Abstrac

Background:

Prostaglandin G/H Synthases (Cyclooxygenases) are enzymes that catalyze the conversion of arachidonic acid to a series of compounds ending in prostaglandins (endogenous compounds triggering many biological & physiological events in many systems including circulatory & renal systems).

Normally, there is a balance between Cox-1 derived thromboxane A2 (TXA2) which acts as a platelet activator enhancing thrombosis, & the antithrombotic cardioprotective effects of prostacyclin (PGI2) which is produced through Cox-2 activity. Thus inhibition of Cox-2 derived PGI2 will exaggerate the cardiovascular effects of TXA2.

Traditional NSAIDs (tNSAIDs) inhibit the formation of both prostanoids and hence mainting this balance normal or near normal. The adjuvant therapies such as α-tocopherol (Vitamin E) & low dose aspirin suggested to act through the reduction of platelet activation, aggregation & hence decreasing thrombosis, with subsequent reduction in cardiovascular events as myocardial infarction and stroke, which could occur as a consequence of Cox-2 inhibitors administration. Our study includes a comparison between the effects of the purely cox-2 selective inhibitor (Celecoxib), and the relatively Cox-2 selective inhibitor (Meloxicam) in cardiovascular consequences, and the effects of adjuvant drugs (vitamin E and low dose aspirin) in modifying these risks.

Setting:

This study has been done at al-Basrah General Hospital under the supervision of a consultant orthopedics with complete authorization from the ministry of health.

Methods:

Sixty patients were selected as having rheumatoid arthritis (RA), or osteoarthritis (OA) with age range of 30-60 years (48±9.72). Fasting blood specimens were obtained to perform specific biochemical investigations based on measuring highly sensitive kit for serum C – reactive protein, serum creatine kinase, serum aspartate aminotransferase, serum urea, serum creatinine, and serum lipid profile. Also blood pressure was measured sphigmomanometrically. Only 36 patients completed the courses of the study, of them 24 patients were with OA, and 12 patients were with RA who were distributed symmetrically among the groups. 12 patients were male, the remainder (24 patients) were female. A group of normal subjects (12) were included as a control group.

The patients were treated as follows:

Group (1): 24 patients with RA (8), or OA (16) treated with celecoxib 400mg/day for 3 months. This group further subdivided into 2 subgroups:

a) Patients with RA (4), or OA (8) given low dose aspirin (100mg/day) co-administered with celecoxib for further 1 month.

b) Patients with RA (4), or OA (8) given vitamin E (800 IU/day) co-administred with celecoxib for further 1 month.

Group (2): 12 patients with RA (4), or OA (8) treated with meloxicam 15mg/day for 3 months.

Assessment to the previously mentioned parameters was done before starting measurement and after 3 months of therapy and for group (1) additional blood specimens were obtained after the addition of the adjuvant therapies i.e. after 1 month.

Results:

In our study, the results indicate that the absolutely selective Cox-2 inhibitor (celecoxib) was not significantly different from the relatively selective Cox-2 inhibitor (meloxicam) in affecting the cardiovascular risk factors.

Both drugs reduced (significantly) the highly sensitive C-reactive protein (hs-CRP) and increase serum total cholesterol, Low Density Lipoprotein /High Density Lipoprotein (LDL/HDL) ratio from pretreatment values. Both drugs have nearly the same effects on renal function where they could deteriorate this function by decreasing glomerular filtration rate (GFR) indicated by elevating serum urea levels. However, the differences that exhibited by meloxicam including a significant increment in systolic blood pressure, and serum creatine kinase (CK), while celecoxib did not exhibit that effect. So this could indicate that meloxicam might aggravate cardiovascular risk factors greater than celecoxib does.

The addition of adjuvant therapies to decrease cardiovascular risk factors produced by celecoxib was not so efficient. Vitamin E reduces (but non significantly) lipid profile, while low dose aspirin does not. Both reduces (but non significantly) hs-CRP levels in serum. These drugs had no effect on systolic blood pressure, or creatine kinase serum levels. However, vitamin E differs from the low dose aspirin in that the former

have had no effect on renal function while the latter aggravated the deteriorated renal function further more investigated by urea level.

Conclusion:

Cyclooxygenase - 2 (Cox-2) inhibitors have different odds on cardiovascular risk factors. Selectivity to that enzyme could play a role in their pharmacological action. The use of adjuvant therapies (vitamin E and low dose aspirin) for a short duration of time can not change significantly the raised cardiovascular risks triggered by celecoxib in patients with arthritis.