Cardiovascular Medications Therapeutic Interchanges: A Narrative Reviews

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ABSTRACT

Objective: To review the cardiovascular medications therapeutic interchanges. **Methods:** It is an extensive search, or fifty databases included the following through the Saudi Digital Library (SDL) searching engine. It included the various types of studies (meta-analysis, randomized controlled studies and observational studies) in the English language with human study only for the update May 2017. The search in terms of therapeutic interchange, medication, therapy, type of disease or medication base on therapeutics class of anti-psychiatric. The medication list and switch from one drug to alternative based on the literature found the search that has included comparative safety, efficacy and cost of the type of medication for each disease and national or international evidence-based guidelines. **Results:** The total number of studies after an extensive search with a specific term search was 487 studies. Of those, there were 107 duplicated studies, and 380 studies included for future evaluation. After evaluation, there were 64 studies about therapeutic interchange of cardiovascular medications. **Conclusion:** The cardiovascular therapeutic interchange studies are wide-ranging and common available findings in the literature. Most of the studies have observational non-randomized. Comparative studies published in management guidelines as an alternative interchange of this matter. Cardiovascular therapeutic interchanges are highly recommended for execution in the Kingdom of Saudi Arabia.

Key words: Cardiovascular, Therapeutic interchanges, Drug, Therapy, Literature, Review.

INTRODUCTION

The shortage of medications in healthcare organizations is critical problems locally or around the world. Various factors cause the medications shortage, for instance, weak inventory management system, overuse of medications without arranging local pharmacy and therapeutic committee or poor formulary management and the pharmaceutical companies stop production the medications.^{1,2} Besides, some shortage of medications might implicate dangerous problems at healthcare services, for instance, cardiovascular medications. Discontinued the medications without healthcare team supervision will sequencing various severe problems with the patients. As a result, one of the vital solutions to solve the shortage of medications is a therapeutic interchange that replaces alternatives medications with the same molecules or different ones with the same class and indicators. Multiple studies have shown the benefit of the therapeutic interchange system implementation.³⁻⁵ Another investigation discussed therapeutic interchange with cardiovascular medications.⁶⁻²⁰ However, the cardiovascular therapeutic interchange has not been discussed before locally or in Middle East countries. The aim of the topic is to review the cardiovascular therapeutic interchange in the Kingdom of Saudi Arabia.

MATERIALS AND METHODS

It is wide-ranging search or fifty databases included the following through Saudi Digital

Library (SDL) searching engine; Willy online library, Web of science, Springer link, Taylor and Francis, Social Science Journal via ProQuest, Science Journal via ProQuest, Scopus, Scifinder, Science Direct, Sage Journal, Royal Society of Medicine, Royal Society of Chemistry, Psychology Journals via ProQuest. Pharmaceutical news index via ProQuest, Patient education via MD consult, Drug via MD consult, Oxford Journals via Oxford University, Ovid Journals, Nursing and Allied Health Sources via ProQuest, Nature Publisher group, Medline index via ProQuest, Medline complete via EBSCO, Medical Evidence Matter via ProQuest, IGI InfoSci Journals, Health Management via ProQuest, Health and Medical complete via ProQuest. Global Health Database-CABI, Family Health via ProQuest, Eric via ProQuest and EBSCO, Emerald, Dynamed via EBSCO, Directory of Open Access Journal (DOAJ), Current Content via Web of Knowledge, Dentistry and Oral Science via EBSCO, Clinical Key-Nursing, Clinical Key- Physician, CINAHL via EBSCO, Central via ProQuest, CBCA via ProQuest, Canadian Science Publishing, Cambridge Journals via Cambridge University, Britannica Academic, BMJ Journals, BMJ Clinical Evidence via BMJ Best Practice, BMJ Best Practice, Biology Journals via ProQuest, ACM Digital Library, Academic Search Ultimate via EBSCO, Cochrane Library PubMed. In addition to Google, Scholar searched alone without SDL. It involved the type of studies

