

New effects of ketamine abuse uncovered

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Research conducted by scientists at the University of York has revealed how recreational ketamine abuse damages the bladder.

In two studies, one of which is published today, the team shows how ketamine present in urine causes damage to the epithelial lining of the [bladder](#), allowing urine to penetrate into underlying tissues which causes inflammation and extreme pain. In some cases this pain can be so extreme that patients need to have their bladder removed (cystectomy).

Led by Dr Simon Baker in the University of York's Department of Biology, in collaboration with clinicians from Middlesbrough and Leeds hospitals, the first study looked at a cystectomy case. This would determine whether bladder damage was caused by direct contact with urinary ketamine or whether the drug causes a systemic change in the whole body that affects the organ.

Reporting a rare physiological coincidence, the team studied [epithelial cells](#) lining the bladder and also in an adjacent remnant of the foetal urinary tract, not in contact with urine, known as an urachus.

Finding that epithelial cells lining the bladder were almost completely absent, having died and been sloughed off into the urine, epithelial cells from the urachus appeared healthy. This shows direct contact with urine is critical to the toxicity of ketamine to the bladder epithelium, ruling out systemic factors.

In the second study, the researchers used epithelium cells taken from

healthy patients to study how ketamine affects the bladder. Used to produce laboratory models, cells were exposed to ketamine and their responses analysed.

The researchers found that ketamine overwhelms the cell's internal power stations, known as mitochondria, causing a catastrophic release of toxins. To avoid this "melt-down", cells commit a controlled form of suicide (apoptosis) resulting in cell death. This occurs in a regulated fashion that does not cause excessive toxicity to other cells in an attempt to protect the remaining tissue; however, in the case of chronic ketamine abuse, all epithelial cells are killed.

Dr Baker, Senior Postdoctoral Research Fellow in York's Jack Birch Unit for Molecular Carcinogenesis, said: "These two studies combine to demonstrate that direct contact with urinary ketamine causes significant bladder damage, and shows how this drug causes the death of previously healthy bladder cells.

"We now have a more detailed understanding of how and why chronic ketamine abuse results in bladder problems and cystitis. Understanding the full side-effects of ketamine is very important as other researchers are currently investigating the potential for this drug to spawn a new generation of anti-depressants."

Ketamine poisoning of the epithelial lining can lead to extreme pain associated with ketamine cystitis. Urologists advise anyone who experiences bladder pain when using ketamine to stop taking the drug immediately, as if too many bladder cells are killed there will not be enough remaining to repair the tissue.

More information: Elizabeth Kidger et al. A Rare Urachal Cyst in a Case of Ketamine-induced Cystitis Provides Mechanistic Insights, *Urology* (2015). [DOI: 10.1016/j.urology.2015.12.015](https://doi.org/10.1016/j.urology.2015.12.015)

Provided by University of York

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