Ibuprofen May Increase AKI Risk in Ultramarathon Runners

Acute kidney injury (AKI) may be more frequent in ultramarathon runners who take ibuprofen, according to a randomized controlled trial in Emergency Medicine Journal.

The study included 91 athletes participating in 50-mile ultramarathon races in desert environments. Runners were randomly assigned to take ibuprofen 400 mg or placebo tablets every 4 hours during their race. Incidence of AKI was compared between groups: “risk” was defined as a 1.5-fold increase in creatinine and “injury” as a twofold increase. Runner characteristics were similar between groups; in the ibuprofen group, average total dose was 1200 mg.

Overall AKI incidence was 44%. On intention-to-treat analysis, AKI occurred in 52% of runners taking ibuprofen versus 34% taking placebo. The 18% difference exceeded the 15% noninferiority threshold. However, the efficacy to harm was 5.5 ibuprofen-treated runners to cause 1 additional case of AKI.

Both categories of AKI were more frequent with ibuprofen: 58% versus 26% for “injury” (nonsignificant) and 14% versus 9% for “risk” (significant). Slower finishers were less likely to develop AKI: odds ratio (OR) 0.67. Greater weight loss was associated with a higher risk of AKI: OR 1.2 at a 1.5% reduction in body weight.

Studies have reported 34% to 85% rates of AKI in ultramarathons. Although it has been suggested that nonsteroidal anti-inflammatory drugs (NSAIDs) might contribute to these rates, up to three-fourths of runners still take NSAIDs during races. The evidence for and causal nature of this association are unclear.

Despite the lack of statistical significance, this trial suggests an increased risk of AKI in ultramarathon runners who use ibuprofen. Taking NSAIDs during endurance running “could exacerbate renal injury,” the researchers write. They note that associations of AKI with finishing time and weight loss suggest a role of dehydration (Lipman GS, et al. Ibuprofen versus placebo effect on acute kidney injury in ultramarathons: a randomised controlled trial. Emerg Med 2017; doi: 10.1136/emerg-2016-206353).

Is it time for a new school of thought?

In CKD, progressive loss of renal function along with chronic inflammation leads to:

- High concentrations and reduced clearance of hepcidin
- Impaired intestinal iron absorption
- Restricted release of iron from storage

Can different thinking help us address these challenges for iron-deficiency anemia in CKD?
Does Contrast Exposure Cause Contrast-Induced AKI?

Contrast media exposure is not a “primary pathogenetic factor” in the development of acute kidney injury (AKI) after primary angioplasty, report a study in the open-access Journal of the American Heart Association.

The researchers analyzed 2025 patients with ST segment-elevation myocardial infarction (STEMI) who underwent primary percutaneous coronary intervention at an Israeli hospital between 2000 and 2015. Median contrast dose was 150 mL. Rates of AKI were compared with those of 1025 patients undergoing fibrinolysis or no reperfusion therapy, who were not exposed to contrast medium. Acute kidney injury was defined as a creatinine level of 0.5 mg/dL or a creatinine increase of greater than 25% within 72 hours. The dose of contrast agent was not a significant factor. A risk score developed from the primary angioplasty group had similar discriminatory performance for AKI in the angioplasty and comparison groups.

Acute kidney injury occurring after primary percutaneous coronary intervention is commonly reported as “contrast-induced” AKI. However, other factors may contribute to this risk; previous studies of this issue have lacked a control group of patients not exposed to contrast medium.

The new analysis suggests that contrast exposure is not the primary cause of AKI after primary angioplasty in patients with STEMI. The increase in adverse outcomes with AKI after angioplasty appears to be independent of contrast exposure. The authors conclude, “A[tempts to reduce AKI rates in STEMI patients likely require targeting mechanisms that are unrelated to contrast media.” (Caspi O, et al. Acute kidney injury after primary angioplasty: is exposure to contrast medium a “primary pathogenetic factor”? J Am Heart Assoc. 2017. doi:10.1161/JAHA.117.005715.)

