

Heavy smoking cuts women's chance of pregnancy – even with donated oocytes

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Heavy smoking may reduce female fertility by directly affecting the uterus – making it less receptive and reducing the chances the embryo will implant, according to research published on line in Europe's leading reproductive medicine journal *Human Reproduction*.

The finding, from a team of fertility experts in Portugal and Spain, comes as a result of comparing the pregnancy rates between non-heavy smokers and heavy smokers, all of whom received donated oocytes.

Smoking has long been known to affect female fertility, but this study is believed to be the first to examine the impact of smoking in women who have received donated oocytes – the situation that allows the most objective assessment of the role of the uterus in the outcome of IVF.

The researchers studied all the first cycles of oocyte-donated IVF treatments carried out at the IVI-Valencia Foundation between the start of 2002 and June 2005 – 741 in non-heavy smokers (under 10 cigarettes a day) and 44 in heavy smokers (over 10 a day). None of the women's partners were smokers and none of the oocyte donors were heavy smokers. The two groups of recipients were comparable and the number of embryos transferred in each cycle (between one and three) was also comparable between the groups.

Lead researcher Dr Sérgio Soares, Director of the IVI Clinic in Lisbon, said: "The non-heavy smokers had a significantly higher pregnancy rate, with over half becoming pregnant (52.2%), compared with just over a



third (34.1%) of the heavy smokers.

"This means we have confirmed previous data that show light smoking has no significant impact on IVF cycles, either through affecting the ooctye or the uterus. But, heavy smokers have a much lower chance of achieving pregnancy. The fact that we see this result in a situation in which the oocytes were donated by other women demonstrates that cigarette smoking negatively affects the receptiveness of the uterus independently of its effect on ovarian function, and this is a new finding."

Although the pregnancy rate was much lower in heavy smokers, for those that did become pregnant the multiple pregnancy rate was much higher, with 60% of the heavy smokers expecting twins against 31% of the non-heavy smokers.

"This is counter-intuitive," said Dr Soares, "and although we controlled for all known interfering variables, it is possible this is not a real association. What would confirm it as a real association is to find it still applies in a large number of cases. However, if it is confirmed as a real association it suggests that, paradoxically, tobacco constituents affect the uterus in different ways in different women, impairing implantation in some and having the opposite effect in others.

"It is already known that there is paradoxical dose-dependent effect of nicotine on ovarian tissue. Maybe the same effect is happening in uterine tissue. The effect of a certain molecule depends, not only on its concentration, but also on the concentration of its receptors and all the other molecules present in the cell. It could be that heavy smoking disrupts the stability of cells in the lining of the uterus differently in some women to others or triggers a response in the embryo itself, resulting in a reduced general pregnancy rate overall, but an increased chance of multiple pregnancy in those who do become pregnant."



Dr Soares said, that as well as confirming these findings in higher numbers of heavy smokers who use donated oocytes, it would be worthwhile studying differences in gene expression in the lining of the uterus of heavy smokers who fail to get pregnant and those whose have twins.

But, for now, the clinical implications of the findings were clear. Tobacco makes the uterus less likely to accept an embryo.

"In spite of all the noise generated about the effects of smoking in a series of health areas, its possible effect on uterine receptiveness has never been evaluated until now," he said.

"Our study is just the first step on this path, and certainly not the last, but it means that we should now be telling patients, if they are heavy smokers, that even if fertilisation takes place they have less chance of achieving a successful pregnancy, whether they are trying to conceive naturally, or through IVF, and particularly with donated ooctyes. Furthermore, we should also warn them of the risks of multiple births, as multiple births are less safe for mothers or babies."

Source: Oxford University

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