Original Article

Prescription Patterns in Valve-replaced Rheumatic Heart Disease Patients in a Tertiary-care Hospital in South India

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The worldwide prevalence of rheumatic valvular heart disease is 15.7 million persons. It was 13.17 million in 2015 in India which is considered the highest among all countries. These patients require valve replacement cardiac surgery. Postoperatively multiple drugs are usually required. The objective of this study was to analyse prescription patterns in such patients: (1) to identify the drugs most commonly prescribed after operation and (2) to ascertain the adherence to World Health Organization prescribing indicators and the recent List of Essential Medicines. A prospective, analysis of prescriptions of patients who underwent valve replacement surgery at the Cardio-Thoraco-Vascular-Surgery Department was undertaken, from January to December, 2017. Demographic data and clinical profile of patients were recorded. Various classes of drugs prescribed and percentage of individual drugs in each class were collected. The drugswere analysed based on WHO prescribing indicators. The most commonly prescribed, antibiotic was combination of intravenous cefuroxime and sulbactam (80%); analgesic &/or antipyretic was oral paracetamol (100%); anticoagulant was either acenocoumarol or warfarin; anti-ulcer agent was oral pantoprazole and antiemetic was intravenous ondansetron. They were used for diseases or surgeries. Polypharmacy, like more than 3 antibiotics per patient and 14 drugs per prescription was universal (100%) as was the use of brand names and the absence of generic names.

Such prescriptions and non-adherence to WHO prescribing indicators leads to increased cost, adverse effects, drug interactions, antibiotic resistance, increased morbidity, increased mortality and prescribing & dispensing errors. Changes in knowledge, attitudes and practice, and intermittent prescription audits are essential to improve prescription habits.

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Key words **: Rheumatic heart disease; surgery; prescriptions; prescribing indicators; polypharmacy.**

Rheumatic Heart Disease (RHD) of the valves primarily involves 2/3rd mitral valve and 1/3rd aortic valve.The disease has a prevalence worldwide of 15.7 million[1] and in India 13.17 million[2]. It is caused by group A Streptococcus (GAS). It begins with sore throat, causing Acute Rheumatic Fever (ARF) and finally it may affect the heart[3]. RHD is putatively due to immune destruction of heart valves[4] and manifests as breathlessness, pedal oedema, fatigue and tachycardia on account of heart failure[3]. Management of ARF includes penicillin prophylaxis, Non-steroidal anti-Inflammatory drugs (NSAID)s, bed rest, fluid restriction, cardiac medications, with prior and intervallic cardiologic assessment including echocardiography, timely surgical referral and replacement of valves[5]. In case of prosthetic valves anticoagulants are frequently used[6]. Till date, our literature search did not find any published articles on the prescription patterns in valve-replaced rheumatic heart disease patients.

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Editor's Comment :

- **Prescribers should avoid polypharmacy and irrational use of medicines.**
- **Always prescribe according to WHO prescribing indicators like 1.4 to 1.8 medicines per prescription, 13.4% to 24.1% injectable, 20% to 27% antibiotics, 100% drugs by generic names and from List of Essential Medicines.**
- **Non-adherence to WHO prescribing indicators can cause adverse effects, anti-microbial resistance, high cost, morbidity and mortality.**
- **Analysis of prescribing pattern or prescription audit should be done periodically to create awareness.**

To make medical care cost-effective and rational, the study of prescribing patterns is essential to monitor, evaluate and suggest modifications, if necessary[7]. Microbial resistance, adverse effects, economic loss, increased morbidity and mortality are related to the irrational use of medications[8]. Prescribing, dispensing, administering and facilitating rational use medicines are

the main focus of prescription pattern monitoring studies[9]. As per World Health Organization (WHO) prescribing indicators the number of drugs per prescription should rang from 1.4 to 1.8 of which antibiotics make up 20% to 27%, injectable medicines constitute 13.4% to 24.1% and all prescription should quote generic names which should also be derived from the Essential Drug List (EDL), currently termed as list of essential medicines (LEM)[10]. The present study was designed to: (1) analyse prescription patterns, identify the most commonly prescribed drugs and (2) ascertain whether the prescriptions for post-operative RHD patients in a tertiary care hospital ward in south India after valve-replacement adhered to WHO prescribing indicators and complied with the 19th WHO List of Essential Medicines (LEM).

