Drug Information Bulletin

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Content

Editorial

A recent publication said that interventions have been made through conducting workshops and seminars involving all stake holders in the health care system promoting the concept of Rational Use of Medicines (RUM). Workshop module consisted of proper selection of medicines, disadvantage of fixed dose combination, avoid Injections where alternative dosage form is available, lack of scientific rational of Tonics, avoid polypharmacy and use of cost effective medicines without compromising quality. The study spanned over semi urban areas covering three districts of West Bengal, India. Community pharmacies mainly serving the prescriptions of private practitioners were selected randomly in this study. Prescriptions were collected from community pharmacies, serving prescriptions of private practitioners in a semi urban area within a month. 30 prescriptions each from 10 pharmacies were collected from those who participated in the workshop/seminars during the last two years. This result was compared with the data obtained from the same 10 pharmacies before intervention. At the end medicine use indicators were analyzed and compared with the data obtained from the same 10 pharmacies before intervention. Results show that the average number of medicines prescribed per encounter reduced from 2.84 to 2.18. Percentage of prescriptions for generics improved significantly from nil to 22.78. Percentage of prescriptions for antibiotics and vitamin tonics reduced significantly, i.e. from 54.33 to 34.66 and from 16 to 12 respectively, percentage of prescriptions for injections reduced from 3.66 to 0.33 .Average number of FDCs reduced from 1.13 to 0.55. Average cost per encounter was calculated, which amounts to INR 322.7 (Max. 1145 Min.3.82). This is less than the average cost per encounter INR 512.4 (Max. 1862.6, Min.102.42) estimated before intervention. Authors concluded that, it appears that medicine use indicators have improved significantly by intervention i.e. disseminating information on rational use of medicines amongst the stake holders of a health care system for cost effective treatment.

More studies involving more number of prescriptions would give clear picture on which basis future action could be chalked out. However, dissemination of information on Rational Use of Medicines (RUM) could improve the situation.

Dr. Subhash C. Mandal
Editor

New Drug: Dolutegravir

Approved indication: HIV infection
Tivicay (ViiV Healthcare)
50 mg film-coated tablets
Australian Medicines Handbook section 5.5.4

Integrase inhibitors, such as elvitegravir and raltegravir, can be used in combination with other antiretroviral drugs to treat HIV infection. Dolutegravir also inhibits HIV integrase to disrupt viral replication. Unlike raltegravir, dolutegravir can be given once daily and unlike elvitegravir it does not need 'boosting' with other drugs to have an effect.

Dolutegravir is rapidly absorbed and although food has some effect on bioavailability it is not clinically significant. The drug's distribution includes the genital tract and cerebrospinal fluid. It is metabolised in the liver with most of the dose being excreted in the faeces. No dose adjustment is required in patients with renal impairment or mild–moderate liver impairment. The half-life is approximately 14 hours.

A combination of once-daily dolutegravir with abacavir and lamivudine was compared to a combination of efavirenz, tenofovir and emtricitabine. The 844 adults in the trial had not previously been treated for HIV and had viral RNA exceeding 1000 copies/mL. After 48 weeks, 88% of the patients who took the dolutegravir combination had less than 50 copies/mL. This was statistically superior to the 81% of patients who responded to the other combination. CD4 lymphocyte counts increased by an average of 267/microlitre with dolutegravir and by 208/microlitre in the control group. This difference was also significant.1

Another trial of previously untreated patients compared dolutegravir with raltegravir. The 827 adults were randomised to take the integrase inhibitors with combinations of tenofovir/emtricitabine or abacavir/lamivudine. After 48 weeks there was no significant difference between the groups. The target of less than 50 copies/mL of viral RNA in the plasma was achieved by 88% of the dolutegravir group and 85% of the raltegravir group. Both drugs increased the CD4 lymphocyte count by a median of 230 cells/microlitre.2

Dolutegravir and raltegravir have also been compared in patients with resistance to two or more classes of antiretroviral drugs. None of the 724 adults in the trial had previously received an integrase inhibitor. After 48 weeks, 71% of the patients treated with a regimen containing dolutegravir had plasma viral RNA concentrations below 50 copies/mL. This was statistically superior to the 64% success rate with regimens containing raltegravir. CD4 lymphocytes increased by a mean of 162 cells/microlitre with dolutegravir and 153 cells/microlitre with raltegravir. Resistance to the integrase inhibitors emerged in 1% of the dolutegravir group and 5% of the raltegravir group.3

Dolutegravir is also being studied in patients who are infected with HIV that is resistant to raltegravir or elvitegravir. Data from 183 patients treated for 24 weeks show that in 69% dolutegravir reduced viral RNA to below 50 copies/mL. The response rate varies depending on which genetic mutation is responsible for the viral resistance. A twice-daily dose of dolutegravir is recommended when there is resistance to integrase inhibitors.

There are insufficient data to guide the use of dolutegravir in children under 12 years old. The effect of dolutegravir in pregnancy is also unknown, but it did cross the placenta in animal studies.

