Drug Information Bulletin

Drug Information Centre (DIC)
Indian Pharmaceutical Association
Bengal Branch
Tele fax: 033 24612776, E-mail: ipabengal.dic@gmail.com
Web Site: http://www.ipabengal.org
Contact: 09830136291

&

Regulatory Affairs Division (RAD), IPA

Volume: 12 ***Number: 11*** ***26th August 2018***

Content

Editorial

Oxytocin-an essential drug is used widely for inducing labour. But unfortunately it is being misused in several means. Medical experts point out that sustained use of the drug can cause hormone imbalance in humans and harms the reproductive system of animals, reducing their life span. Similarly, it was reported that minor girls were given repeated and unregulated shots of oxytocin injection to speed up their sexual maturation. Moreover, consuming this hormone unknowingly through Milk, vegetables, which causes several dysfunctions in human body. It is very harmful for humans who unwittingly are made to consume this hormone. Humans face all the harmful effects of this drug. Children are most susceptible to its effects and it is known to have caused imbalanced hearing and weak eyesight. Common symptoms are exhaustion and loss of energy. Govt. of India has taken several steps to curb this menace, through a notification vide no. 29 E dated 17.01.2014 and a recent circular dated 22.10.2014. They has adopted further restrictions on movement of Oxytocin vide G.S.R.411(E) dtd. 27.04.2018, which are-

The manufacture of Oxytocin formulations for domestic use shall be by public sector undertakings or companies only and the label of the product shall bear barcodes.

(i) The manufacture of Oxytocin formulations for export purposes shall be open to both public and private sector companies and the packs of such manufacture for exports shall bear barcodes.

(ii) The manufacturers of active pharmaceutical ingredient of Oxytocin shall supply the active pharmaceutical ingredient only to the public sector manufacturers licensed under the Drugs and Cosmetics Rules, 1945 for manufacture of formulations of the said drug for domestic use.

(iii) The manufacturers of active pharmaceutical ingredient of Oxytocin shall supply the said active pharmaceutical ingredient to the manufacturers in public and private sector licensed under the Drugs and Cosmetics Rules, 1945 for manufacture of formulations of the said drug for export purpose.

(iv) The Oxytocin formulations manufactured by the public sector companies or undertakings licensed under the Drugs and Cosmetics Rules, 1945 for domestic use shall supply the formulations meant for human and veterinary use only,- (a) to the registered hospitals and clinics in public and private sector directly; or (b) to the Pradhan Mantri Bhartiya Janaushadhi Pariyojana (PMBJP) and Affordable Medicines and Reliable Implants for Treatment (AMRIT) outlets or any other Government entity which may be specified by the Central Government for this purpose in the country which shall further supply the drug to the registered hospitals and clinics in public and private sector.

(v) The Oxytocin in any form or name shall not be allowed to be sold through retail Chemist.

Subsequently it was further amended to make Oxytocin available from retail outlets and for further regulation Oxytocin was included in the Schedule H1vide G.S.R. 795(E) dtd.21.08.2018.

Dr. Subhash C. Mandal
Editor
E mail: subhash.mandaldr@gmail.com
Mob. 9830136291

New Drug: Silodosin for benign prostatic hypertrophy

Approved indication: benign prostatic hypertrophy
Urorec
4 mg and 8 mg capsules

Benign prostatic hyperplasia can cause lower urinary tract symptoms such as slow urine flow, nocturia and incomplete emptying of the bladder. If these symptoms are sufficiently bothersome as to require treatment, selective alpha-blockers such as alfuzosin and tamsulosin are one option. These drugs block alpha1 adrenoreceptors in the smooth muscle of the prostate and bladder to reduce resistance and so improve urinary flow. Silodosin is another selective alpha-blocker. It has much greater affinity for the $alpha_{1A}$ receptor than the $alpha_{1B}$ receptor found in vascular smooth muscle.

Silodosin is taken once a day with food. The dose is halved if the patient has moderate kidney impairment (creatinine clearance 30–59 mL/min) and silodosin is not recommended for those with severe impairment (creatinine clearance <30 mL/min). Most of the dose is metabolised, but no data are available on the effect of severe hepatic impairment. The terminal half-life of silodosin is about 11 hours. As the metabolism of silodosin involves cytochrome P450 3A4, it should not be used with strong inhibitors of this enzyme system, such as ketoconazole and ritonavir. Silodosin is also a substrate of P-glycoprotein so using it with strong inhibitors (amiodarone, verapamil) of this transporter is not recommended.

