Oral contraceptives and diabetes mellitus: an update

There has long been interest in the possible relationship between oral contraceptive (OC) use and diabetes mellitus. In 1991, we reported our findings (in this Journal) on 45 women who had been referred to hospital for diabetes during follow-up in the Oxford-Family Planning Association (Oxford-FPA) contraceptive study. No association was found with OC use.1 Nonetheless we believed that it would be of interest to comment briefly on the findings for this disease up to the time that individual follow-up of the study participants ceased in July 1994 (follow-up of cancer registrations and death notifications is still continuing).

The Oxford-FPA study methods have been described in detail elsewhere.2 In brief, the study included 17 032 white women who, when recruited between 1968 and 1974, were married and aged between 25 and 39 years. At entry, 56% were using OCs, 25% a diaphragm and 19% an intrauterine device. These women (save for certain subgroups – see Vessey and Painter3) were followed up annually and information was collected about changes in contraceptive methods, pregnancies and their outcome, hospital referrals and deaths. Women who at entry to the study reported that they were suffering from diabetes were excluded from the present analysis. Only the first hospital referral (inpatient or outpatient) was taken into account in the analysis.

As expected, hospital referral was strongly positively related to age and body mass index (BMI). In addition, referral was three times as common in women of lower social class (IV-VI) as in women of upper social class (I-II), a difference only partly explained by BMI. Analyses of hospital referral rates in relation to OC use were therefore adjusted for age, BMI and social class.

Our first analysis compared women ever using OCs with those never doing so. The rate ratio was 0.9 with a 95% confidence interval (CI) ranging from 0.5 to 1.3. Rate ratios for hospital referral to any total duration of OC use were as follows (95% CIs are given in parentheses): never used, 1.0 (reference category); current–48 months, 0.9 (0.3–2.1); 49–96 months, 0.7 (0.3–1.7); 97–144 months, 0.9 (0.5–1.7); 145 months or more, 0.6 (0.2–1.6). Corresponding rate ratios in relation to duration since last use of OCs were as follows: never used, 1.0 (reference category); current–48 months, 0.7 (0.3–1.4); 49–96 months, 0.7 (0.3–1.7); 97–144 months, 0.6 (0.2–1.5); 145 months or more, 0.7 (0.2–2.8). The data were too few to enable analyses to be done by type of OC, but it should be noted that preparations containing 50 μg oestrogen made up 67% of OC exposure. OCs containing a greater amount of oestrogen provided only 2% of exposure.

We recognise the shortcomings of our data, which include the small number of affected women and the associated fact that only those referred to hospital with diabetes were identified. Nonetheless we believe that our case finding has been unbiased with respect to OC use. Furthermore, as we have pointed out previously,1 if such a bias existed it might be expected to lead to hospital referral of more OC users than non-users.

In conclusion, the final results of the Oxford-FPA study with respect to diabetes mellitus offer further support to the view that OC use does not increase the risk of clinical diabetes mellitus, a finding in keeping with most other studies.1-4

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References

Increase in IUD expulsions

We write to raise awareness of an apparent increase in intrauterine device (IUD) expulsions noted since we started using the TT380 Slimline® in Autumn 2005.

As clinic policy we changed our preferred first-choice copper IUD to TT380 Slimline, mainly because of its 10-year licence compared with a 9-year licence for the T-Safe Cu380A. In early 2006 we noticed that a number of women were returning soon after insertion with either full or partial expulsion.

Two experienced doctors fit the majority of IUDs, either personally or as part of supervision for the FPFHRIC Letter of Competence in Intrauterine Techniques (LoC IUT). We reviewed their IUD data from 1 January 2005 to 1 March 2006, choosing the dates to give roughly equivalent numbers of T-Safe Cu380A and TT380 Slimline insertions. We excluded insertions done by any other clinicians.

From January 2005 to March 2006 we were able to identify those women who had not returned for follow-up and those who did not continue with the IUD. Only women in whom follow-up was completed in the first 3 months after insertion were included, although later expulsions also appear to be increased. We also noted an increase in women asking to have their IUD removed within the first 3 months. The results are shown in Table 1.

Table 1 Summary of IUD fitting data

<table>
<thead>
<tr>
<th>Device</th>
<th>Total</th>
<th>No data</th>
<th>No follow-up</th>
<th>Expelled (presence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-Safe Cu380A</td>
<td>115</td>
<td>3</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>TT380 Slimline®</td>
<td>104</td>
<td>9</td>
<td>17</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Nova-T® 380</td>
<td>15</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Gyna-Damas-Taban</td>
<td>184</td>
<td>6</td>
<td>18</td>
<td>3</td>
</tr>
<tr>
<td>Mirena® (IUS)</td>
<td>196</td>
<td>2</td>
<td>39</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

IUS, intrauterine system.

Of the seven women who expelled the TT380 Slimline, four also expelled a replacement device. Similarly, of the two women who expelled the T-Safe Cu380A, one was known to have a fibroid uterus and also expelled her replacement device. None of the expelled devices had been fitted as part of LoC IUT training.