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(meta-analysis, randomized controlled studies and observational studies) in the English language with human study only for the update May 2017. The search in terms of therapeutic interchange and medication, therapy and type of disease or medication base on therapeutics class. The medication list and switch from one drug to alternative based on the literature found the search that has included comparative safety, efficacy and cost of the type of medication for each disease and national or international evidence-based guidelines.²¹⁻²⁶ The Cardiovascular medication interchange list included drug name, general dosing and frequency. All settings of patient care services, inpatient or ambulatory care or community services oral medication included. All dosage form medication will be included in the. All medications should include the Ministry of Health formulary. The location of studies included Saudi Arabia as top propriety if hasn't existed Gulf or Middle East counties included, if not found overall counties included. If not existed, the table suggested from the author's experiences.

RESULTS

The total number of studies after an extensive search with a specific term search was 487 studies. Of those, there were 107 duplicated studies, and 380 studies included for future evaluation. After evaluation, there were 64 studies about therapeutic interchange of cardiovascular medications. Of those 64 studies, fifteen studies included for evaluation. Other studies have not fitted with criteria, as explored in Figure 1. Seven studies for statins for hyperlipidemia, three studies about calcium channel blocker interchange, one research about angiotensin-converting enzyme inhibitors, two studies about angiotensin II receptor blockers therapeutic interchange, one study about beta-blocker oral interchange in heart failure and one study discussed Low Molecular Weight Heparin (LMWH) therapeutic interchange therapy. All studies had been done in the USA, France, Tideland, Singapore and Saudi Arabia within the period 1997-2017. The number of patients in a range (20-3,636), while the duration of the studies exceeds more than one year. That means the number of patients was little and the number of cardiovascular medications interchange was little. The majority of studies were non-randomized controlled studies; most of the studies were observational studies (Table 1). The cost-saving did not exceed (500,000 USD).

DISCUSSION

Cardiovascular medications are very critical to be compliant and adherence administration. If any drug-related problem occurred and the

drug not available in the market, the alternative or equivalent therapeutic interchange should be replaced. After a comprehensive search based on proposed criteria, the article was only twelve studies had been included. The majority of studies were observational design and there were not randomized studies was conducted except one study of lipid disorders management. The number of patients varies from the small number of patients with a significant amount during the studies. The most type of research was about statin therapy for cholesterol disorders with duration up to in years, period and up to more 3500 patients. There is no significant difference after the therapeutic interchange, with very high-cost savings reach to half a million USD annually. Therapeutic interchange of using calcium channel blocker was observational studies with up to 300 patients and up to 12 months duration of therapy with a non-significant difference after the therapeutic interchange with up to 300,000 USD saving cost annually. The studies about the angiotensin II receptor blocker's therapeutic interchange, where the non-significant difference to acceptable saving cost. The studies about angiotensin-converting enzyme inhibitors in hypertension patients and beta-blocker oral interchange in

heart failure patients were not significant differences after the therapeutic interchange with justifiable saving cost. Other medications like diuretics, vasodilation agents and other anti-coagulant medications not included in the studies. One study discussed the therapeutic interchange of LMWH and there are significant differences between them. The authors and his colleagues suggested the cardiovascular therapeutic interchange list for most popular drugs based on literature and international guidelines on management of cardiovascular diseases (Table 2). Further studies request the randomized controlled investigation to validate cardiovascular medications and therapeutic interchange. An interchangeable therapeutic system of cardiovascular medicines is mandatory to set up in the kingdom of Saudi Arabia through the implementation of therapeutic interchange system guidelines.²⁷⁻³¹

CONCLUSION

Cardiovascular medications, therapeutic interchange system regulated by the international heart society of various regulations, policies and procedures. Various studies conducted as a therapeutic interchange on cardiovascular medications with different results and more

Figure 1: Results of searching the literature Records identified through database searching (n = 487).

Table 1: Cardiovascular medications therapeutic interchanges literature review.

