Drug Information Bulletin

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Editorial

Access to essential medicines is a problem throughout the globe especially in the developing and under developed countries. As per WHO India is not an exception, where only 35-50 percent of its population has access to essential medicines, though India is the third largest producer of medicines and is exporting to about 170 countries. Experts believe there are several complex reasons behind it. One of them is irrational use of medicines. Prescribing in generic name is considered as one of the important tools for improving rational use of medicines. In India Central Government, several State Governments and some agencies have instructed the doctors under Govt. sector to prescribe in generic name but unfortunately it has not been strictly implemented.

Though a small fraction of our population is covered by Government sector health facilities and mostly depends on private health care facilities that are not coming under ambit of Government regulation is really a problem to implement the above idea. Recent amendment notified on 21st September 2016 vide No. MCI-211 (2)/2016 (Ethics)/131118 by Medical Council of India under the "Indian Medical Council (Professional Conduct, Etiquette and Ethics) Regulation 2002 states that "Every physician should prescribe drugs with generic names legibly and preferably in capital letters and he/she shall ensure that there is a rational prescription and use of drugs" is a one step forward to implement rational use of medicines. Though there is apprehension amongst a section about its implementation, it is expected that it may bring tangible change in the health care system towards improving access to medicines.

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New Drug: Idarucizumab

Approved indication: dabigatran reversal
Praxbind (Boehringer Ingelheim)
vials containing 2.5 g/50 mL
Australian Medicines Handbook section 7.4

A limiting factor in the use of the newer oral anticoagulants is that, unlike warfarin, there have been no antidotes. Reversal of anticoagulation may be required if the patient develops severe bleeding or requires emergency surgery. Idarucizumab has been developed to reverse the effect of dabigatran, a direct thrombin inhibitor.

The development of idarucizumab involved genetically engineering a humanised monoclonal antibody fragment. The affinity of this antibody for dabigatran is greater than the affinity of dabigatran for thrombin.

To test the concept that idarucizumab would reverse the effect of dabigatran a trial was carried out in 47 healthy men. They were given dabigatran for a few days then, within two hours of the last dose, they were infused with idarucizumab or a placebo. Idarucizumab immediately bound to dabigatran so unbound dabigatran concentrations fell quickly. After idarucizumab doses of 2 g or more, they remained close to the lower limit of quantification during 72 hours of observation.[1] There was a rapid improvement in clotting studies such as thrombin time and activated partial thromboplastin time.

Idarucizumab is rapidly cleared. It is probably catabolised with 32% of the dose being excreted in the urine within six hours of infusion. There may be a transient proteinuria. Clearance is reduced in patients with renal impairment, but no dose adjustment is currently recommended by the manufacturer.

A prospective cohort study is investigating patients taking dabigatran who present with life-threatening bleeding or require surgery that cannot be delayed. The dose of idarucizumab used in this trial is two infusions of 2.5 g given no more than 15 minutes apart. Interim results on 51 patients with bleeding and 39 surgical patients have been published.[2] Most of these patients had atrial fibrillation and had been using dabigatran for stroke prevention. They had a median age of 76.5 years.

Compared to clotting tests taken before the first infusion, there was a complete reversal of the anticoagulant effect in almost all patients before the second infusion was given. The concentrations of unbound dabigatran had fallen to levels that would have little effect on coagulation. At 24 hours after the second infusion, the thrombin time was within the upper limit of the normal range in 90% of the patients with bleeding and 81% of the surgical patients. Normal haemostasis was reported in 33 of the 36 patients (92%) who had urgent surgery.[2]

The interim analysis reported nine deaths in each group of patients. Most of these were related to the presenting problem, particularly bleeding. Reversing the anticoagulant effect was associated with thrombosis in five patients.[2] While it is difficult to attribute adverse effects to idarucizumab, problems such as fever, rash and pruritus may be signs of hypersensitivity.

The idarucizumab solution contains a large amount of sorbitol and sodium. Patients with hereditary fructose intolerance are potentially at risk of adverse reactions from the sorbitol.

In some patients the anticoagulant effects of dabigatran may re-emerge up to 24 hours after an infusion of idarucizumab. Repeating the treatment may need to be considered. If the anticoagulant effect has been completely reversed, the patient will be at risk of thrombosis. A decision has to be made when to resume anticoagulant therapy. If dabigatran is still indicated, it can be resumed 24 hours after idarucizumab.

Although idarucizumab effectively reverses the anticoagulant effect of dabigatran, patients still require other supportive treatments. In the interim analysis the

mortality rate was 20% and, without a control group, it is difficult to know if this was a significant improvement on supportive care. Interestingly, 24% of the patients presented with thrombin times that were within the normal range at baseline, so they would not have derived much benefit from idarucizumab. As these patients were excluded from the analysis, the assessment of effectiveness was limited.[2] More data will be required to define the role of idarucizumab especially in patient populations, such as those with renal impairment. As the drug is specific for dabigatran it should not be used to reverse the effects of other anticoagulants.

