

NASID in Sports Medicine: A Plea for More Considerate Use

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Editorial

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are commonly used by physically active people to reduce existing or prevent anticipated musculoskeletal pain related to physical exercise [1,2]. The reported prevalence of NSAIDs among athletes widely differs between various sports and ranges from 12% in cyclists to 90% in professional soccer players [3,4]. This suggests that the use of these drugs is safe. However, NSAIDs are associated with a variety of adverse gastrointestinal and cardiovascular events and we have recently published a study that adds to the evidence that NSAIDs (ibuprofen) cause significant small intestinal injury if used during strenuous exercise in healthy individuals.

Evidence is accumulating that NSAIDs have hazardous effects on more the cardiovascular, renal, musculoskeletal and gastrointestinal system. Studies have demonstrated a significant increase in cardiovascular events associated with the use of NSAIDs, with an elevated risk of approximately 25% for non-fatal myocardial infarction [5]. The use of NSAIDs is also associated with a number of contra-indications such as an active gastro duodenal ulcer, renal dysfunction and the use of specific drugs.

With regard to the musculoskeletal system, the use of conventional NSAIDs as analgesic by patients with healing fractures was reported to impair bone healing. The question was also raised whether the use of NSAIDs had a detrimental effect on soft tissue healing; however, there is insufficient human data reported to draw conclusions [6].

The extent to which NSAIDs cause intestinal injury in healthy individuals was recently demonstrated. Strenuous physical exercise itself can compromise the gastrointestinal tract. Complications such as mucosal ulceration, diarrhea and ischemic colitis have been reported during and after completion of long-distance runs [7,8]. The exact causes of these complications remain to be determined, but one of the main contributors in the pathogenesis is thought to be the physiological reduction of gastrointestinal perfusion, leading to hypo perfusion of the gut.

Such a physiological reduction of blood flow is the result of a redistribution of the blood flow during exercise, directing the blood towards the active muscles, heart and lungs, away from the gastrointestinal system [9,10]. We previously demonstrated that the resulting intestinal hypoperfusion leads to small intestinal injury and temporary loss of gut barrier function in otherwise healthy individuals [11]. Such injury occurred in all of the tested subjects, but it remains subclinical in the majority of athletes, which means that this intestinal injury is usually not accompanied by gastrointestinal problems. It generally lasts as long as the exercise bout and resolves spontaneously within approximately one hour after exercise, depending on the intensity and duration of the exercise bout [11]. However, it does contribute to the pathogenesis of gastrointestinal complaints [12], and

in combination with other risk factors, such as the use of NSAIDs, it may cause severe abdominal distress.

Our recent study describes that the use of NSAIDs during strenuous physical exercise aggravates the hypoperfusion-induced intestinal injury during exercise [13]. The mechanism for these effects is presumed to be worsened gastrointestinal blood flow, since NSAIDs have been described to impair local gastrointestinal perfusion due to inhibition of the enzyme cyclo-oxygenase (COX)-1 [14].

In addition, reduced production of local nitric oxide via regulation of the NF-kappa-B pathway and COX-2 inhibition, leading to immunodisregulation, are thought to further compromise the gastrointestinal tract [15]. Therefore, we hypothesized that the use of NSAIDs in combination with strenuous exercise causes profound intestinal injury. Healthy, young individuals were studied on four different occasions to determine the effects of exercise and the oral intake of the NSAID Ibuprofen (two doses of 400 mg), either alone or combined. As expected, we observed subclinical exercise-induced intestinal injury. The levels of intestinal injury however, were twice as high after exercise with prior intake of Ibuprofen. In line with these observations, loss of gut barrier function was most pronounced in case of the combination of Ibuprofen and exercise. Taken together, our data clearly demonstrated that two single doses of ibuprofen prior to exercise aggravate exercise-induced intestinal injury and gut barrier dysfunction in healthy individuals. It remains to be determined whether such intestinal injury has implications for musculoskeletal and gastrointestinal tissue recovery after strenuous exercise.

In conclusion, the use of NSAID supplementation in combination with strenuous physical exercise induces small intestinal injury and gut barrier dysfunction in healthy individuals, which may have implications for recovery after exercise. These data and the previous reports on cardiovascular complications and contra-indications led us to conclude that NSAID consumption by athletes is not harmless and its pre-emptive use should be strongly discouraged. Therefore, NSAIDs should only be considered for patients in need of pain treatment without contra-indications for these drugs. If a clear indication for NSAIDs is present, we would recommend topical NSAID application since this is reported to be beneficial in improving pain, without the gastrointestinal side effects associated with oral administration [16,17].

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