphadenopathy	2 (6.45)
Skin condition	
Rash areas > 50% of the surface	24 (77.42)
The rash that is compatible with DRESS	31 (100.00)
- MP rash	28 (90.32)
- agioedema	5 (16.13)
- facial edema	5 (16.13)
- mucous involvement	5 (16.13)
- conjunctivitis	3 (9.68)
- patch	3 (9.68)
Other body system symptoms	
1 organ involvement	23 (74.19)
2 or more organ involvement	4 (12.90)
- liver	25 (80.65)
alanine aminotransferase level IU/L (IQR median)	225 (149 - 273)
- kidney	5 (16.13)
- heart	2 (6.45)
Blood system	
eosinophilia	18 (58.06)
- % eosinophil (IQR median)	15 (9.3 - 18.9)
- eosinophil cell count /µL (IQR median)	1,066 (847 - 1,711.50)
atypical lymphacyte	13 (41.94)
- % atypical lymphocyte (IQR median)	2 (2 - 4)
lymphocytosis	28 (90.32)
- lymphocyte count /µL (IQR median)	8,000 (5,900 - 10,875)
thrombocytopenia	6 (19.35)
- platelet count /µL (IQR median)	122,000 (100,750 - 134,250)

2 patients died during the study, both of whom were taken phenytoin, one as an unknown cause, and the other was unrelated to drug allergy.

DISCUSSION

The study found that the occurrence of DRESS from anticonvulsants in the aromatic ring class was 34.21% of all patients, and the main cause drug was phenytoin (28.95%) (Figure 4). The research of this study is in line with other as well.[1-4] However, for anticonvulsants in the aromatic ring class allergy, there is clear evidence that there is an approximately 70-80% chance of cross-reactivity. Whereas in this study, no cross-reactivity was found. Therefore, 11 patients diagnosed with phenytoin-induced DRESS should be switched to anticonvulsants in the non-aromatic ring class, such as levetiracetam or valproic acid.

The number of patients with DRESS from nevirapine was 10.53%, with the second most common cause following phenytoin (Figure 4), by the median number of days that the patient received the drug until the patient's diagnosis was 21.5 days (IQR 16.75 - 32.75 days). Consistent with other studies conducted in Thailand, the study by Pranee Wongkitsophon et al.[6] collected data from 27 patients who were diagnosed with DRESS. 4 patients were treated with nevirapine (14.80%), which was second after phenytoin. The median time from the drug received until patients were diagnosed with drug allergy was 10 days (range between 5 and 25 days). In the study of Akarin Hiransuthikul et al.,[7] which found 17.30% or 9 of those received nevirapine which was also second only to phenytoin. This was associated with a statistically significant increase in ALT two weeks after being diagnosed with DRESS (p=0.005). In this study, one female patent who started receiving nevirapine while having a CD4 level > 250 cells/mm3, could increase the risk of rash by 50% with symptoms associated with severe hepatitis up to 11%, which is one of the symptoms of DRESS. Currently, Thailand has guidelines for the treatment and

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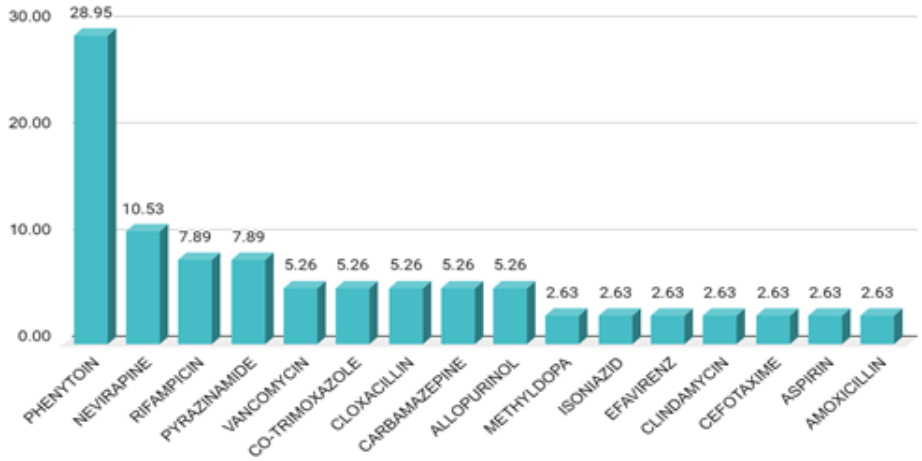

Figure 4. Drugs-induced DRESS in 2016-2020

prevention of HIV,[8] it will recommend the efavirenz in the class of non-nucleoside reverse transcriptase inhibitors (NNRTIs) instead of nevirapine. In this regard, when considering the structural formula, it was found that both drugs have different chemical formulas, so there is a low chance of cross-reactivity. According to the study by Manosuthi et al.[9] However, the World Health Organization's anti-HIV drug treatment guidelines recommend that NNRTIs should not be given in cases of severe drug allergy.[10]