Adverse events in patients infected with HIV may be caused by the treatment or the disease itself. When multiple drugs are used it can be difficult to determine which one is causing an adverse event. Some problems such as immune reconstitution syndrome may be associated with any retroviral therapy. In the studies which compared dolutegravir and raltegravir there were similar adverse effects.2,3 These include diarrhoea, nausea and headache. Rashes may be a sign of hypersensitivity. As hypersensitivity reactions may also affect the liver, liver function should be checked.

Dolutegravir will be used in combination with other antiretroviral drugs. While there are some interactions these may not require dose adjustment. Efavirenz reduces dolutegravir concentrations so this combination should be avoided or a twice-daily dose of dolutegravir will be needed. Antacids containing magnesium, aluminium or calcium should not be taken within several hours of dolutegravir as they reduce its absorption. The combined oral contraceptive pill and methadone do not have a significant interaction with dolutegravir.

Adherence to treatment is very important in managing HIV infection. An effective once-daily drug will help adherence and it is likely that dolutegravir will be formulated with other drugs to allow patients to take a single daily dose of all their drugs. When used in previously untreated patients viral resistance to dolutegravir did not seem to be a problem.1 This may give it another advantage over other integrase inhibitors, but the development of resistance will need to be monitored once dolutegravir is more widely used.

References:

1. Walmsley SL, Antela A, Clumeck N, Duiculescu D, Eberhard A, Gutiérrez F, et al; SINGLE Investigators. Dolutegravir plus abacavir-lamivudine for the treatment of HIV-1 infection. N Engl J Med 2013;369:1807-18.
2. Raffi F, Rachlis A, Stellbrink HJ, Hardy WD, Torti C, Orkin C, et al; SPRING-2 Study Group. Once-daily dolutegravir versus raltegravir in antiretroviral-naive adults with HIV-1 infection: 48 week results from the randomised, double-blind, non- inferiority SPRING-2 study. Lancet 2013;381:735-43.
3. Cahn P, Pozniak AL, Mingrone H, Shuldyakov A, Brites C, Andrade-Villanueva JF, el al; extended SAILING Study Team. Dolutegravir versus raltegravir in antiretroviral-experienced, integrase-inhibitor-naive adults with HIV: week 48 results from the randomised, double-blind, non-inferiority SAILING study. Lancet 2013;382:700-8.

Source: Australian Prescriber

FDA unveils drug compounding rules

Regulations of compounding pharmacies were released Tuesday by the FDA to establish manufacturing standards and update the list of drugs considered too dangerous to be changed. Noncompliant compounders could face seizures and prosecution. The regulations outline a risk-based approach, but action can be taken without the identification of a safety issue.

Source: The Hill

David Cameron calls for global effort against drug-resistant infections

U.K. Prime Minister David Cameron says an international campaign is needed to combat the misuse of antibiotics and the rising threat of drug-resistant infections. He announced the creation of an independent commission led by Jim O'Neill, former Goldman Sachs chief economist, to examine why the antibiotic pipeline is so small. "We are in danger of going back to the dark ages in medicine, to see infections that were treatable not be treatable," Cameron said.
Source: NewsDaily/Reuters

Guideline Calls Routine Exams of the Pelvis Unnecessary

The New York Times reports "There is no evidence that such pelvic exams are useful and plenty to suggest that the procedure provokes fear, anxiety and pain in many women, the American College of Physicians said in a new practice guideline for doctors...The new guideline comes as more routine procedures are critically evaluated in light of scientific studies, part of a move toward evidence-based medicine."
For details: http://www.nytimes.com/2014/07/01/health/doctors-group-advises-against-regular-pelvic-exams.html?_r=0

DBT to begin research on HPV prevention & control, calls for proposals from biotech companies

Even as the academia and industries worldwide are actively involved in finding a solution to the growing Human Papilloma Virus (HPV) infection in terms of new screening/diagnostic tests, vaccines and therapeutic options, the Department of Biotechnology (DBT) will soon begin research on HPV prevention and control. The DBT's initiative in this regard is significant as HPV infection is the leading cause of cervical cancer in the world. India bears 30 per cent of the burden of cervical cancer worldwide. The lack of awareness in rural areas and the lifestyle of women in urban areas worsen the situation of cervical cancer in the country. Low-cost, effective solutions are required for the prevention and treatment of HPV infections.

The DBT will conduct this research programme under its Biotechnology Industry Partnership Programme (BIPP). The DBT has invited proposals from eligible biotech companies to conduct research on HPV prevention and control.

Some of the indicative priority areas for submitting proposals include simple, sensitive, accurate and affordable screening tests (standard self-screening methods that are independent of individual interpretation); simple, sensitive, specific and acceptable diagnostic tests (cost effective and applicable to low resource settings); vaccines covering additional number of HPV types; process optimization for cost effective vaccine production; development of vaccines with specified duration of protection; and development of new therapeutic options including products of natural origin.

Source: Pharmabiz

Forthcoming Event

IPA Convention
(Inaugural function of the IPA Platinum Jubilee year)
8th August 2014
Venue: NIMHANS Convention Centre, Bangalore