No.	Author	Year of publication	Country	No of participants	Duration	Study design	Outcome	Comments
1.	Grace, Karen A. et al. (6)	2002	USA	942	4 month	cerivastatin and simvastatin as the therapeutic interchange	The percentage of patients achieving their targeted low-density-lipoprotein cholesterol concentration increased from 65% to 75%	the conversion policy saved an average of \$115 per patient in the first year. Further Adverse events resulting in drug discontinuation occurred in 28 (3%) of the 942 patients
2.	Clay, D. R. et al. (7)	2000	USA	113	8 month	All patients who were switched from amlodipine to felodipine between	One year after the switch to felodipine, 67 patients (59.3%) were using a concomitant antihypertensive; this rate was not significantly different from that for amlodipine	No adverse effects were considered related to felodipine, Of the 113 patients reviewed, 19 (16.8%) discontinued felodipine because of adverse effects scored as probably due to the drug. An amlodipine-to- felodipine interchange program resulted in a higher than expected rate of drug discontinuation because of adverse effects inpatient
3.	Javelot, Hervé et al. (8)	2017	France	20 patients	6 months	evaluate the clinical impact (efficacy and tolerance) of a therapeutic interchange program for non-complicated hypertension. 13 patients receiving angiotensin enzyme converting inhibitors interchange to Ramipril and 7 patients under sartans to valsartan	all the substitutions were well tolerated, and no significant difference was observed for diastolic and systolic pressure after the therapeutic interchange	non
4.	Mohammed, Khurram et al (9)	2010	Saudi Arabia	NA	One year	Evaluate the impact of therapeutic interchange from Atorvastatin to Simvastatin on the pharmacy budget at the Saudi Aramco Medical Services Organization (SAMSO).	Approximately 50% of patients have been switched from atorvastatin to simvastatin	The cost savings of approximately The US \$500 000 over a one year
5.	MEISSNER, BRIAN et al(10)	2006	USA	3,636 patients	12 months	A retrospective, the quasi-experimental within-subjects design was used in this study. From Atorvastatin to any of statins therapy	3,636 patients who met the study inclusion criteria and were converted from atorvastatin to an alternate statin drug. 129 patients (3.5%) switch back to Atorvastatin therapy	Total costs for medical management of dyslipidemia with statin therapy decreased following implementation of the TI intervention for atorvastatin
6.	Hilleman, Daniel E et al(11)	1997	USA	36 patients	11 months	determine the cost-effectiveness and outcomes of a therapeutic interchange from captopril, enalapril, or lisinopril to quinapril with mild-to-moderate hypertension with open non-randomized	(97%) were successfully switched to quinapril with similar blood pressure control. Four of the 36 patients (11%) complained of cough while on quinapril;	cost savings of \$4,956 per year

Continued...

Table 1: Cont'd.

No.	Author	Year of publication	Country	No of participants	Duration	Study design	Outcome	Comments
7.	Mamdani, Muhammad M et al(12)	2000	USA	101	9 months	pre/post analysis involving retrospective cohort study design patients receiving extended-release nifedipine(ProcardiaXL) were converted- ed to either amlodipine (Norvasc) or felodipine (Plendil) through the institute- nation's conversion program	The grade of hypertension was observed from the pre-conversion period to the post-conversion period, although there were statistically significant drops in both systolic (mean reduction of 7.5 mm Hg; $p<0.001$) and diastolic blood pressures (mean reduction of 5.6 mm Hg; $p<0.001$).	the total cost of drug therapy was significantly higher during the nine-month post-conversion period relative to the nine-month
8.	Patel, Rachana I et al (13)	1999	USA	170 patients	9 months	Evaluate the impact of a therapeutic interchange from pravastatin to lovastatin on treatment outcomes, quality of life, patient satisfaction, and costs. It was a prospective cohort study	Lipid values and liver function test results were similar for pravastatin and lovastatin treatment. There were no significant differences between pravastatin and lovastatin in QOL, medication tolerance, and patient satisfaction.	Cost savings from this therapeutic interchange was approximately \$211,000 annually.
9.	Lee, Yen-ying et al (14)	2012	Taiwan	444 outpatients	6 months	Evaluate the Therapeutic interchange program involving angiotensin II receptor blockers (ARBs) to candesartan. Evaluate therapeutic efficacy, adverse effects associated with therapy, and drug costs was conducted before and after	no statistically significant differences in blood pressure, and the average number of antihypertensive agents used per patient remained unchanged. Only 3.15% of the patients developed adverse drug reactions potentially related to candesartan	The cost savings of US\$62,237 of 444 patients
10.	Cruz, Joseph E et al(15)	2016	USA	300 patients	One year	describe the implementation and cost avoidance achieved by utilizing clevidipine as an alternative therapeutic interchange to SNP in cardiac surgery patients	Clevidipine was implemented successfully in our cardiac surgery patients	net cost avoidance of approximately \$300,000 in one year
11.	Li, Pengxiang et al. (16)	2016	USA	801 patients	3 months	This quasi-experimental study examined patients with hyperlipidemia who filled prescriptions for atorvastatin or rosuvastatin between January and March 2006. Propensity score matching and difference-in-difference regressions were used to compare changes in statin	Compared to the control group, the study group had a more considerable decline in any monthly brand-name statin use (0.24 30-day fills, $P<0.001$). This was only partially offset by increased monthly generic statin use (+0.06 30-day fill, $P<0.001$), with an overall drop in any monthly statin use (0.18 30-day fills, $P<0.001$). Overall adherence with statins declined (OR 0.81, $P<0.001$), and statin discontinuation increased (OR 1.62, $P<0.001$) in the study group as compared to the control group.	

