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Decision Support System for Drug-Drug Interaction Pertaining to COPD and its Comorbidities

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Abstract: A Drug-Drug Interaction is an alteration in the impact of a drug when consolidated with another drug or group of drugs. Drug interactions are common and have caused increased hospital admission rates, treatment failures, avoidable medical complications, and even deaths. Studies have found multiple drug usage, and age-related comorbidities to be the reasons for the interactions and this demands a general study. Here in this paper, we discuss the Drug-Drug Interactions between Chronic Obstructive Pulmonary Disease (COPD) and its associated comorbidity diseases. We have designed a Drug Decision Support System which helps the Physicians to check the Drug-Drug interaction between Chronic Obstructive Pulmonary Disease and its associated comorbidity diseases. COPD is a fourth decade disease means after age 40 it may be diagnosed and is currently fourth largest killing disease. Study says one of the major causes for COPD is smoking (active/passive). As there is no cure for COPD yet. The patient's life can be improved by providing better treatment and management strategies. Once the patient is diagnosed with COPD the patient may also end up suffering with the comorbidity diseases associated with COPD like Asthma, Depression, Dementia, Diabetics, Heart Failure, Hypertension, Hypotension, Obesity, and Osteoporosis. The patient has no choice but taking the prescribed drugs for COPD and other comorbidity disease he is suffering from. Therefore the proposed work plays a vital role in avoiding the drug-drug interaction between COPD and its associated comorbidity diseases.

Index Terms: Drug-Drug Interaction (DDI), Drug Decision Support System (DDSS), Chronic Obstructive Pulmonary Disease (COPD).

1. Introduction

Drug-Drug Interaction (DDI) is nothing but the interaction between one drug with another drug. When two drugs such as one being antacid and another being acidic, react nullify the effect of each other. In such cases when patient is required to take both, it is advised to have a minimum gap of two hours. A drug interaction occurs when one drug hinders responses of another drug or alters a pharmacological effect of another drug or the pharmacological effects of two drugs may be increased or decreased. This interaction is called pharmacokinetic which can easily be demonstrated by ADME (Adsorption, Distribution, Metabolism and Excretion) [1].

Mechanism of drug interactions can be broadly classified into two [2] Pharmacokinetics [3] and Pharmacodynamics [4]. Pharmacokinetics is the study of how the organism effects the drug. Pharmacodynamics is the study of how a drug effects an organism. Drug Interactions are typically classified into four categories: Antagonism, Synergism, Potentiation, and interaction with Metabolism. Antagonism can be described as, one drug decreases or restricts the effect of another drug. Synergism can be described as, two or more drugs work together in contradiction of one goal, creating a result that is superior to the individual result of the two drugs composed. For example when we add five to five the result will be twelve instead of ten. Potentiation can be described as, a drug that increases the outcome of another drug. COPD is a type of obstructive lung disease characterized by long-term poor airflow. The major risk factors for COPD are smoking, air pollution and occupational chemicals. Smoking being the top most cause for COPD. The main symptoms include shortness of breath, cough with sputum production and easily tiring. The other causes of COPD are low level of AAt

proteins and genetics. COPD cough may produce mucus, phlegm or spots of blood. As COPD progresses there may be swelling in the legs and feet. COPD is a fourth decade disease because of its slow progression it is not detected until the age forty. There is no enduring medication for COPD, but by the treatment we can lower the risk of life and improve the quality of life. It has become one of the key public health problem globally. It is the fourth foremost reason of death globally. The WHO approximates that about 210 million people globally have COPD [5]. By 2030 COPD is forecasted to be the third leading cause for death globally.

Here, in this paper we have developed a Drug Decision Support System (DDSS) for COPD and its comorbidities. The Drug-Drug interaction is checked between COPD and its comorbidity diseases. The COPD patient normally suffers from the comorbidities like Asthma, Depression, Dementia, Diabetics, Heart Failure, Hypertension, Hypotension, Obesity, and Osteoporosis. The main objective of this work is to present a working architecture which can be used by both physician and patients for checking the drug-drug interaction if the patient is taking two or more drugs at a time for COPD and the other disease he is suffering from.

2. Literature Review

According to the National Health of Statics Report in each year 195000 are hospitalized and 74000 long suffering are stayed due to the DDI states. DDI are implications can be approximately 3% of patient are admitted in hospital and 4.8% elders are admitted and 3% to 5% of patients are intolerant due to the suppository errors [6].

Tatoneetti et.al, [7] conducted a study on DDI, during the study drug and adverse effect of the drugs. The study was designed on based on predefined classes and spontaneous data to identify the drug interaction. In this study, DFA's and ARS methods were used to train models that were used to predict the drug interaction between the two or more drugs. The adverse effect of 171 novel drug interactions can be predicted in this paper.