Drugs that induced the DRESS next in line were rifampicin (7.89%), pyrazinamide (7.89%), and isoniazid (2.63%), which were included in the treatment for Tuberculosis. The median and duration of the received until the patient was diagnosed with the allergy were 30, 13 and 30 days, respectively. It is consistent with the Tipsiri Chaikong[11] study showed 229 data from the Health Product Vigilance Center, the Food and Drug Administration of the Ministry of Public Health. The estimated incidence of DRESS was 1 - 3 patients per 10,000 patients per year. Drugs like rifampicin and isoniazid were the main cause of SCARs, with 23.30% and 21.36%, respectively, while ethambutol, streptomycin, and pyrazinamide were found to be 19.42%, 19.42%, and 16.50%, respectively. Duration from drug received to the occurrence of DRESS for the study was a median of 31 days. In the process of treating Tuberculosis, patients should be starting at low doses, approximately 1/10th of the usual daily dose based on the low to the high incidence of skin reactions were streptomycin, followed by ethambutol, pyrazinamide, rifampicin, and isoniazid, respectively.[12]

The median number of days in which patients were dosed to the date of diagnosis of patients for this study was 18 days, which was close to that of the previous RegiSCAR study, which was 22 days,[13] and for Akarin Hiransuthikul's study was16 days.[7]

For skin rashes, it was found that the rash caused by the DRESS drug allergy was different in many forms. In this study, the majority of MP rash was found in 28 patients (90.32%). Other symptoms included angioedema in 5 patients (16.13%), facial edema in 5 patients (16.13%), and mucosal inflammation symptoms were also found, such as mouth ulcers, eye inflammation, and genital ulcers in 5 patients (16.13%).

In the proportion of patients experiencing dysfunction in internal organs liver dysfunction was found the most (80.65%), consistent with the study in Thailand by Akarin Hiransuthikul et al.,[7] which also showed the highest proportion of DRESS patients with liver dysfunction. It includes the study of Cacoub et al.,[15] which found 172 DRESS patients, and according to RegiSCARS, 94.00% of patients had the most liver dysfunction.

The proportion of kidney dysfunction was similar to the previous study at 16.00 - 53.00%, 2 of 5 patients with phenytoin-related kidney dysfunction without a medical history of underlying kidney disease before had been diagnosed with a drug allergy. In this study, phenytoin caused an increase in serum creatinine, but no statistically significant difference was found.

For blood system disorders, eosinophilia was found at 58.06%. Studies inside and outside Thailand showed a wide range from 48.00 to 95.00% [15-17]–and found similar values in the study of Akarin Hiransuthikul et al.[7], who found 57.70%. Patients treated with phenytoin had statistical significantly higher eosinophilia than other groups (p=0.044)

Treatment of patients diagnosed with DRESS drug allergy found that most were evaluated at first and then considered the choice of medication for symptomatic treatment. Patients who have no abnormalities in internal organs were given drugs in antihistamines class, antipyretics, or antihistamines to cure the patient's skin conditions, which was found 83.87% in this study. In the cases of dysfunctions of the internal organs, the drug given is systemic corticosteroids, which is dexamethasone — an intravenous given drug, before converted to oral prednisolone. The median patient dose was 0.5 mg/kg/day, the median time to systemic corticosteroids was 7 days, and the most commonly used is prednisolone 40 - 50 mg/day. The dose is gradually reduced by 5 - 10 mg every 2 weeks it should be in the range of 4 - 8 weeks,[16,17] in order to reduce the symptoms of recurring rashes. In this study was found that some patients with recurrence of the rash by reasons of discontinuation of systemic corticosteroids. It is recommended that the dose should be reduced slowly, as well as in planning the timing of systemic corticosteroids appropriately, together with the assessment of the patient's condition.

The study found a positive HLAB*5801 allergy gene after one allergic reaction to allopurinol. Only 2 (6.45%) allergic reactions to allopurinol were found. It was quite different from other studies that often found the DRESS incidence of drug allergy being second at 14.8% and third at 15.39%. These are a result of the policy of the Ministry of Public Health to recommend the HLAB*5801 allergy gene test in the Thai population, which currently, in 2020, the genotyping test is available free of charge in all public healthcare programmes. Samutsakhon Hospital has designated guidelines for using this gene test in all patients who started taking allopurinol, resulting in a decrease in the number of people allergic to DRESS from allopurinol and an HLAB*1513 gene test as positive after phenytoin allergy. If these genes were found, the risk of drug allergy for SJS/TEN was statistically significant at 11.28 times (p=0.003), and DRESS was 59.00 times (p=0.003).

The limitation of this study was that the number of years of the retrospective study was only four years because of limitations in data from hospital electronic medical records databases, small study populations, and lack of data on days, including follow up the rash after discontinuation of the suspected drugs until symptoms have healed. Even with such limitations, we can begin to see the clinical characteristics of each drug as well as better understand the tendency of surveillance of some drug classes and the guidelines for organising them.

Conclusions from the operational research, designed by hospital pharmacists, data collection, and the transfer of information to the PTC can support and push the policy and the management of DRESS in the hospital more clearly. Collaborative practice with other professionals, such as physicians who give prescription medication and DRESS diagnosis, using RegiSCAR criteria to the appropriate and timely treatment as well as a gene-based screening system that prevents the occurrence of DRESS effectively. In addition, the tendency of DRESS was reduced in drugs that PTC allowed for the genotyping test. Based on ongoing surveillance and monitoring through 2020, it can be concluded that the 4 drugs with the highest incidence are phenytoin, nevirapine, rifampicin, and pyrazinamide to induce DRESS. For that reason, healthcare professionals play key roles starting with surveillance. When the initial symptoms of severe drug allergy are found, it will assess the cause of the occurrence by considering the drugs that often use. This make the possibility to stop the drugs on time and to provide appropriate treatment, as well as prevent the recurrence of drug allergies.

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