Continued...

Table 1: Cont'd.

No.	Author	Year of publication	Country	No of participants	Duration	Study design	Outcome	Comments
12.	Tan, Doreen S. et al.(17)	2012	Singapore	161 patients	6 months	determine the impact of a carvedilol-bisoprolol therapeutic interchange program in chronic heart failure (HF) patients on cost savings and outcomes	There was no statistical difference ($P = .826$, paired t-test) in the patients' QoL scores pre- and post-conversion. Readmission rates in the 6 months post-conversion were not statistically different compared with the rates in the 6 months before conversion; $P = .332$. Admission rates for unswitched carvedilol patients were higher than for the converted patients	Sixty- three percent ($n = 85$) of the patients were switched to generic bisoprolol, leading to a cost savings of \$12,321 (US\$9857), or approximately \$145 (US\$116) per patient-year.
13.	Hilleman, Daniel E. et al. (18)	2001	UAS	80 Patients	6 months	patients with coronary artery disease switch from pravastatin and simvastatin to atorvastatin	Baseline demographic and clinical characteristics of the treatment groups were not significantly different The frequency of side effects was similar for all three statins.	The change from simvastatin 40 mg/day to atorvastatin 10 mg/day was associated with cost savings and an equivalent reduction in LDL
14.	Taylor, A. J. et al. (19)	2001	USA	942	6 week	Patients were converted from their current statin therapy to either cerivastatin or simvastatin, using a conversion algorithm. Efficacy and safety were evaluated at baseline and after 6 weeks of therapy; costs were also measured	Statin therapeutic interchange can improve lipid control at reduced costs.	Overall costs were reduced by \$115/ patient treatment-year.
15.	KRISTEN A. BOLLINGER et al. (20)	2000	USA	90	12 months	This observational study was conducted to assess the clinical outcomes associated with the use of dalteparin to Enoxaparin	In the overall comparison (including results pooled from all enoxaparin trials) the incidence of DVT was lower in the dalteparin patients than in the unadjusted enoxaparin group (2.2% versus 14.8%) These findings support the development and implementation of LMWH therapeutic interchange programs and	non

Table 2: Suggested Cardiovascular medications therapeutic interchanges.