Isabel Segura-Bedmar et.al. [8] developed an extraction of drug interaction from biomedical scripts. Here in this research the classification of drug name and their drug classes based on the chemical substance. DDI amount consists of 784 Drug banks and 233 medical line abstracts and Drug- Drug interaction is between 5021 drugs and much more drug intention. Recognizing the drug and the classification of drug according to the pharmacological substance based on the generic name of a drug. Drug information is collected based on the DEC and CLA for detection and classification, it can classify based pharmacological substance and generic brand name. Drug extraction can provide the score based on the interaction of drug, drug bank test data set is composed, constructed on the CLA performance rank has been given in the similar way drug interaction Medicine Line test data is collected.

In 2015, Sathien Hunta et.al. [9] conducted study using enzyme action crossing attribute formulation for Drug-Drug Interaction. In his study he used various Machine Learning techniques like k-Nearest Neighbor, Neural Networks and Support Vector Machine. The best accuracy was yielded by Support Vector Machine. The accurateness was of 70.40% and of 81.85% with the balance and unbalanced datasets used for the study.

3. Problem Definition

Study says there are many patients who are hospitalized because of drug-drug interactions. Therefore an application can help both physician and patient to avoid drug-drug interaction. Most of the time, the physicians prescribe the drugs without having adequate and complete knowledge about comorbidities associated with diseases the patient is suffering from. Due to the lack of time, doctors do not check any drug interactions. In order to avoid such adverse interactions, we have developed a DDSS to check DDI for COPD and its comorbidities. If the physician employs the DDI checker this will help many patients to avoid the reactions caused by the Drug – Drug interactions some of which are life threatening. Drug Interactions have become major causes in the hospital admission rates, treatment failures, and even deaths.

4. Architecture for Drug Decision Support System

The components of the Architecture for Drug Decision Support System are - User Interface, Rule Engine and Drug Database which are discussed below.

The User Interface: The UI has been designed for different users (Admin, Physician, and Pharmacist). The Admin adds the new Drug-Drug interactions to the Database of COPD and its comorbidities. And he/she can also accept/reject the registration of Physician or a Pharmacist. The Physician (Pulmonologist) uses this application for checking the Drug-Drug interaction for COPD and its comorbidities. The Physician can also send any new Drug-Drug interaction found to the Admin. The Pharmacist can also send any new Drug-Drug interaction found for the COPD disease and its associated comorbidities to the Admin.

Rule Engine: The task of the rule engine is to link the given data with the procedures in the engine, triggering those precise procedures [10]. The Rule Engine plays a vital role in the proposed architecture. The Rule Engine has been designed using Python Language. The procedure is described in the pseudocode shown below.

Step1. If a patient suffering from COPD else (go to Step 8).
Step 2. Select stage Mild, Moderate, Severe or Very severe.
Step 3. Check whether patient is suffering from any other
Disease (COPD Comorbidity) else (go to Step 8).
Step 4. Select the prescribed drug for COPD.
Step 5. Select the comorbidity disease.
Step6.Select the drug prescribed for comorbidity disease. Step 7.Displays Interaction Report.
Step 8. End

Drug Database: The Drug Database has been built considering COPD, Asthma, Depression, Dementia, Diabetics, Heart Failure, Hypertension, Hypotension, Obesity, and Osteoporosis diseases where in which commonly prescribed drugs for all the above-mentioned diseases have been added to the database.
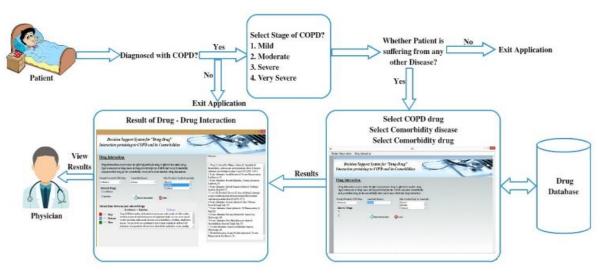

Fig.1. Drug-Drug Interaction Checker for COPD and its Comorbidities

All the Drug-Drug Interactions between the COPD disease and its comorbidities diseases have been added with references. In the results we can see the references available for the drug interactions.

Table 1. Description of Drug Database used in the Study

SL. No	Co-morbidities Associated with COPD	No. of Drugs
1	Asthma	122
2	Depression	101
3	Dementia	98
4	Diabetics	121
5	Heart Failure	139
6	Hypertension	176
7	Hypotension	145
8	Obesity	86
9	Osteoporosis	154

5. Results and Discussions

The proposed application was designed using C# and Python as code behind the technology, ASP.NET as presenation layer and MS SQL Server 2008 as data layer to store the information. Drugs inforamtion was collected from MedSpace.com, Drugs.com and Webmd.com. We have collected the list of all drugs prescribed for COPD and its associated comborbidities and prepared the database. Few results are discussed below.

