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Editorial

ASPIRIN MARCHES ON

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Even though aspirin has entered the second century since its discovery, the onward march of this remarkable chemical continues. Newer applications emerge, data accumulates and finally get established as indications in the face of overwhelming and convincing evidence. New entrants as definite indications are given below:

Early use of Aspirin in CABG Surgery

The vital need of long term aspirin use after CABG to prevent thrombosis of the graft has long been recognized. However, the use of Aspirin in early hours after CABG has been very controversial and an editorial[1] in NEJM has mentioned that use of aspirin in immediately postoperatively was considered a taboo as a practice in many centres. This is primarily because of risk of bleeding complications. Inspite of the advances in surgical technique, myocardial preservation, hemodynamic monitoring and intensive care, complication rate in CABG surgery continue to be 15% or higher[2], which affects heart, brain, kidneys and intestines. Several studies have also emphasized that aspirin administration leads to more mediastinal blood loss, transfusions and repeated operations[3].

A recent study by Mangano and colleagues[4] have presented the data on the use of aspirin during 48 hours after CABG. The results of the study are very striking. In patients receiving aspirin during first 48 hours, the rate of death was lower by more that 60% compared to those without aspirin. The rates of non-fatal ischemic complications including myocardial infarction, stroke, renal failure and bowel infarction was reduced by a similar magnitude. Interestingly the frequency of bleeding complications was significantly lower in aspirin-treated patients; rate of re-operation was reduced by 63% and frequency of GI bleeding was reduced by 50%. With these results, it seems likely that taboo of yesterday would change into new standard practice of today for early use of aspirin in the immediate post-operative period in CABG surgery.

Antiphospholipid Syndrome

Women with antiphospholipid syndrome (Hugh's syndrome) suffer from recurrent miscarriages, increased fetal losses and maternal thrombosis during pregnancy. Heparin has been the drug of choice but aspirin in low-dose has also been emerging as a strong contender vs heparin. In a recent study[5], aspirin alone (75 mg daily) has been demonstrated to be as effective as aspirin plus low-molecular-weight heparin (5000 U subcutaneously daily) in improving the live birth rate to 72-74% and without any episodes of maternal thrombosis. The authors recommend to use aspirin in low doses as a routine and discourage the use of heparin, for improving the outcome of pregnancies in anti-phospholipid syndrome.

Pulmonary Embolism & DVT

Landmark study, Pulmonary Embolism Prevention (PEP) trial[6] has shown that in

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patients undergoing hip replacement and other major surgeries Aspirin therapy produced 43% reduction in pulmonary embolism and 36% reduction in symptomatic deep vein thrombosis. The incidence of fatal pulmonary embolism was reduced by 58% with aspirin. Based on these results, it is now recommended that all patients undergoing major surgery should be given aspirin 150 mg daily for 6 weeks postoperatively.

Established and new emerging indications

Antiplatelet therapy is now the mainstay of treatment as well as primary or secondary prevention of acute and chronic cardiovascular diseases[7,8]. These diseases included :

Myocardial infarction, coronary syndromes, ischemic stroke, transient ischemic attacks, hypertension, diabetes etc. However, there are several other clinical conditions for which the data for the benefits of aspirin is still emerging and has not reached the consensus stage. The examples are:

Cancer especially colonic, toxemia of pregnancy, dementia, cataract etc. It is expected that at least for some of these conditions aspirin will find a definite place in their treatment in due course.

Untoward aspects

Like any other drug, aspirin also has its share of untoward effects. The most important side effects with aspirin are related to GIT, resulting from mucosal irritation. Here the most significant effect is that GI bleeding. However, this is highly dependent on the dosage and duration of aspirin administration. Smaller doses, recommended for most of the conditions discussed above (75-150 mg daily) especially with protective coating is considered to be safer. It is interesting to note that the toxicity index score of aspirin is lowest compared to all the non-steroidal anti-inflammatory drugs[9].

Aspirin sensitivity or allergy is another relevant issue. 3-10% of asthmatics are sensitive to aspirin. This is based on an increased basal biosynthesis of cystinyl leukotrienes, probably coming from mast cells as well as eosinophils. Increased severity of asthma may be accompanied by rhinorrhoea, hives, flushing and abdominal pain[10].

Aspirin resistance is another phenomenon which has come to surface in the recent years. There are conflicting reports on the incidence and clinical relevance of this phenomenon. Probably what it means is that some patients, inspite of taking aspirin, may still be exposed to higher risk of cardiovascular events[11].

The profile of the patients who are likely to be aspirin-resistant is still emerging. According to a recent study these patients are likely to be women and less likely to be smokers[12]. However, there does not seems to be a difference in aspirin sensitivity based on race, diabetes, platelet count, renal or hepatic disease. There is still no standardised method of detection of aspirin resistance. Heart Outcomes Prevention Evaluation (HOPE) study [13] suggested that in patients with increased 11-dehydro thromboxane B2, a metabolite of thromboxane A2 in the urine, had an increased risk of cardiovascular events. The HOPE study implicates that alternate pathways for thromboxane synthesis may exist. Thromboxin B2 could be used in future as a marker to identify patients who are receiving suboptimal aspirin or those who are aspirin resistant.

Another implication of aspirin resistance is that these patients, in addition to those who are intolerant to aspirin or aspirin is contraindicated, alternatives to aspirin therapy would have to be used. The newer antiplatelet agents target different sites of the platelet aggregation pathway. This subject has elegantly been covered in an article by Fahim Jafary[14] in this issue of Pakistan Journal of Medical Sciences.

CONCLUSIONS

Clinical use of aspirin continues to increase with its inherent life-saving benefits to the patients. Newer indications are getting established while others are in their emerging stage. Aspirin is remarkably safe; however, it has its

share of adverse effects. Aspirin allergy is already known while aspirin resistance is also emerging. However, this phenomenon is awaiting full elucidation in terms of its definition, incidence and detection. In situations where aspirin can not be used for various reasons, alternative antiplatelet agents are now available but these agents can not match the ease of use and economy of aspirin.

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