Materials and Methods

The study was conducted among Cardio-Thoraco-Vascular Surgery (CTVS) inpatients department (IPD) of Vydehi Hospital affiliated to Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, after taking approval from the Institutional Ethics Committee. This was a prospective study of one year duration, from January 2017 to December 2017. Prescriptions included for analysis were those issued post-operatively after aortic, mitral or double, valve replacement surgery using mechanical prosthetic valves, for RHD. Prescriptions were excluded for any combined surgery like two different categories of CTVS operations or history of known drug hypersensitivity or history of embolism or hemorrhagic diathesis. Demographic data (age and sex) and clinical profile of patients (diagnosis and operation or surgery) were recorded. Various classes of drugs prescribed and percentage of individual drugs in each class were collected. The drugs utilized were assembled into groups and analysed based on WHO prescribing indicators. Collected data were entered on Microsoft Office Word and Excel spreadsheet formats. The baseline data like demography (age, sex), diagnosis, treatment or operation were subjected to descriptive statistical analysis and expressed as mean + SD, frequencies and percentages. The drug utilization results were expressed as percentages.

Observations

A total of 60 prescriptions were analysed. The results are as follows :

(1) Demographic details :

Age and sex : The mean age ± SD was 41.07 ± 11.808. 20 (33.33%) patients were belonged to age group of 41 to 50 years, 16 (26.66%) patients were belonged to 51 to 60 years, 14 (23.33%)patients were belonged to 21 to 30 years, 8 (13.33%) patients were belonged to 31 to 40 years and 2 (3.33%) patients were belonged to 18 to 20 years. There was male preponderance; 39 (65%) were male and 21 (35%) were female.

(2) Clinical profile :

The clinical profile of patients were noted as shown in Table 1.

(3) Prescription analysis :

(I) Prescribed drugs — The drugs utilized post-operatively were assembled into groups of various classes and percentage of individual drugs, as shown in Table 2, Fig 1, Table 3, Fig 2 and Table 4. Drugs were prescribed for

Table 1 — *Clinical profile*

Diagnosis	Operation or surgery	Distribution (n=60)
Mitral stenosis (MS), Mitral regurgitation (MR)	Mitral valve replacement (MVR)	29 (48.33%)
Aortic stenosis (AS) and Aortic regurgitation (AR)	Aortic valve replacement (AVR)	14 (23.33%)
MS, MR, AS and AR	Double valve replacement (DVR)	17 (28.33%)

Table 2 — *Antimicrobial, Analgesics and/or Antipyretics*

Antimicrobial agents

Drug	Dose	Route	Frequency	Overall %
Cefuroxime & sulbactam	1gm & 500 mg	Intravenous	BID	80%
Meropenem	500 mg	Intravenous	TID	52.72%
Imipenem	500 mg	Intravenous	QID	52.72%
Gentamicin	80 mg	Intravenous	BID	47.27%
Colistin	5mg/kg/day	Intravenous	BID	7.27%
Vancomycin	500 mg	Intravenous	BID	7.27%
Teicoplanin	200 mg	Intravenous	BID	5.45%
Benzathine Penicillin	2.4 Million Unit	Intramuscular	4 weekly	52.72%
Amoxicillin & potassium clavulanate	500 mg &125 mg	Oral	TID	67.27%
Cefixime	200 mg	Oral	BID	65.45%
Cefuroxime	500 mg	Oral	BID	52.72%
Linezolid	600 mg	Oral	BID	50.9%
Ciprofloxacin	500 mg	Oral	BID	20%
Faropenem	200 mg	Oral	TID	14.54%
Moxifloxacin	400 mg	Oral	OD	12.72%
Nitrofurantoin	100 mg	Oral	BID	10.9%
Rifaximin	200 mg	Oral	BID	7.27%