The Australian approval of silodosin is mainly based on three randomised trials. Two of them compared silodosin with placebo in a total of 923 men.[1] These patients had an average baseline score of 21.3 on the 35-point International-Prostate Symptom Score (I-PSS). After 12 weeks of treatment this had reduced by 6.4 points in the 466 men who took silodosin 8 mg daily and by 3.5 points in the 457 who took placebo. There was also a significant difference in urine flow rate. Patient satisfaction was higher with silodosin, with 32% of the men who took it being 'delighted, pleased or mostly satisfied' compared with 22.5% of the placebo group.[1]

The third trial compared silodosin with tamsulosin, as well as placebo.[2] In this trial the baseline I-PSS was 19.1. After 12 weeks of treatment it had reduced by a mean of 7.0 points in the 371 men taking silodosin 8 mg daily and by 6.7 points in the 376 taking tamsulosin 0.4 mg. The average reduction for the 185 taking placebo was 4.7 points. The proportions of patients who had an improvement of at least 25% in the I-PSS were 66.8% with silodosin and 65.4% with tamsulosin. These results were significantly better than the 50.8% response rate to placebo. While 44–45% of the men were 'delighted, pleased or mostly satisfied' with the active treatments, only 34% of the placebo group agreed.[2]

Silodosin was generally well tolerated, but caused more adverse effects than placebo. In the placebo controlled trials, 6.4% of the silodosin group withdrew because of adverse events compared with 2.2% of the placebo group. Problems that were more frequent with silodosin included dizziness, orthostatic hypotension, diarrhoea and headache. A major difference between silodosin and placebo was the adverse effect of retrograde ejaculation (28.1% vs 0.9%).[1] This abnormal ejaculation is thought to be a consequence of the selective blockade of the $alpha_{1A}$ receptors. This specificity should reduce cardiovascular adverse effects, but in the comparative study silodosin did not have significantly different effects from tamsulosin on pulse and blood pressure.[2] Alpha-blockers may cause floppy iris syndrome so the patient's ophthalmologist should be informed when cataract surgery is being planned.

There can be a high placebo response when treating symptoms associated with benign prostatic hyperplasia. The trials controlled for this by only randomising patients who had not responded during a placebo run-in phase. Despite this the differences between silodosin and placebo were small. Although it is statistically significant, a difference of 2–3 points in the I-PSS is only a slight advantage. The mean difference in maximum urine flow rates was 1 mL/second.[1] Such a small advantage over placebo is of questionable value.[3] The overall efficacy of silodosin is non-inferior to tamsulosin, but silodosin is more likely to cause retrograde ejaculation (14.2% vs 2.1%).[2]

References:
1. Marks LS, Gittelman MC, Hill LA, Volinn W, Hoel G. Rapid efficacy of the highly selective alpha1A-adrenoceptor antagonist silodosin in men with signs and symptoms of benign prostatic hyperplasia: pooled results of 2 phase 3 studies. J Urol 2009;181:2634-40.
2. Chapple CR, Montorsi F, Tammela TL, Wirth M, Koldewijn E, Fernández Fernández E; European Silodosin Study Group. Silodosin therapy for lower urinary tract symptoms in men with suspected benign prostatic hyperplasia: results of an international, randomized, double-blind, placebo and active-controlled clinical trial performed in Europe. Eur Urol 2011;59:342-52.
3. Dawson A. The price of urine. Aust Prescr 1995;18:26-7.

Source: Australian Prescriber

Lamivudine Risk of hearing loss

NCC-PvPI, IPC has made a recommendation to CDSCO requesting that the drug safety label for lamivudine is revised to include hearing loss as an adverse reaction. Lamivudine is used for the treatment of HIV infection in combination of at least two other antiretroviral drugs. Between July 2011 and March 2018, NCC-PvPI received eight ICSRs that reported hearing loss with lamivudine use. A review of cases by the Signal Review Panel (SRP)-PvPI, IPC suggested a strong causal relationship between lamivudine and hearing loss. Reference: Based on the communication from IPC, NCC-PvPI, India (http://ipc.nic.in)

Propofol Contraindication in pregnant women removed

MHLW and PMDA have announced that precautions of propofol preparations (Diprivan®) should be revised to remove the contraindication of use during pregnancy. Propofol can be used by pregnant women or women who may be pregnant provided the potential benefits outweigh the risks. Propofol is indicated for induction and maintenance of general anesthesia. Propofol is used for therapy in pregnant women in Europe and the United States. For this reason the MHLW requested the PMDA to conduct an investigation into the use of propofol during pregnancy. As a result, PMDA concluded that the above-mentioned revision to safety precautions of propofol is acceptable. Reference: Revision of Precautions, MHLW/PMDA, 27 March 2018 (www.pmda.go.jp/english/)