No.	Ordered Oral Drug or Interchange Oral Drug (4)(21)(22)(24)(25)(26)				Ordered Oral Drug or Interchange Oral Drug			Registration (22) (23)
	Regular Days	Doses/ Day	Frequency Per day		Regular Days	Doses/Day	Frequency Per day	
1.	Atenolol OR	25- 100 mg	In 1-2 doses	Atenolol OR	25- 100 mg	In 1-2 doses	In 1-2 doses	RSFDA , MOHDF
	Betoxalol OR	5-40 mg	In 1 dose	Betoxalol OR	5-40 mg	In 1 dose	In 1 dose	
	Metoprolol Succinate SR	50- 400 mg	Divided in 1-2 doses	Metoprolol Succinate SR	50-400 mg	Divided in 1-2 doses	Divided in 1-2 doses	
	Metoprolol Tartrate OR	50-200 mg	Divided in 1-2 doses	Metoprolol Tartrate OR	50-300 mg	Divided in 1-2 doses	Divided in 1-2 doses	
	Propranolol HCl OR	40-480 mg	Divided in 2-3 doses	Propranolol HCl OR	40-480 mg	In 1 dose	In 1 dose	
	Carteolol OR	2.5-10 mg	In 1 dose	Carteolol OR	2.5-10 mg	In 1 dose	In 1 dose	
	Nadolol OR	20-320 mg	In 1 dose	Nadolol OR	20-320 mg	In 1 dose	In 1 dose	
	Carvedilol OR	12.5- 50 mg	Divided in 2 doses	Carvedilol OR	12.5- 50 mg	Divided in 2 doses	Divided in 2 doses	
	Bisoprolol	5-20 mg	In 1 dose	Bisoprolol	5-20 mg	In 1 dose	In 1 dose	
	Amlodipine besylate OR	2.5- 10 mg	In 1 dose	Amlodipine besylate OR	2.5- 10 mg	In 1 dose	In 1 dose	
	Felodipine OR	2.5- 10 mg	In 1 dose	Felodipine OR	2.5- 10 mg	In 1 dose	In 1 dose	
2.	Nifedipine SR OR	20-120 mg	Divided in 1-2 doses	Nifedipine SR OR	20-120 mg	Divided in 1-2 doses	Divided in 1-2 doses	RSFDA , MOHDF
	Nifedipine SR OR	30-90 mg	In 1 dose	Nifedipine SR OR	30-90 mg	In 1 dose	In 1 dose	
	Nifedipine OR	10-120 mg	Divided in 3 doses	Nifedipine OR	20-120 mg	Divided in 1-2 doses	Divided in 1-2 doses	
	Nicardipine hydrochloride	60-120 mg	Divided in 3 doses	Nicardipine hydrochloride	60-120 mg	Divided in 3 doses	Divided in 3 doses	
	Diltiazem HCl OR	60-360 mg	Divided in 3 doses	Diltiazem HCl OR	120 -360 mg	Divided in 1-2 doses	Divided in 1-2 doses	
3.	Verpamil HCl	40-480 mg	Divided in 3 doses	Verpamil HCl	90-480 mg	Divided in 1-2 doses	Divided in 1-2 doses	RSFDA , MOHDF
	Pravastatin OR	10-80 mg	In 1 dose	Pravastatin OR	20-40 mg	In 1 dose	In 1 dose	
4.	Simvastatin	10-80 mg	In 1 dose	Simvastatin	20-40 mg	In 1 dose	In 1 dose	RSFDA , MOHDF
	Rosuvastatin OR	5-40 mg	In 1 dose	Rosuvastatin OR	10-40 mg	In 1 dose	In 1 dose	
5.	Atorvastatine	10-80 mg	In 1 dose	Atorvastatine	10-80 mg	In 1 dose	In 1 dose	RSFDA , MOHDF
	Enalapril maleate OR	5- 40 mg	Divided in 1-2 doses	Enalapril maleate OR	5- 40 mg	Divided in 1-2 doses	Divided in 1-2 doses	
6.	Captopril OR	12.5-150 mg	In 2-3 doses	Captopril OR	12.5-150 mg	In 2-3 doses	In 2-3 doses	RSFDA , MOHDF
	Fosinopril sodium OR	10- 80 mg	Divided in 1-2 doses	Fosinopril sodium OR	10-80 mg	Divided in 1-2 doses	Divided in 1-2 doses	
	Lisinopril OR	5- 40 mg	In 1 dose	Lisinopril OR	5-40 mg	In 1 dose	In 1 dose	
	Perindopril OR	4-8 mg	In 1-2 doses	Perindopril OR	4-8 mg	In 1-2 doses	In 1-2 doses	
	Quinapril HCl OR	5-80 mg	Divided in 1-2 doses	Quinapril HCl OR	5-80 mg	Divided in 1-2	Divided in 1-2	
	Ramipril	1.25-20 mg	In 1-2 doses	Ramipril	1.25-20 mg	In 1-2 doses	In 1-2 doses	
	Losartan OR	25- 100 mg	Divided in 1-2 doses	Losartan OR	25- 100 mg	Divided in 1-2 doses	Divided in 1-2 doses	
	Ibuprofen OR	150- 300 mg	In 1 dose	Ibuprofen OR	150- 300 mg	In 1 dose	In 1 dose	
7.	Olmesartan OR	20-40 mg	In 1 dose	Olmesartan OR	20-40 mg	In 1 dose	In 1 dose	RSFDA , MOHDF
	Candesartan OR	8-32 mg	In 1 dose	Candesartan OR	8-32 mg	In 1 dose	In 1 dose	
	Telmisartan OR	40-80 mg	In 1 dose	Telmisartan OR	40-80 mg	In 1 dose	In 1 dose	
	Valsartan	80-320 mg	In 1 dose	Valsartan	80-320 mg	In 1 dose	In 1 dose	

