

# Synthetic cannabinoid may aid fertility in smokers

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A reproductive medicine specialist at the University at Buffalo has shown that a new compound may improve the fertility of tobacco smokers who have low sperm count and low percentage sperm motility.

The sperm from male smokers were washed with a synthetic chemical called AM-1346. After incubation, there was a doubling in the fertilizing capacity of sperm from poor quality semen, results showed.

Lani Burkman, Ph.D., and colleagues presented the findings at the 2006 meeting of the American Society of Reproductive Medicine held recently in New Orleans. "Based on our previous data and published literature, it is clear that most tobacco smokers will exhibit a small or a significant decline in fertility," she stated. "Nicotine addiction is quite powerful. The best solution is to stop smoking and then wean yourself off of all nicotine products. But for smokers who can't quit, the in vitro use of AM-1346 may significantly improve their fertilizing capacity."

Burkman, associate professor in the departments of gynecology/obstetrics and urology and head of the Section on Andrology in the UB School of Medicine and Biomedical Sciences, previously demonstrated that sperm functions critical for fertilization are altered by nicotine exposure, whether in vitro, or through long-term tobacco use. Two-thirds of the male smokers studied had decreased fertility; some showed a serious loss.

The new study involved nine selected smokers (22 experiments) who had

been evaluated previously for sperm fertilizing potential using the outside cover of a human egg, called the zona pellucida. Four men had a high number of sperm attaching to the zona (normal, Group I), while five other smokers had sperm with poor egg binding (poor fertilizing potential, Group II).

The new experiments were designed to evaluate whether sperm with poor fertilizing capacity from smokers could be treated so that egg binding was improved. Specifically, the researchers studied a potential interaction between two chemical systems that control sperm.

"Human sperm carry the cholinergic receptor, which responds to the neurotransmitter acetylcholine," noted Burkman. "Nicotine mimics acetylcholine and binds to the cholinergic receptor." In earlier research, Burkman and colleagues also showed that human sperm contain cannabinoid receptors, which respond to marijuana, as well as natural cannabinoids occurring in the body.

"Research from other scientists indicates that the cholinergic system and the cannabinoid system naturally regulate human sperm and help prepare them for fertilizing an egg," she said. "Our research suggests that this natural regulation is out of balance for the majority of smokers when sperm are continuously exposed to nicotine.

"We think there is an important communication between the cannabinoid and cholinergic receptor systems in human sperm," said Burkman. "No one has shown this interaction before when looking at human tissue. AM-1346, the drug that we tested, is a synthetic version of a natural cannabinoid found in the body.

"In 22 Hemizona tests, we showed that the response to AM-1346 depended on the initial fertility of the tobacco smoker, and if his semen showed poor quality, meaning low sperm count and low percentage

motility."

The sperm from Group II volunteers were incubated with AM-1346 for several hours and then retested in the Hemizona Assay. Six experiments in Group II started with semen of low quality and all six resulted in stimulation of sperm binding to the zona ranging from 133 percent to 330 percent, with a mean of 201 percent, when compared to their own untreated sperm, results showed.

"In contrast," said Burkman, "samples from Group I (normal fertility, normal semen quality) reacted in the opposite manner. This two-way, or biphasic, response is common for cannabinoid action. With Group I, the drug AM-1346 caused a substantial decrease in sperm binding to the zona for eight out of nine samples.

"This opposite response must be studied further," Burkman said. "It might be tied to early-versus-late steps in fertilization, where it is expected that one process is slowed down while another process is stimulated.

"It does appear that sperm functioning in tobacco smokers with low fertility and low semen quality is quite different when compared to smokers with higher fertility and good semen quality. Nicotine appears to change the sperm membranes and sperm receptors. It also raises the question of why sperm from some smokers are protected from the effects of tobacco and nicotine."

Source: University at Buffalo

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