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Assessment of renal function after administration different doses of aspirin

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Abstract
Aspirin is commonly used by elderly patients. In previous studies we found transient changes in renal function induced by low doses of aspirin. Hence from the above literature findings the present study was planned to assess the effect of low dose aspirin altering renal function or not. As low dose aspirin has been reported to be a risk factor of hyperuricemia.
The present study was planned in the VMMC & Safdarjung Hospital, New Delhi in total 40 patients without any complications. The patients were those enrolled in long-term care, as well as new patients with various medical conditions necessitating the use of low dose aspirin that were in stable clinical conditions throughout the study. The patients were divided in two study groups based on the dose of the administered aspirin. The group: A patients received the 100 mg/day Aspirin for 4 weeks and Group: B patients were received the 300 mg/day Aspirin for 4 weeks.
In conclusion, the results of the present study indicate that low dose aspirin administration in elderly inpatients for a short time has a significant effect on their renal tubular function. The dose dependent study concluded that the dosage of 300 mg/day aspirin was found to induce a considerably higher changes in renal function and secretion of uric than 100 mg/day. The dosage of 100 mg/day aspirin can be used with more safety during the treatment.

Keywords: low dose aspirin, renal function, uric acid, creatinine

Introduction
The terms "renal function" and "kidney function" mean the same thing. Health professionals use the term "renal function" to talk about how efficiently the kidneys filter blood. People with two healthy kidneys have 100 percent of their kidney function. Small or mild declines in kidney function-as much as 30 to 40 percent-would rarely be noticeable. Kidney function is calculated using a blood sample and a formula to find the estimated glomerular filtration rate (eGFR). The eGFR corresponds to the percent of kidney function available.
For many people with reduced kidney function, a kidney disease is also present and will get worse. Serious health problems occur when people have less than 25 percent of their kidney function. When kidney function drops below 10 to 15 percent, a person needs some form of renal replacement therapy-either blood-cleansing treatments called dialysis or a kidney transplant-to sustain life.

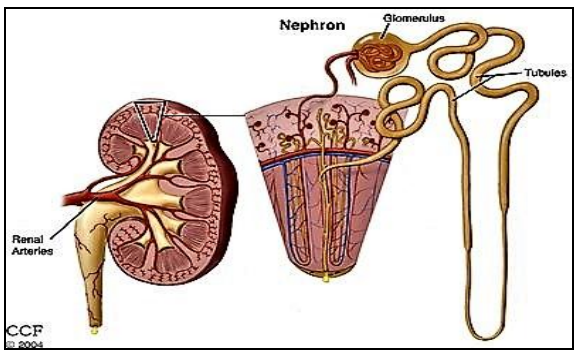

Fig 1

In clinical practice, however, creatinine clearance or estimates of creatinine clearance based on the serum creatinine level are used to measure GFR. Creatinine is produced naturally by the body (creatinine is a breakdown product of creatine phosphate, which is found in muscle). It is freely filtered by the glomerulus, but also actively secreted by the peritubular capillaries in very small amounts such that creatinine clearance overestimates actual GFR by 10% to 20%. This margin of error is acceptable, considering the ease with which creatinine clearance is measured. Unlike precise GFR measurements involving constant infusions of inulin, creatinine is already at a steady-state concentration in the blood, and so measuring creatinine clearance is much less cumbersome. However, creatinine estimates of GFR have their limitations. All of the estimating equations depend on a prediction of the 24-hour creatinine excretion rate, which is a function of muscle mass which is quite variable. One of the equations, the Cockcroft and Gault equation (see below) does not correct for race. With a higher muscle mass, serum creatinine will be higher for any given rate of clearance.
The normal range of GFR, adjusted for body surface area, is 100 mL/min/1.73m2 to 130 mL/min/1.73m2 in men and 90 mL/min/1.73m2 to 120 ml/min/1.73m2 in women younger than the age of 40. In children, GFR measured by inulin clearance is 110 mL/min/1.73 m2 until 2 years of age in both sexes, and then it progressively decreases. After age 40, GFR decreases progressively with age, by about 0.4 mL/min to 1.2 mL/min per year [1].
Risk factors for kidney disease include diabetes, high blood pressure, family history, older age, ethnic group and smoking. For most patients, a GFR over 60 mL/min/1.73m2

is adequate. But significant decline of the GFR from a previous test result can be an early indicator of kidney disease requiring medical intervention. The sooner kidney dysfunction is diagnosed and treated the greater odds of preserving remaining nephrons, and preventing the need for dialysis.

Aspirin, also known as acetylsalicylic acid (ASA), is a medication used to treat pain, fever, or inflammation. Specific inflammatory conditions in which aspirin is used include Kawasaki disease, pericarditis, and rheumatic fever. Aspirin given shortly after a heart attack decreases the risk of death. Aspirin is also used long-term to help prevent heart attacks, ischaemic strokes, and blood clots, in people at high risk. Aspirin may also decrease the risk of certain types of cancer, particularly colorectal cancer. For pain or fever, effects typically begin within 30 minutes. Aspirin is a nonsteroidal anti-inflammatory drug (NSAID) and works similar to other NSAIDs but also suppresses the normal functioning of platelets [2].

Common side effects include an upset stomach. More significant side effects include stomach ulcers, stomach bleeding, and worsening asthma. Bleeding risk is greater among those who are older, drink alcohol, take other NSAIDs, or are on blood thinners. Aspirin is not recommended in the last part of pregnancy. It is not generally recommended in children with infections because of the risk of Reye's syndrome. High doses may result in ringing in the ears [2].

