

Painkillers may threaten power of vaccines

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With flu-shot season in full swing and widespread anticipation of the HPV vaccine to prevent cervical cancer, a new University of Rochester study suggests that using common painkillers around the time of vaccination might not be a good idea.

Researchers showed that certain nonsteroidal anti-inflammatory drugs (NSAIDs), also known as cyclooxygenase inhibitors, react with the immune system in such a way that might reduce the effectiveness of vaccines.

The research has widespread implications: study authors report that an estimated 50 to 70 percent of Americans use NSAIDs for relief from pain and inflammation, even though NSAIDs blunt the body's natural response to infection and may prolong it.

“For years we have known that elderly people are poor responders to the influenza vaccine and vaccines in general,” said principal investigator Richard P. Phipps, Ph.D., a professor of Environmental Medicine, and of Microbiology and Immunology, Oncology and Pediatrics. “And we also know that elderly people tend to be heavy users of inhibitors of cyclooxygenase such as Advil, aspirin, or Celebrex. This study could help explain the immune response problem.”

The study is available online in the Dec. 1, 2006, Journal of Immunology, and was funded in part by the National Institutes of Health. (See full study at:

<http://www.jimmunol.org/cgi/content/full/177/11/7811>)

When a person is vaccinated, the goal is to produce as many antibodies as possible to effectively neutralize the infection. To do this, white blood cells called B-lymphocytes, or B cells, spring into action to produce those antibodies. B cells also serve as the immune system's memory for future protection against the illness.

But Phipps and colleagues discovered that human B cells also highly express the cyclooxygenase-2 (cox-2) enzyme, which is not intrinsically bad unless it is overproduced, causing pain and fever. So, when a person takes a drug to block the cox-2 enzyme – and thereby reduce pain and fever – the drug also reduces the ability of B cells to make antibodies.

“The next step is to figure out the worst time to take drugs that inhibit cox-2 in the context of getting vaccinated. Is it the day before, the day of, or the day after” The timing is likely to be very important,” Phipps said. “But meanwhile, we believe that when you reach for the medicine cabinet to reduce pain at the injection site, that is probably the wrong thing to do.”

The findings are based on laboratory studies of blood samples from people who participated in early clinical trials for the HPV vaccine, and on studies of mice.

For the animal portion of the study, researchers vaccinated normal mice and mice engineered to be cox-2 deficient with a component form of the HPV vaccine. They analyzed the amount of antibodies the animals produced, focusing on the critical virus-neutralizing antibodies. The cox-2 deficient mice made 50 to 70 percent less of these key antibodies.

The same experiment was done on preserved blood samples from people who had been vaccinated against HPV-16, the strain linked to cervical cancer. Scientists reactivated the B cells in the blood samples and watched them churn out antibodies, as expected. But when researchers

treated the B cells with a cox-2 inhibiting drug, the cells significantly diminished their production of antibodies – showing that cox-2 is essential for an optimal immune response against HPV 16.

This study is not questioning the effectiveness of the newly marketed HPV vaccine, the Rochester scientists said. They pointed out that in many clinical trials involving thousands of women, the vaccine offered complete protection against the development of cervical cancer. And presumably some of these women were taking NSAIDs at the time.

“There’s no doubt the HPV vaccine showed 100 percent efficacy. Still, our data does suggest that it might be wise to limit the use of NSAIDs when you receive any vaccine,” said co-author Robert Rose, Ph.D., associate professor of Medicine and Microbiology and Immunology at the University of Rochester, and one of the virologists whose work led to the development of the new cancer vaccine.

Scientists do not completely understand the mechanism by which cox-2 influences the immune response in humans. They do believe the response may depend upon the dose and frequency of NSAID use.

The negative effects of blocking cox-2 could be more pronounced in people with compromised immune systems, such as AIDS or cancer patients, the study noted. Moreover, if a vaccine is in short supply and needs to be given in lower-than-optimal doses, taking an NSAID could hamper the immune response even more.

Source: University of Rochester Medical Center

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