Analgesics &/or Antipyretics

Drug	Dose	Route	Frequency	Regularity
Diclofenac	75 mg	Intramuscular	BID/SOS	58.18%
Tramadol	100 mg	Intramuscular	TID/SOS	29.09%
Paracetamol	650 mg	Oral	TID/SOS	100%
Indomethacin	75 mg	Oral	BID	16.36%
Pregabalin	75 mg	Oral	OD	12.72%
Diclofenac, Menthol,Methyl salicylate & Oleum Lini	1.16%, 5%, 10% & 3%	Topical	BID	32.72%
Choline Salicylate, Magnesium Salicylate & Benzalkonium Chloride	9%, 9% & 0.02%	Topical	BID	29.09%

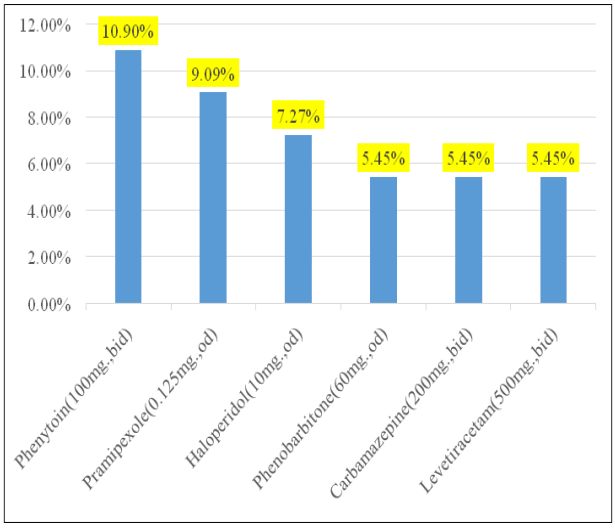

Fig 1 — Drugs (oral) affecting Central Nervous System

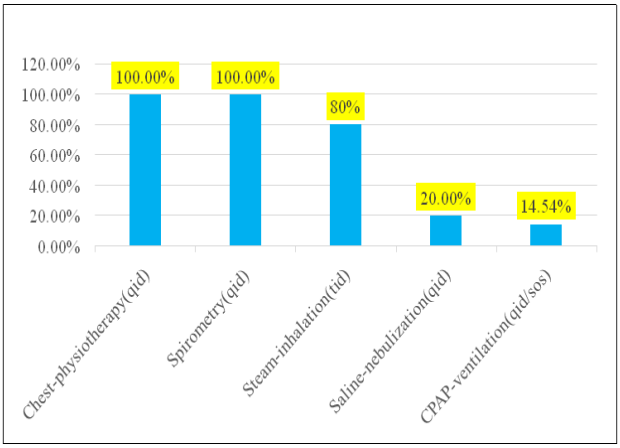

Fig 2 — Miscellaneous or Supportive therapy

7 days after operation, in different doses like in gram (gm.), milli-gram (mg), micro-gram (µg) and in different frequencies daily like once (OD), twice (BID), thrice (TID), four times (QID) daily, SOS (as and when required).

As dietary supplement egg white (TID, 52.72%) and protein powder (TID, 38.18%) was given to the patients.

(II) Analysis of prescribed drugs based on WHO prescribing indicators and the 19th WHO List of Essential Medicines — A total of 60 prescriptions were analysed for (60 participants. A total of 840 drugs (92 types) were prescribed, and an average of 14 drugs were prescribed per patient.Out of 17 antibiotics prescribed none was given as monotherapy. All 92 types (100%) of 840 drugs (100%) were prescribed as per 19th WHO List of Essential Medicines. No drug was prescribed by generic name. Out of the 92 types of drugs prescribed, 17 (15.64%) were prescribed as injections. Every prescription had more than 3 antibiotics. Brand names were used in all prescriptions.