Aspirin and other NSAIDs can cause abnormally high blood levels of potassium by inducing a hyporeninemic hypoaldosteronism state via inhibition of prostaglandin synthesis; however, these agents do not typically cause hyperkalemia by themselves in the setting of normal renal function and euvolemic state [3]. When taken as directed, regular use of aspirin does not seem to increase the risk of kidney disease in people who have normal kidney function. However, taking doses that are too large (usually more than six or eight tablets a day) may temporarily- and possibly permanently- reduce kidney function. In people with kidney disease, aspirin may increase the tendency to bleed. People who already have reduced kidney function, or other health problems such as liver disease or severe heart failure, should not use aspirin without speaking to their doctor [4].

Hence from the above literature findings the present study was planned to assess the effect of low dose aspirin altering renal function or not. As low dose aspirin has been reported to be a risk factor of hyperuricemia.

Methodology

The present study was planned in the VMMC & Safdarjung Hospital, New Delhi in total 40 patients without any complications. The patients were those enrolled in long-term care, as well as new patients with various medical conditions necessitating the use of low dose aspirin that were in stable clinical conditions throughout the study. The patients were divided in two study groups based on the dose of the administered aspirin. The group: A patients received the 100 mg/day Aspirin for 4 weeks and Group: B patients were received the 300 mg/day Aspirin for 4 weeks.

The Patients having history of Urinary tract infection (UTI), renal stone, Hematuria, and Renal stones were excluded from the present study as per study protocol. Excluded patients from the study were with a history of active peptic ulcer, gastrointestinal bleeding, chronic liver diseases, hyperuricemia, serum creatinine > 1.5 mg/dL (132.6 μmol/L), a significant history of alcohol consumption, or recent use of anticoagulants, aspirin, or nonsteroidal anti-inflammatory drugs.

Clearances of creatinine, uric acid and urea were calculated as the products of urine concentrations and 24-hour urine collection divided by the serum concentrations and expressed as ml/min.

Results and Discussion

The data from the both the study group was collected and presented as below. The patients were divided in two study groups based on the dose of the administered aspirin. The group: A patients received the 100 mg/day Aspirin for 4 weeks and Group: B patients were received the 300 mg/day Aspirin for 4 weeks.

Table 1: Demographic data

Group	Group A	Group B
No. of Patients	20	20
Dose of Administered Aspirin	100 mg/day	300 mg/day
Age in years	35-65	32-63
Males	16	14
Females	4	6

Group	Group A		Group B	
Dose of Administered Aspirin	100 mg/day		300 mg/day	
Parameters	Baseline	After 4 weeks	Baseline	After 4 weeks
Serum Uric Acid (mg/dl)	5.5±1.2	4.9±1.3	5.6±1.2	5.2±0.8
Fractional Excretion of Uric Acid (mg/dl	46.4±10.5	35.70±8.2	43.8±9.5	26.3±6.8
Uric Acid Clearance (ml/min)	8.6±0.6	7.2±0.9	8.9±0.8	6.9±1.1
Serum Creatinine (mg/dl)	1.3±0.2	1.1±0.1	0.85±0.2	1.2±0.1
Urine Creatinine (mg/dl)	122±28	127±22	112±13	95±13
CrCl (ml/min)	110±15	102±13	115±10	97±12
Serum Urea (mg/dl)	26±8	33±5	27±5	32±4
Urine Urea (mg/dl)	1860±290	1810±330	1840±280	1590±290

The dose of 100 mg/d of aspirin did not significantly affect serum uric acid, creatinine and urea levels, whereas it significantly decreased urinary uric acid fraction and uric acid clearance rate respectively. While 300 mg/d aspirin, caused a significant elevation in serum uric acid, creatinine and urea levels, with a significant reduction in the 24h-urinary fractional excretion, and the 24 urine uric acid, creatinine clearance.

Comparing our results with those of previous studies, Louthrenoo *et al*. [5] found that both 300 mg/d and 60 mg/d doses of aspirin decreased the fractional excretion of uric acid after 2 weeks of therapy. A relatively significant decreased uric acid clearance and creatinine clearance was found in those who were on 300 mg/day aspirin therapy only. While serum creatinine and uric acid concentration, remained stable during both drug administration periods. The important differences between these studies included aspirin dosages and duration of therapy.

A related result on the effects of the current low dose aspirin regimens (75-325 mg/day) for cardiovascular disease prevention were previously studied in two groups of elderly patients [6-7]. They found that these doses of aspirin were capable of inducing a significant decrease in both creatinine and uric acid excretion within 1-2 weeks. One week after the drug was withdrawn, uric acid excretion returned to normal while creatinine clearance remained low. In another trial Segal *et al*. [7] reported that Mini-dose aspirin, even at a dosage of 75 mg/day, caused significant changes in renal function and UA handling within 1 week in a group of elderly inpatients, mainly in those with preexisting hypoalbuminemia. In contrast, when Low doses (100 mg/ day) of aspirin were administered in gouty arthritis patients treated with allopurinol or benzbromarone for 4 weeks did not influence serum uric acid level or urinary uric acid excretion [8].

A limitation of our study relates to the true GFR estimations. Based on the American National Kidney Foundation guidelines, the estimates of glomerular function by C-G and MDRD equations are the best overall indices of the level of kidney function. We also estimated GFR by the MDRD formula and the results were absolutely similar to the results obtained from C-G formula (data not shown). However, in older patients these methods may under-or overestimate the GFR [9-11].

Conclusion

In conclusion, the results of the present study indicate that low dose aspirin administration in elderly inpatients for a short time has a significant effect on their renal tubular function. The dose dependent study concluded that the dosage of 300 mg/day aspirin was found to induce a considerably higher changes in renal function and secretion of uric than 100 mg/day. The dosage of 100 mg/day aspirin can be used with more safety during the treatment.

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