The drug selected for COPD was Theophylline (Fig. 2) and the Comorbidity disease selected was Hypertension and the drug selected for Hypertension was Lasix (Furosemide). For this combination the DDSS showed Minor level of interaction.
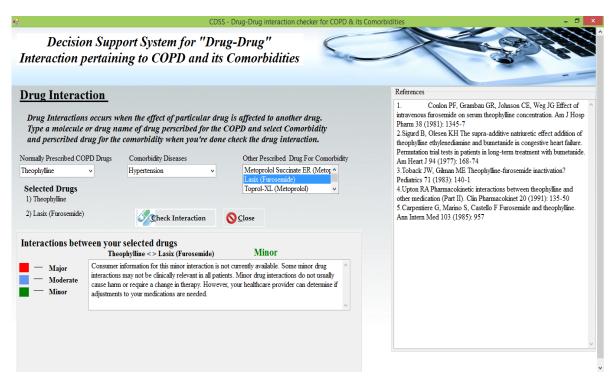
Fig.2. Results showing the Minor Interaction

The drug selected for COPD was Salmeterol (Fig. 3) and the Comorbidity disease selected was Dementia and the drug selected for Dementia was Haloperidol. For this combination the DDSS showed Moderate level of interaction.
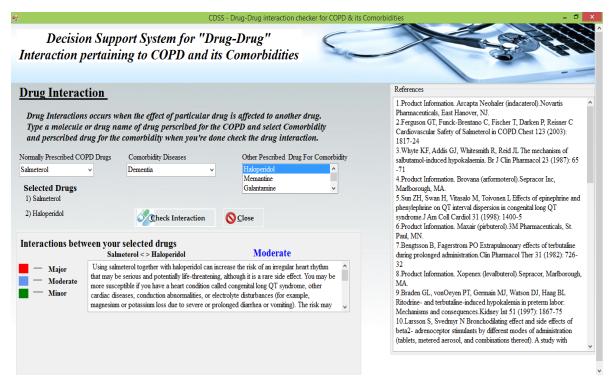

Fig.3. Results showing the Moderate Interaction

The drug selected for COPD was Aminophylline (Fig. 4) and the Comorbidity disease selected was Depression and the drug selected for Depression was Wellbutrin (Bupropion). For this combination the DDSS showed Major level of interaction.
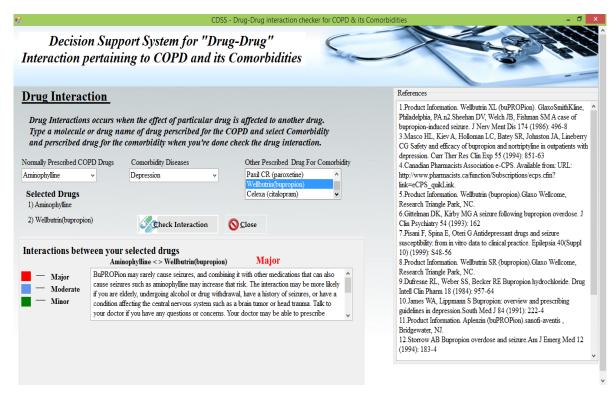
Fig.4. Results showing the Major Interaction

Table 2. Few Outputs of the Drug Interactions between COPD disease and its comorbidities

Disease	Medication	Drugs for COPD	Stage	Interactions
Asthma	Albuterol	Levalbuterol	Moderate	Albuterol together with levalbuterol may increase cardiovascular side effects such as elevations in heart rate and blood pressure or irregular heart rhythm.
Asthma	Metoprolol	Aminophylline	Major	These medications together can make metoprolol less effective and increase the effects of aminophylline.
Hyper tension	Midodrine	Umeclidinium / Vilanterol	Moderate	Midodrine together with vilanterol may increase cardiovascular side effects such as elevations in heart rate and blood pressure or irregular heart rhythm.
Hypotension	Midodrine	Albuterol (Salbutamol)	Moderate	Cardiovascular side effects such as elevations in heart rate and blood pressure or irregular heart rhythm.
Dementia	Wellbutrin/Bupr opion	Methylprednisolone	Major	Bupropion may rarely cause seizures, and combining it with other medications that can also cause seizures such as methylprednisolone may increase that risk.
Depression	Humulin N (Insulin Isophane)	Vilanterol/Fluticasone	Moderate	Vilanterol may interfere with blood glucose control and reduce the effectiveness of insulin isophane (NPH) and other diabetic medications. Monitor your blood sugar levels closely.
Diabetics	Choleca-lciferol	Salmeterol	N/A	No interaction Found

6. Conclusion

Drug Decision Support System is need of the hour for doctors to check the interaction between the drugs taken by the patients. Normally if a patient is suffering from COPD the doctor prescribes drugs for the COPD but does not look into the other comorbidities associated with the drugs being consumed by the patients. Hence, this DDSS shall be of enormous use to the doctors to check drug interactions and take appropriate steps to avoid such drug interactions. The proposed work is a web application which can be easily accessed by the physician as well as patients. In this experiment study we have considered standard drugs prescribed for COPD in GOLD criteria, for other disease which as comorbidity as COPD are the common drugs prescribed by the physicians.

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