News

Hormonal contraception use among teenagers linked to depression

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Re: Hormonal contraception use among teenagers linked to depression - Yet another example of a never ending confusion between relative and absolute risks?

Millions of women worldwide use hormonal contraception (HC) and it is recognised that some women report that they experience mood changes associated with HC (1) . But is there an increased frequency (or risk) of depression among women using HC compared to non-users? If so, would this imply a causal link between HC and depression? Would it then be reasonable to expect that stopping contraceptive use would reverse the symptoms in many women who suffer from depression?

Based on data collected from a large registry-based cohort study of more than one million women in Denmark, Skovlund et al (1) assessed the influence of HC on the risk of subsequent use of antidepressants and subsequent diagnosis of depression at a psychiatric hospital. They found that women who used combined oral contraceptives had a risk of first use of antidepressants that was increased by 23% compared with non-users (adjusted RR = 1.23, 95% CI 1.22 – 1.25), independent of age, calendar year, educational level, history of polycystic syndrome and endometrioses. A “slightly lower” increase by 10% in the risk of a first confirmed diagnosis of depression was found for women on combined oral contraceptives compared to non-users (adjusted RR = 1.10, 95% CI 1.08 – 1.31). In adolescents, the relative risk increases were even more dramatic: HC was associated with an increase in the risk of antidepressant use of 80% (adjusted RR = 1.8, 95% CI 1.75 – 1.84) and an increase by 70% in the risk of having a confirmed diagnosis of depression (adjusted RR = 1.7, 95% CI 1.63 –1.81). The authors implied a causal link by stating in their abstract that these findings are “suggesting depression as a potential adverse effect of HC use”.

Within few days following its publication in JAMA Psychiatry, the study grabbed much attention in the media and alarming headlines made it in the news , such as “If you take hormonal contraceptives, you need to know about this new study” (Business Insider UK, 11/10/2016) or “The pill: From sexual revolution to cancer and depression links (The Independent, 2/11/2016)” or even “‘It’s not in your head’: Striking new study links birth control to depression” (The Washington Post, 5/10/2016)”. The study also attracted the attention of the British Medical Journal (2), but readers’ rapid responses were conflicting. One gynaecologist wrote that “it is not new news that HC can cause depression” and then referred to findings of studies performed in the 1960s that “have mostly been ignored for 50 years” (3). Another gynaecologist prudently noted that the Skovlund et al findings may show over-prescription of antidepressants in Denmark and cause concern that local psychiatrists may be overlooking indications for these drugs (4). The Faculty of Sexual & Reproductive Healthcare of the Royal College of Obstetricians and Gynaecologists issued a rapid statement to acknowledge that the Skovlund et al study only “adds to the existing conflicting evidence regarding a potential association between

HC and depression, but does not demonstrate any causal association" (5). The latter was because the study was "an observational study and not a randomised controlled trial and other significant confounding factors cannot be excluded" (5).

Intricate issues in study design are of major importance in making causal inferences, but these were not the reason why the Skovlund et al study has caught our attention. What seems to have fuelled our interest in this study is that it reported that HC is associated with an increase in the risk of first use of antidepressants by 23%, which rises to 80% for adolescents. And this sounds terrifyingly high.

However, the 23% (or the 80%) is a relative risk increase and does not help us assess the actual risk of someone on HC subsequently using antidepressants - because it doesn't tell us how many women would be using antidepressants anyway. Looking at the raw data reported in Skovlund et al (1), the actual baseline risk of subsequent use of antidepressants was 1.66 cases per 100 women per year for those not using HC, which increased to 2.11 cases per 100 women per year for users of any oral HC. This corresponds to an impressive relative risk increase of 27% (that reduces to 23% after accounting for the effect of factors other than HC). But the absolute risk increase is only 0.45 cases per 100 women per year, i.e. an ultimately unimpressive risk of 0.45% in a year. Even more unimpressive is the absolute risk increase for a confirmed diagnosis of depression: 0.04%.

The Royal College of Obstetricians & Gynaecologists recommended that women should be informed by their contraceptive provider that there is no clear evidence that HC causes depression (5). However, an honest doctor would simply have to tell her patient that, on average, only 1 in 221 women exposed to HC over a year is likely to subsequently be prescribed an antidepressant because of HC (number needed to harm [NNH] is 1/0.045 = 221), and only 1 in 2,441 women is likely to be diagnosed with depression at a psychiatric hospital (NNH is 1/0.0004 = 2441). For adolescents, the NNH is 1 in 92 for use of antidepressants and 1 in 556 for depression diagnosis (Table).

Do any of these absolute risk increases counterweight the benefits from birth control?

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Competing interests: No competing interests

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Table. Calculation of measures of absolute and relative risk and number needed to harm (NNH) using the raw data from Skovlund et al (1). Note that these statistics have not been adjusted for other factors prognostic of depression.

	Events	Person-years (PY)	Rate per 100 PY	Risk Ratio	Risk Excess (%)	NNH (95% CI)
Antidepressants, all women						
No HC	50346	3041595	1.66	1.00	0.00	
All oral HC combined	74126	3518381	2.11	1.27	0.45	221 (212 - 232)
All progestin-only	1884	74540	2.53	1.53	0.87	115 (101 - 132)
Depression diagnosis, all women						
No HC	9310	3041595	0.31	1.00	0.00	
All oral HC combined	12211	3518381	0.35	1.13	0.04	2441 (2011 - 3104)
All progestin-only	296	74540	0.40	1.30	0.09	1099 (732 - 2205)
Antidepressants, adolescents						
No HC	10257	1094654	0.94	1.00	0.00	
All oral HC combined	18597	916691	2.03	2.17	1.09	92 (89 - 95)
All progestin-only	287	10277	2.79	2.98	1.86	54 (46 - 65)
Depression diagnosis, adolescents						
No HC	2496	1094654	0.23	1.00	0.00	
All oral HC combined	3738	916691	0.41	1.79	0.18	556 (511 - 610)
All progestin-only	56	10277	0.54	2.39	0.32	316 (217 - 575)