Policy Update

NIH Gains in Appropriations Budget, but Falls Short of Need

By Zachary Kribs

On Thursday, July 13, 2017, the House Labor, Health and Human Services, Education, and Related Agencies Appropriations (LHHS) Subcommittee approved the Fiscal Year 2018 budget by a party-line vote. One of the largest of 12 annual appropriations bills, the LHHS bill provides a $5 billion reduction in funding to the Department of Health and Human Services as compared to enacted 2017 funding. However, the legislation provides for a few exemptions from the cuts, including a $1.1 billion increase for the National Institutes of Health.

Under the normal appropriations process as outlined by the Congressional Budget Act, the President presents their budget blueprint to Congress the first Monday of February. By mid-April, Congress completes action on the budget resolution, which sets topline spending levels for the government. Congress then begins to craft appropriations legislation, which specify exact funding levels for all discretionary programs. This process must be complete by the beginning of the fiscal year on October 1, otherwise the government runs out of money and shuts down.

However, this year, as in previous years, the budget process is far from on schedule. Congressional leadership in charge of determining the budget has yet to complete negotiations on topline spending levels, while appropriators, shuffling off normal order, are crafting appropriations legislation without the guidance of a budget resolution. Discrepancies between the appropriations bills and the budget resolution could further delay the budget process, and with just over a month of scheduled work days before the end of the fiscal year, many legislators are predicting the need for emergency funding measures like last year’s series of continuing resolutions.

While the LHHS appropriations bill is a far cry from the Trump administration’s budget proposal, whose drastic cuts the American Society of Nephrology (ASN) spoke out against earlier this year, the bill falls short of ASN’s asks. A $1.1 billion increase for the National Institutes of Health is much more preferable than a $6 billion cut, but the amount is basically half of the $2 billion increase necessary to keep pace with medical inflation and sustain current research levels. Kidney diseases in particular deserve special attention. The government has already pledged $53 billion annually to support dialysis; greater emphasis on funding kidney research will foster breakthrough developments that would change the lives of the nearly 700,000 Americans living with kidney failure, and greatly reduce the burden kidney diseases place on the economy.

ASN will watch the bill closely as it moves through Congress. The legislation is scheduled for a full markup by the House Appropriations Committee on Wednesday, July 18, and will then be voted on in the full House floor before being sent to the Senate. Many amendments are expected to be made, and ASN will continue to advocate for both a $2 billion increase and the establishment of a Special Kidney Program to address the outsourcing toll kidney diseases place on the American public.

Cuts Proposed for NIH Funding for Facilities and Operating Costs

By Ryan Murray

In addition to the “proposed” sweeping reduction to the National Institutes of Health (NIH) budget, which is not expected to be supported by Congress, President Trump’s fiscal year 2018 budget includes significant reductions to NIH support for costs associated with conducting federally supported research, causing concern within the medical research community.

The total cost of federally sponsored research includes both direct and facilities and administrative (F&A) expenses (previously referred to as “indirect costs”). Direct costs are used to cover portions of researcher salaries and necessary equipment and supplies, while F&A costs refer to necessary research infrastructure and operating expenses that the university provides to support research.

Despite F&A costs as a percentage of federal funding remaining relatively unchanged at approximately 27% for more than a decade, they have become a popular target among politicians looking to reduce federal expenses because of a misconception by the public that F&A costs do not support research. F&A expenses are essential research costs including but not limited to personnel support, physical infrastructure, energy and utility expenses, costs of regulatory compliance, and other government-mandated expenses. These expenses are necessary to conduct high-quality medical research. A reduction in F&A costs would make research unaffordable for many institutions and lead to a reduction in critical biomedical research.

The proposed reduction in F&A costs can be achieved through two routes. Congress could pass a statute that caps the F&A costs an institution can be reimbursed for; this, however, is seen as unlikely due to the bipartisan support for medical research.

The more likely route is a lengthy process in which the Office of Management and Budget could issue new guidance. This process would occur over several years and would require public comment on the proposed guidance. The American Society of Nephrology has encouraged the administration to support medical research and reconsider its proposal on F&A costs, and will continue to track this issue.