Study supports link between injectable hormonal contraceptive and HIV risk

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Women using depot medroxyprogesterone acetate (DMPA), commonly known as Depo-Provera or the birth control shot, have a moderately increased risk of becoming infected with HIV, a large meta-analysis of 12 studies involving more than 39 500 women published in *The Lancet Infectious Diseases* has found. Other forms of hormonal contraception, including oral contraceptive pills, do not appear to increase this risk.

Worldwide about 144 million women use hormonal contraception—around 41 million use the injectable forms and 103 million take the oral contraceptive pill. Whether or not use of hormonal contraceptives increases women's risk of HIV acquisition has been hotly debated for more than two decades. But research so far has been inconclusive.

Researchers from the University of California at Berkeley in the USA conducted a meta-analysis of all existing data examining the effect of using the most commonly prescribed forms of hormonal contraception (combined oral contraceptives, progestin-only pills, and the injectable contraceptives DMPA and norethisterone enanthate) on HIV risk up to June, 2014.

Analysis of 12 observational studies from sub-Saharan Africa involving 39 560 women suggest that DMPA use increases a woman's chance of becoming infected with HIV by 40% compared with women using other contraceptive methods or no method. Although statistically significant, this represents only a moderate increase in relative risk. This risk appears to be lower among women in the general population (increase 31%) than for women already at high risk of acquiring HIV such as sex workers. However, the limited number of studies on high risk women leaves uncertainty for this important subgroup of women. No increased risk was noted for users of oral contraceptive pills, combined oral contraceptives, or norethisterone enanthate.

"The moderate elevation in risk observed in our study is not enough to justify a complete withdrawal of DMPA for women in the general population", cautions Lauren Ralph, lead author and an epidemiologist at the University of California at Berkeley. "Banning DMPA would leave many women without immediate access to alternative, effective contraceptive options. This is likely to lead to more unintended pregnancies, and because childbirth remains life-threatening in many developing countries, could increase overall deaths among women."

She adds, "Further evidence regarding the magnitude and mechanisms of the DMPA and HIV link among high risk women, such as commercial sex workers and women in serodiscordant partnerships (where one partner is HIV-positive and the other is not), is urgently needed."

Writing in a linked Comment, Christopher Colvin from the University of Cape Town in South Africa, and Abigail Harrison from Brown University School of Public Health in the USA say, "Currently, the increasingly narrow and fierce debates over the HIV and *depot medroxyprogesterone acetate* link have focused on whether a large randomised controlled trial should be done to better understand this link. Like many scientific controversies, views have become hardened, personal, financial, or political agendas have been suggested, and there has even been intrigue in the form of leaked copies of articles under peer review. Both sides have raised important, compelling arguments, but their partisan character can weaken the quality of the debates and restrict the view of the complex relation between evidence, policy, and practice."

They add, "Ralph and colleagues' signature contribution is their nuanced discussion of what their research adds and what is possible with current and future evidence...They describe an approach to evidence, policy, and practice rooted in an "ecology of evidence" as the foundation for..."
thinking through the next steps. The current polarised environment around the proposed trial makes this more holistic approach all the more difficult, but necessary.

More information: The Lancet Infectious Diseases, www.thelancet.com/journals/lanc ... (14)71052-7/abstract

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