Correspondence

with hospital formulary and practicing of generic drugs. More prospective studies from different regions of India are required in this field. However, we believe data of this study are more representative of developing country like India than any other western studies.

2. We discussed intravenously administered ranitidine as inappropriate. It was prescribed in patients who were on other oral medicines. We agree that safer alternative of metoclopramide and deriphyllin may not be affordable to all patients. Factors promoting irrational prescription are many and one of the factors for it is lack of availability of medicine in hospitals. The present study was aimed to find out the drug utilization pattern and pharmacoeconomic analysis but not toward the factors affecting particular pattern of drug use. This type of study will identify the areas where efforts can be made to identify the safer alternatives. The further study can be conducted to find out the various factors responsible for irrational use of some drugs in the hospital.

3. We have already mentioned the multiple comorbidities as a reason of poly-pharmacy in geriatric patients in discussion. In government hospitals whenever medicines are not available which patient requires, clinicians advise them to purchase them from the medical store if the patient is willing to do so. We agree that majority patients come from poor socio‑economic status. The generic prescriptions could be one of the practical solutions of this theoretical problem. Total 51.21% of the drugs were prescribed by the brand name in our study. We observed that diabetes mellitus increases the cost burden to the patients. Efforts should be made to available anti‑diabetic drugs though hospital formulary or physician should prescribe the generic or branded generics for the same. There is a need to generate prescription guidelines, to identify the potentially inappropriate medications and their safer economical alternatives for the geriatric patients based on the drugs available on Indian market similar to the western countries.

REFERENCES

1. Jhaveri BN, Patel TK, Barvaliya MJ, Tripathi CB. Drug utilization pattern and pharmacoeconomic analysis in geriatric medical in‑patients of a tertiary care hospital of India. J Pharmacol Pharmacother 2014;5:15‑20.

Sir,

Medical science is witnessing a progressive revolution and evolution throughout the globe with continual improvement in diagnostics and therapeutic interventions. The literary and practical updates in medical sciences are highly essential for the betterment of patients well-being. The article “new factor Xa inhibitor” published in the current issue of the journal by Bhanwra and Ahluwalia is a comprehensive review of orally active anticoagulant apixaban.[1] The article definitely adds to our current knowledge about these new revolutionary drugs for
the prevention of thrombosis, stroke and other clinical diseases associated coagulation abnormalities. A comprehensive review of new orally active anticoagulants—new orally active anticoagulants in critical care and anesthesia practice: the good, the bad and the ugly—was published in annals of cardiac anesthesia that had emphasized the lack of consideration for drug drug interaction and renal insufficiency which can jeopardize the safe and efficacious use of new oral anticoagulant (NOAC) and make them look bad or ugly.\[2\]

It had also been emphasized that there is a strong need for guidelines on drug drug interaction and renal dosing to promote the safe and more efficacious use of NOACs. European heart and rhythm association (EHRA) have come out with definitive guidelines on the drug drug interaction and renal dosing which is a bold new step forward in promoting the safe and efficacious use of NOACs.

NOACs have ushered a new era in anticoagulation.\[3\] Vitamin K antagonists (VKA) have traditionally been the standard of care for treating patients with venous thromboembolism (VTE) or at risk of VTE. With their predictable pharmacokinetics and pharmacodynamics, they are an excellent replacement for VKA.\[4\] Clinicians around the world have approached NOACs with trepidation and caution secondary to their drug interactions and variable renal clearance and rightly so.\[5\] EHRA have come out with guidelines on drug drug interactions and definitive recommendations so as when to stop NOACs prior to elective surgical procedures in patient with underlying renal insufficiency.

In view of lack of monitoring tests it is very important that drug drug interactions be taken into consideration prior to and after starting these medications. EHRA has come out with tabulated drug drug interactions with NOAC with definitive guidelines so as what to do in a particular clinical scenario. Color coding has been done to define the clinical impact of the drug drug interaction [Table 1].\[6\] The red code indicates that the drug is contraindicated, orange indicates that dose reduction is needed and presence of two or more yellow codes indicate that either the NOAC may not be used or dose reduction to be done or use with caution. The interpretation of yellow code has been left to the discretion of clinician as to take appropriate action in the given clinical scenario. Furthermore, the drug interaction where data is lacking but significant interaction is expected has been hatched. Again caution has been advised in use of NOAC in those particular drugs. Definitive dose changes have been advised where warranted. For apixaban dose needs to be decreased to 2.5 mg BID from 5 mg BID. For rivaroxaban dose reduction to 15 mg daily from 20 mg daily and for dabigatran etexilate dose reduction from 150 mg BID to 110 mg BID is needed.