Amarasate extract Anaphylaxis

The Medicines and Medical Devices Safety Authority (Medsafe) has issued a warning about the risk of anaphylaxis with the use of amarasate extract (Calocurb®). Amarasate extract is a dietary supplement marketed to support weight loss and appetite control. Medsafe continues to monitor reports of adverse reactions for this product and all other dietary supplements. Reference: Safety Information, Medsafe, 9 May 2018 (www.medsafe.govt.nz/)

Obeticholic acid Risk of serious liver injury

The MHRA has issued advice to healthcare professionals about the risk of serious liver injury in patients with pre-existing moderate or severe liver impairment, taking obeticholic acid (Ocaliva®). Health-care professionals are reminded to adjust dosing according to liver function. Obeticholic acid is indicated in the treatment of primary biliary cholangitis in combination with ursodeoxycholic acid. An EU review assessed reports of serious liver injuries and deaths in patients with primary biliary cholangitis with preexisting moderate or severe liver impairment who were not adequately dose-adjusted. Liver-related adverse events have occurred both early in exposure and after months of treatment. The review concluded that no changes to the product information are required but suggested that health-care professionals should be reminded of the dosing recommendations. The MHRA has received two Yellow Card reports of hepatobiliary disorders in the UK associated with obeticholic acid. One case was lifethreatening and required hospital admission. Obeticholic acid is subject to additional monitoring, allowing quick identification of new safety information. Reference: Drug Safety Update, MHRA, 24 April 2018 (www.gov.uk/mhra) (See WHO Pharmaceuticals Newsletters No.5, 2017: Risk of serious liver injury in USA)

Over 40 Techs in Pharma up for grabs for Gujarat companies

Over 40 technologies developed by the National Research Development Corporation (NRDC) in drugs and pharmaceuticals have huge potential to be commercialised by Gujarat-based companies, a senior NRDC official said on Tuesday. With a share of about 20%, Gujarat is one of the largest recipients of technologies developed by NRDC.

NRDC has over 80 technologies in pharmaceuticals and drugs, for which it is seeking partners, through Transfer of Technology (ToT) for commercialisation. "Of these, over 40 licenses have high potential to be used by Gujarat based companies," said Amitabh Mishra, senior manager of biotechnology in NRDC, while interacting with media persons on the sidelines of a seminar on NRDC Industry Meet on Technology Transfer Opportunities in Pharma, Biotech and Health in Ahmedabad on Tuesday.

"Non-invasive diagnostic technologies targeted and new-borns, solutions for control of diseases like Hepatitis-B, as well as herbal medicines need to be adapted by private companies," said Mishra.

Jaimin Vasa, president of Gujarat Chamber of Commerce and Industry (GCCI), said that small businesses do not have the financial or human resource to conduct research, during the seminar. "SMEs need hand-holding during commercialisation of technologies and to minimise risks. We need more interactions of industries with research institutions," said Vasa.

Arvind Kukreti, Deputy Drug Controller of Central Drug Standard Control Organization (CDSCO) called for better coordination between regulators, Research and Development (R&D) institutions and industry to ensure that the interests of the consumers are met. Anil Jain, MD of Ascent Finechem Private Ltd said that R&D is also needed to bring down the cost and improve affordability. Experts feel that there is a strong need to develop technologies to cater to the future needs of the society. With Gujarat being a hub of pharmaceuticals and chemicals, it has an important role to play, said Mishra.

With Maharashtra and Gujarat being one of the most industrialised states, they are also the largest recipients of technologies developed by NRDC. While Gujarat companies are seeking licenses in drugs and pharmaceuticals, Maharashtra-based companies are also major recipients of technologies in agriculture and food sector.

Source: DNA Money

DISCLAIMER:

The Newsletter intends to provide updated and reliable information on medicines and other related issues in an attempt to equip healthcare professionals to take informed decision in recommending medicines to the patients. However, they are encouraged to validate the contents. None of the people associated with the publication of the Newsletter nor the organization shall be responsible for any liability for any damage incurred as a result of use of contents of this publication. The brand names of medicines, if mentioned, are for illustration only and the Newsletter does not endorse them.