Table 3 — *Drugs affecting Cardiovascular &/or Renal and Respiratory system*

Drugs affecting Cardiovascular &/or Renal system

Drug	Dose	Route	Frequency	Regularity
Furosemide	20 mg	Intravenous	BID	56.36%
Spironolactone	25 mg	Intravenous	BID	25.45%
Furosemide	20-40 mg	Oral	OD	90.9%
Digoxin	0.125-0.25 mg	Oral	OD	74.54%
Sildenafil	20 mg	Oral	BID/TID	67.27%
Spironolactone & Furosemide	25 mg & 20/40mg	Oral	BID	60%
Verapamil	20-40 mg	Oral	OD/BID/ TID	52.72%
Atorvastatin	10 mg	Oral	OD	50.9%
Metoprolol	25 mg	Oral	OD/BID	49.09%
Aspirin & Atorvastatin	150 mg & 20mg	Oral	OD	40%
Spironolactone	25 mg	Oral	BID/TID	40%
Potassium chloride	0.5 gm	Oral	TID	40%
Nifedipine	10-20 mg	Oral	BID/TID	38.18%
Amiodarone	200 mg	Oral	TID	38.18%
Ramipril	1.25-5 mg	Oral	OD	34.54%
Bisoprolol	1.25 mg	Oral	OD	29.09%
Nitroglycerin	6.5 mg	Oral	OD	25.45%
Mannitol	20%	Oral	SOS	20%
Diltiazem	60 mg	Oral	OD	9.09%

Drugs related to Respiratory system, like, Expectorants, Bronchodilators, Mucolytics and Mucokinetics

Drug	Dose	Route	Frequency	Regularity
Hydrocortisone	100 mg	Intravenous	TID	30.9%
Guaifenesin & Terbutaline	50 mg & 2.5 mg	Oral	TID	52.72%
Ambroxol	15 mg	Oral	TID	52.72%
Terbutaline & Bromhexine	2.5 mg & 8 mg	Oral	TID	49.09%
N - Acetyl cysteine	600 mg	Oral	BID	43.63%
Dexamethasone	8 mg	Oral	BID	40%
Bromhexine	8 mg	Oral	TID	38.18%
Deriphyllin	150 mg	Oral	TID	34.54%
Orciprenaline	10 mg	Oral	TID	12.72%
Acetyl cysteine	20%	Inhalational (Nebulization)	TID	56.36%
Normal Saline, Salbutamol & N - Acetyl cysteine	0.09 %, 200 µg & 20 %	Inhalational (Nebulization)	TID	43.63%
Levosalbutamol & Budesonide	200 µg & 200 µg	Inhalational (Nebulization)	BID	38.18%
Budesonide	200 µg	Inhalational (Nebulization)	TID	25.45%
Formoterol & Budesonide	12 µg & 200 µg	Inhalational (Nebulization)	BID	25.45%

It was noticed that directions for drug, dose, route, time, duration, doctor'ssignature, doctor's medical registration number and signature of the dispensing person was not completely written everywhere. In all prescriptions

Table 4 — *Drugs affecting blood coagulation, Gastro-intestinal system, Haematinics and/or Multivitamins and/or Multiminerals supplements and Endocrine system or Hormones*

Drugs affecting blood coagulation, bleeding thrombosis, like, Anticoagulants, Antiplatelets				
Drug	Dose	Route	Frequency	Regularity
Heparin	5000 Unit	Subcutaneous	QID	25.45%
Acenocoumarol	2-4 mg	Oral	OD	50%
Warfarin	2-5 mg	Oral	OD	50%
Aspirin	75 mg	Oral	OD/BID	40%
Clopidogrel & Aspirin	10vmg & 75 mg.	Oral	OD	16.36%
Drugs affecting Gastro-intestinal system				
Drug	Dose	Route	Frequency	Regularity
Ondansetron	4 mg	Intravenous	OD	43.63%
Ramosetron	0.3 mg	Intravenous	OD	7.27%
Pantoprazole	40 mg	Oral	OD	74.54%
Pantoprazole & Domperidone	40 mg & 30 mg	Oral	OD	25.45%
Ursodeoxycholic acid	150-300 mg	Oral	BID	10.9%
Haematinics and/or Multivitamins and/or Multiminerals supplements				
Drug	Dose	Route	Frequency	Regularity
Multiple Vitamins	-	Intravenous	OD	34.54%
Iron,Cyanocobalamin & Folic acid	40mg, 7.5mg and 0.5mg	Oral	OD	71 %
Vitamin-C	500 mg	Oral	OD	67.27%
Vitamin B complexes	-	Oral	OD	61.81%
Zinc, Vitamin B1, B2, B6 & Folic acid	41.4 mg, 10 mg, 10 mg, 3mg & 1.5mg	Oral	OD	43.63%
Calcium, Magnesium, Zinc, Vitamin B, D, E, H	-	Oral	OD	30.90%
Drug affecting Endocrine system or Hormones				
Drug	Dose	Route	Frequency	Regularity
Levothyroxine sodium or Tetraiodothyronine	100 µg	Oral	OD	5.45%

abbreviations were used. Capital letters were not used in writing the majority of prescriptions.