Furthermore, they have come up with specific guidelines as when to stop the NOACs prior to elective surgeries.\[6\] For all NOACs, holding period before elective surgeries is 1–2 days depending on whether there is low or high risk of bleed. These aspects are highly significant in renal diseases where strategies have to be worked out for peri-operative renal protection.\[7\] In case of renal insufficiency with creatinine clearance (CrCL) <30 the holding time is 36-48 h for Xa inhibitors. For dabigatran holding time varies depending on CrCL as it is 90% excreted renally [Table 2]. It has also been advised not to use NOACs in patients with CrCL <30 as there is no outcome data. These facts make it mandatory to adopt an evidence based approach rather than switching to logical empiricism.\[8\] Furthermore, Cockroft method was used previously to calculate CrCL which uses ideal body weight in calculating CrCL.

Drug interactions of NOACs are mediated through P-glycoprotein and cytochrome 3A4. These are involved in the metabolism of large number of drugs in clinical use. The tabulated color coded drug drug interaction is an excellent and bold attempt to make the use of NOACs safer and more efficacious. Continued improvisation of this would go a long way in making NOACs safer and more efficacious and thereby reducing the morbidity and mortality associated with VTE and atrial fibrillation.

**Vishal Sehgal, Sukhminder Jit Singh Bajwa**

*Department of Medicine, The Commonwealth Medical College, Scranton, PA 18510, USA, Department of Anaesthesiology and Intensive Care Medicine, Gian Sagar Medical College, Banur, Patiala, Punjab, India*

**Address for correspondence:**
Sukhminder Jit Singh Bajwa, House No. 27-A,

---

### Table 1: Drugs affecting plasma levels of NOAC from drug-drug interaction

| Color | Drugs and changed body physiology affecting NOAC metabolism |
|-------|------------------------------------------------------------|
| Red   | Dabigatran, azoles except fluconazole, protease inhibitors, rifampin, St. John's Wort, Dilantin, carbamazepine, phenytoin |
| Orange| Verapamil, quinidine, weight <60 kg |
| Yellow| Cardizem, cyclosporine, tacrolimus, macrolides, fluconazole, age <75, renal function impairment, antiplatelets, NSAIDS, h/o GI bleed, thrombocytopenia, HAS-BLED >2, recent surgery on critical organ |

NOAC=New oral anticoagulant, NSAIDS=Non-steroidal anti-inflammatory drugs, GI=Gastrointestinal

### Table 2: Holding time for dabigatran etexilate prior to elective surgery

| Dabigatran CrCL (ml/min) | Low risk (H) | High risk |
|--------------------------|-------------|-----------|
| CrCL>79                  | >24         | >48       |
| CrCL 50-80               | >36         | >72       |
| CrCL>30-50               | >48         | >96       |
| CrCL=15-30               | Not indicated | Not indicated |

CrCL=Creatinine clearance
Correspondence

Ratan Nagar, Tripuri, Patiala, Punjab, India.
E-mail: sukhminder_bajwa2001@yahoo.com

Received: 18-01-2014
Revised: 15-02-2014
Accepted: 15-02-2014

REFERENCES

1. Bhanwra S, Ahlawalia K. The new factor Xa inhibitor: Apixaban. J Pharmacol Pharmacother 2014;5:12-4.
2. Sehgal V, Bajwa SJ, Bajaj A. New orally active anticoagulants in critical care and anesthesia practice: The good, the bad and the ugly. Ann Card Anaesth 2013;16:193-200.
3. Mantha S, Cabral K, Ansell J. New avenues for anticoagulation in atrial fibrillation. Clin Pharmacol Ther 2013;93:68-77.
4. Alberts MJ, Eikelboom JW, Hankey GJ. Antithrombotic therapy for stroke prevention in non-valvular atrial fibrillation. Lancet Neurol 2012;11:1066-81.
5. Rivaroxaban and atrial fibrillation: Continue to use warfarin or in some cases, dabigatran. Prescrire Int 2012;21:257-60.
6. Heidbuchel H, Verhamme P, Alings M, Antz M, Hacke W, Oldgren J, et al. EHRA practical guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation: Executive summary. Eur Heart J 2013;34:2094-106.
7. Bajwa SJ, Sharma V. Peri-operative renal protection: The strategies revisited. Indian J Urol 2012;28:248-55.
8. Bajwa SJ, Kalra S. Logical empiricism in anesthesia: A step forward in modern day clinical practice. J Anaesthesiol Clin Pharmacol 2013;29:160-1.

Access this article online

Quick Response Code:
Website: www.jpharmacol.com
DOI: 10.4103/0976-500X.130147

Drugs administered during anesthesia can act as antigens able to induce anaphylactic reactions. Such reactions may appear during various stages and especially during induction, maintenance, and post anesthesia care. It is known that anaphylaxis occurs when 2000 nearby antibodies attached to mast cell surface are bridged by corresponding