At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA and the European Medicines Agency.

References:

1. Glund S, Stangier J, Schmohl M, Gansser D, Norris S, van Ryn J, et al. Safety, tolerability, and efficacy of idarucizumab for the reversal of the anticoagulant effect of dabigatran in healthy male volunteers: a randomised, placebocontrolled,double-blind phase 1 trial. Lancet 2015;386:680-90.
2. Pollack CV Jr, Reilly PA, Eikelboom J, Glund S, Verhamme P, Bernstein RA, et al. Idarucizumab for dabigatran reversal. N Engl J Med 2015;373:511-20.

NICE proposes fast-track options for cost-effective new drugs

The National Institute of Health and Care Excellence proposed a plan to fast-track its recommendations for the most cost-effective new drugs that would clear them as much as three months faster than the current system. The new process will apply to drugs with a likely cost per quality adjusted life year of up to $12,500.

Ref. Reuters

New adjunctive treatment for Parkinson's launched in UK

Bial launched Ongentys, or opicapone, in the UK for Parkinson's patients taking levodopa/DOPA decarboxylase inhibitors who are experiencing end-of-dose motor difficulties. Opicapoone can improve motor symptoms as levodopa wears off, noted neurologist Andrew Lees of London's National Hospital for Neurology and Neurosurgery.

Ref. PharmaTimes (U.K.)

Centre can fix drug prices to check profiteering: SC

In a major relief to patients, the Supreme Court upheld on Friday the Centre's power to specify prices of essential medicines to curb profiteering by pharmaceutical companies.

A bench of Justices Madan B Lokur and R K Agrawal allowed the Centre's appeal against many high court orders either staying the operation of Drug Price Control Order (DPCO) notifications enforced by National Pharmaceutical Pricing Authority or restraining coercive action against defaulting pharma firms.

As a result, 350 bulk drugs and more than 2,000 formulations, including Diosmin, Glipizide, Norfloxacine, Salbutamol, Theophylline and Ciprofloxacin, would come under the government's price control regime.

Those who had got relief from the various HCs were Cipla, Martin and Harris Laboratories, Dr Reddy's Laboratories, Ishaan Labs, Remidex Pharmaceuticals and Johnson & Smith Co. They had challenged the DPCO and resultant notifications on the ground that Centre was resorting to a mechanical process for fixing price of bulk drugs and medicines without fixing norms for conversion cost, packaging charges and its material cost .

The court, however, said it was wrong on the part of the pharmaceutical majors to allege that the Centre had arbitrarily fixed norms for determining the price of medicines and formulations. It said the task of fixing retail price and ceiling price of formulations was not only gargantuan but also extremely complex.

Writing the judgment for the bench, Justice Lokur said: "It is important to remember that the purpose of fixing the retail price and ceiling price of formulations is to make them affordable and ultimately benefit the consumer of medicines. Profits earned by manufacturers/formulators are secondary and 'profiteering' is certainly out of question."

Asking the HCs to go slow in interfering in matters relating to public interest and government's economic policy, the bench said: "Not only is the drug industry in the country extremely large with heavy financial stakes, but there is a lot at stake in it not only for the industry, but also for the consumers."

"For this reason, the courts have to be extremely cautious in interfering in any manner whatsoever with the working of the drug industry. Any interference by the courts would have wide ranging repercussions not only in commercial terms but also for the people of the country," the SC said agreeing with the submissions of solicitor general Ranjit Kumar.

Ref. The Times of India

Centre bans over 350 drug combinations

The Union government, through Drugs Controller General of India (DCGI), informed the Nagpur bench of Bombay High Court on Thursday that it had banned over 350 fixed drugs combinations (FDC), which the experts believed have irreversible and adverse effects on vital human organs.

The reply came while hearing a suo motu PIL (No 18/2010) on a media report over sale of spurious drugs in Nagpur district. Anand Parchure was appointed as amicus curiae.

Earlier, the India Medical Association (IMA) filed an affidavit stating that it was creating awareness among doctors and patients regarding use of banned drugs through seminars and other events.

Parchure had made a prayer in this regard in the PIL along with banning of drugs. A division bench comprising justice Bhushan Gavai and justice Vinay Deshpande then disposed of the case stating that purpose of PIL was served.

The IMA had submitted a list of about 87 drug combinations terming them as "irrational". It was prepared by a court appointed expert panel headed by the Department of Pharmacology, Government Medical College & Hospital in the city, in 2010. IMA pointed out that majority of these combinations were prohibited in many countries.

Parchure then pointed out that DCGI had met in this regard in 2011 after the panel submitted its report to the court. Then it again met after four years in February last year, but failed to take any concrete action against these 87 drugs.

The judges tersely observed that the DCGI's work was going on at a snail's pace and warned its director that he would have to personally remain present if decision was not taken within stipulated period.

Ref. The Times of India

Forthcoming Event:

National workshop on

"Pharmacists for a Healthy India"

27th November 2016

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