

Withdrawal of rofecoxib- a wake up call for drug safety

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Cyclooxygenase-2 (COX-2) inhibitors have been developed with the goal of providing similar efficacy and greater safety, compared with that of traditional Non-Steroidal Anti Inflammatory Drugs (NSAIDs)¹. United States Food and Drug Administration (USFDA) has approved rofecoxib in May 1999 for the reduction of pain and inflammation caused by osteoarthritis, as well as for acute pain in adults and for the treatment of menstrual pain with added advantage of minimal gastrointestinal side effects. Subsequently, the USFDA approved this drug to treat the signs and symptoms of rheumatoid arthritis².

Unlike conventional NSAIDs, COX-2 inhibitors do not reduce the endogenous production of thromboxane A₂, a potent activator and aggregator, there by causing a potentially thrombotic cascade of events that could lead to an increase in the risk for thrombotic cardiovascular system events³.

In a large randomized study of 8076 patients receiving long-term daily treatment for rheumatoid arthritis with either rofecoxib 50 mg/day or naproxen 1000mg/day [(VIOXX Gastrointestinal Outcomes Research Study (VIGOR); aspirin was not administered], patients receiving rofecoxib had a relative risk of 2.38 for developing serious thrombotic cardiovascular adverse events [Myocardial Infarction (MI), ischemia stroke, unstable angina, cardiac thrombus, sudden or unexplained death, transient ischemic attack, resuscitated cardiac arrest] compared with patients treated with naproxen^{3, 4}. This result prompted new warning statements regarding use of rofecoxib in patients with a history of ischemic cardiac conditions including angina and heart attacks. New labeling specifically cites a significant difference in the rates of non-fatal MI (18 versus 4) for rofecoxib and naproxen, respectively, in VIGOR trial⁵.

On September 30, 2004, rofecoxib has been voluntarily withdrawn by its manufacturer Merck & Co, INC, USA from the market in relation with its risks associated with cardiovascular events including heart attacks and strokes².

This drug is not approved by the Department of Drug Administration (DDA) Kathmandu, the national drug regulatory authority of Nepal and hence not available in Nepal for use. However, similar drugs of this category like celecoxib, valdecoxib etc are being widely used in some parts of the world and hence the possible risks still persist.

This issue can be considered as a wake-up call for all the health care workers and drug regulatory authority of the country to impose strict vigilance over the drugs which do not have long-term safety studies in human subjects. This event also suggests that every country should have their own pharmacovigilance program which should be focused towards patient safety.

References

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