McGowan Institute for Regenerative Medicine
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Erectile Dysfunction Drugs Could Protect Liver from Sepsis-Induced Damage

Drugs that are on the market to treat erectile dysfunction (ED) could have another use—they might be able to protect the liver from damage caused by sepsis, a systemic inflammatory response to infection, says senior investigator and McGowan Institute for Regenerative Medicine faculty member Timothy Billiar, MD, and researchers at the University of Pittsburgh School of Medicine. They recently published their findings in *Science Signaling*.

Infection can lead to the release of chemicals that cause whole-body inflammation, which can cause life-threatening damage to organs including the liver and kidneys, explained Dr. Billiar, professor and chair of surgery, Pitt School of Medicine. Sepsis is a leading cause of death in the intensive care unit.

"Sepsis is a very challenging problem, so the possibility that we might be able to repurpose a drug that is in use and well understood is very exciting," Dr. Billiar said.

Sepsis triggers production of a protein called tumor necrosis factor, or TNF, which helps fight infection but is harmful at sustained high levels. The researchers found in a mouse model of sepsis that sildenafil, more commonly known as Viagra, induced the liver to produce greater amounts of a protein called cyclic GMP, which in turn led cells to shed surface proteins called TNF receptor, reducing TNF signaling in the cells and preventing liver damage. Experiments with human liver cells also showed the protective effects of the drug.

"Our study suggests that increasing the bioavailability of cyclic GMP might be beneficial in ameliorating the inflammation associated with sepsis," Dr. Billiar said. "Sildenafil and other ED drugs might be a good approach to try early in the course of the illness to forestall organ damage."

The research team plans to verify their findings in a large animal model of sepsis.

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Abstract (Shedding of the tumor necrosis factor (TNF) receptor from the surface of hepatocytes during sepsis limits inflammation through cGMP signaling. Deng M, Loughran PA, Zhang L, Scott MJ, Billiar TR. Science Signaling; 2015 Jan 27;8(361):ra11.)

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