Discussion

Duration is comparable to studies like Kolasani *et al*[8] and Gambre *et al*[11]. Mean age ±SD is similar to study done by Kolasani *et al*[8]. Sex ratio is comparable to study like Vakade *et al*[7]. Carapetis e*t al*, mentioned similar findings of valve replacement cardiac surgery being done in MS, MR, AS and AR cases of RHD patients[5]. Drugs affecting cardiovascular and/or renal system are similar to other studies likeVakade *et al*[7], Rajathilagam *et al*[12] and Teng *et al*[13]. Laudari *et al*, mentioned that RHD patients require surgical treatment[14]. Here various classes of drugs and their percentages were evaluated. Similar analysis was done by Vakade *et al*[7], Teng *et al*[13], Kolasani *et al*[8], Begum *et al*[15] and Shah *et al*[16]. Same analysis procedures based on WHO prescribing indicators were used in other studies like Pallavi *et al*[9], Sidamo *et al*[10], Gambre *et al*[11] and Rajathilagam *et al*[12]. Commonly (80%) prescribed injectable antibiotic class (Cephalosporins) is comparable to other studies like Pallavi *et al*[9], Begum *et al*[15] and Shah *et al*[16]. Commonly (67.27%) prescribed oral antibiotic was Amoxicillin & potassium clavulanate. Here, most commonly used analgesic was injectable Diclofenac (58.18%), which is similar with other studies like Kolasani *et al*[8] and Qoul *et al*[17]. Paracetamol was most commonly (100%) used oral analgesic, which is comparable to other studies like Begum *et al*[15] and Sandvik *et al*[18]. Intravenous Furosemide (56.36%), intravenous Spironolactone (25.45%), oral Furosemide (90.9%), Oral Digoxin (74.54%), oral Sildenafil (67.27%), oral Spironolactone and Furosemide combination (60%), oral Verapamil (52.72%) and oral Atorvastatin (50.9%) were the mostly prescribed drugs affecting cardiovascular and/or renal system. Chest physiotherapy (QID, 100%), Spirometry (QID, 100%) and steam inhalation (tid, 80%) were the mostly prescribed miscellaneous or supportive therapy. Vitamin K antagonists like acenocoumarol (50%) or warfarin (50%) were used in all participants, which is comparable to other studies like Saksena *et al*[6] and Harter *et al*[19]. Subcutaneous Heparin (5000 unit, QID) was used in 25.45% patients. Here, oral Pantoprazole was used most commonly (74.54%). In another study Gamelas *et al*, mentioned that the main appropriate indication for prescribing proton pump inhibitor was anticoagulation alone, mostly to prevent gastrointestinal bleeding[20]. The most commonly used injectable antiemetic was Ondansetron, similar to another study done by Kolasani *et al*[8]. Levothyroxine sodium or Tetraiodothyronine was prescribed for hypothyroidism in 5.45% patients. No patients were detected as diabetes mellitus.

Limitations :

Less numbers of prescriptions (only 60) of valve-replaced rheumatic heart disease patients were analysed and the duration of the study was less (only 1 year).

Conclusion:

Polypharmacy, use of trade names, no generic name and non-adherence to WHO prescribing indicators were observed in this study. All these lead to increased cost,

adverse effects, drug interactions, antibiotics resistance, increased morbidity and mortality. All the afore mentioned may cause prescribing and dispensing errors. Awareness, education on drug prescription methodology, standard treatment guidelines, hospital formulary and periodic prescription audits are essential to improve prescription habits. To ensure safe medication preparation and administration "7 rights" like right patient, right drug, right dose, right time, right route, right reason and right documentation"should be followed.

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