Continued...

Table 2: Cont'd						
No.	Ordered Oral Drug or Interchange Oral Drug (4)(21)(22)(24)(25)(26)			Ordered Oral Drug or Interchange Oral Drug		Registration (22) (23)
8.	Tinzaparin OR Heparin (Unfractionated) OR	175 IU/kg SC daily 60-100 units/kg IV bolus, then 12-18 units/kg/hr IV; or, 5000 units SC q8-12h	In 1 dose Divided in 2-3 doses	Tinzaparin OR Heparin (Unfractionated) OR	175 IU/kg SC daily 1 mg/kg bid or 1.5 mg/kg SC daily;	RSFDA, MOHDF
	Dalteparin OR	5000-10,000 IU SC daily or q12h	In 1-2 doses	Dalteparin OR	5000-10,000 IU SC daily or q12h	In 1-2 doses
	Enoxaparin OR	1 mg/kg bid or 1.5 mg/kg SC daily;	In 1-2 doses	Enoxaparin OR	1 mg/kg bid or 1.5 mg/kg SC daily;	In 1-2 doses
	Hydrochlorothiazide OR Indapamide	12.5- 50 mg 1.25- 5 mg	In 1 dose In 1 dose	Hydrochlorothiazide OR Indapamide	12.5- 50 mg 1.25- 5 mg	RSFDA , MOHDF
10.	Aspirin OR	100 mg (prophylactic dose)	In 1 dose	Aspirin OR	100 mg (prophylactic dose)	RSFDA , MOHDF
	Clopidogrel	75 mg PO daily	In 1 dose	Clopidogrel	75 mg PO daily	In 1 dose
11.	Furosemide OR	40- 120 mg	Divided in 1-2 doses	Furosemide OR	20- 320 mg	Divided in 2 doses
	Torsemide	5-40 mg	Divided in 1-2 doses	Torsemide	5-40 mg	Divided in 1-2 doses

Note: The prescriber should adjust the dose after interchange according to the patient condition

RSFDA: The Drug had been registered in Saudi Food and Drug Authority, MOHDF: The Drug is Ministry of Health Drug Formulary

half of the results were positive. Further randomized controlled studies high demand cardiovascular medications, therapeutic interchange to standardize the interchange systems. The cardiovascular medications, therapeutic interchange can be implemented with close monitoring of patients unless validated with comparative safety and efficacy studies. Using of generic cardiovascular medications, therapeutic interchange can be widely used and therapeutic interchange medications for cardiovascular disease is suggested to start with close monitoring of efficacy, safety and drug-related problems of interchange medications at healthcare services in the Kingdom of Saudi Arabia.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

MOH: Ministry of Health; **KSA:** Kingdom of Saudi Arabia; **USA:** United States of America; **TI:** Therapeutic Interchange; **USD:** United States Dollar; **SDL:** Saudi Digital Library; **LMWH:** Low Molecular Weight Heparin.

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