Although this is only a small observational study, we are concerned that this may be early evidence of a problem with the design of the TT380 Slimline. None of the IUDs provided to this frame of device seems to be softer and less springy than the T-Safe Cu380A and the discontinued, but similar, Ortho Gynae T380®. The TT380 Slimline takes longer to open fully and post-fitting in vitro. We are careful to fit the device immediately after loading so the device is compressed within the tube for as little time as possible.

We value feedback from colleagues on their experience of using the TT380 Slimline.

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Liquid-based cytology

We very much welcome Dr Williams’ commentary1 in the July 2006 issue of the Journal on any advantage that liquid-based cytology (LBC) may offer and his critical analysis of the systematic review by Davey et al.2 It is surprising that the favourable results of the large five pilots on Liquid-based Cytology of England, Scotland and Wales2 were not included. Two recent publications from this country echo the LBC pilots as regards significant reductions in inadequate rates with LBC.3,4

Our positive experience at PathLinks with LBC are in line with these publications. PathLinks is a pathology group which serves Greater Lincolnshire and Goole; the catchment population is approximately one million. The laboratory processes around 65 000 cervical cytology samples annually and therefore LBC service implementation of LBC began in June 2005, with one of the six PCTs converting every 6 weeks coinciding with training completion of a pathologist, a checker and three cytoscreeners. A total of 30 staff converted and provided the present service. Turnaround time just prior to conversion was 6 weeks. Presently this is 2 weeks, with around 90% of results being reported within a week. The inadequate rates were as follows: pre-conversion (April 2004–March 2005) 7.75%, during conversion (April 2005–March 2006) 4.9% and post-conversion 0.8%. The high-grade rates during these periods were 0.95% and 1.1%, respectively, suggesting concordance with the expectation of increased sensitivity of LBC. Our cytoscreeners have found the LBC slides to be ‘clean’ and easier to read compared to conventional smears. Detection of endometrial cells is more frequent although this offers no advantage, the diagnosis of these cells and other variants, and cytoscreeners would be reluctant to return to interpreting conventional smears.

Whether the LBC can be made more cytoscreener-friendly is being explored by the NHS Health Technology Assessment Programme through the MAVARIC trial. Automated technology may make identification of abnormal cells easier. The computerised software will direct the cytoscreeners to probe some 20 locations on a slide rather than painstakingly scanning the whole slide. Furthermore, one of the machines (FocalPoint®) can sort the abnormal slides into quintiles. Up to 25% of the samples are likely to be classified as ‘no further review’ meaning that manual reading is not required. The MAVARIC trial set up in August 2005 compares two automated cervical screening technologies and manual screening. Cytology samples are randomly allocated to reading by manual screening alone or by one of the two automated technologies backed up by manual screening. The trial is expected to end in 2009 and the published results are due in 2011. Further uses of LBC are being actively researched. LBC lends itself to the hybrid capillary technique for the human papillomavirus test5 and for chlamydia screening.6

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Clinical Department

1 FRRC: Reproductive Health Care 2006: 32(4) 267-269 - JFPRHC Oct 06  9/20/06  4:09 PM  Page 1
LETTERS

Williams\(^1\) has already eloquently answered the question as to whether LBC offers any real advantage over the conventional smear technique. We agree that LBC is a very welcome technique in the current screening programme and would encourage ongoing endeavours to explore how LBC can bring further benefits to women’s health.

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References


I was interested to read the articles in the July 2006 issue of the Journal regarding problems related to Implanon\(^\text{®}\) insertion.

I recently inserted an Implanon device into the left arm of a 23-year-old, right-handed patient. The procedure went smoothly. Eleven days after the insertion the patient presented with a 3-day history of a red rash around the site of the implant. On examination she had a lymphangitis-type reaction extending proximally and distally from the site of the implant. She was otherwise well with no systemic symptoms. The patient was commenced on oral Flucloxacillin.

Three days later the patient was reviewed. The erythema had resolved. A scrotal vessel was palpable extending from just deep to the implant to the mid-forearm. It was not tender. The patient experienced some discomfort on full extension of the arm but as she was otherwise well had opted to leave the implant in situ. A diagnosis of thrombophlebitis was made.

I can find no mention of this complication in the product or FPPRHC literature. I wonder if others have also seen similar cases?

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References


Reply

Dr Arunakumari identifies several important points. The negative urine pregnancy tests remain puzzling since the ultrasound scan performed at 27 4 2 weeks would suggest the Implanon\(^\text{®}\) was inserted when the patient was 8 weeks pregnant (i.e. 6 weeks after conception). This means, however, that oogenesis might not have been completed by the time of insertion.

Dr Arunakumari is, of course, correct that pregnancy is a contraindication to use of Implanon. However, the issue in this case, as in Dr Melrose’s case, is that removal and postnatal re-insertion of Implanon at this late stage in pregnancy subjects the patient to two extra

Full-term pregnancy with Implanon\(^\text{®}\) in situ

I write in regard to the letter on full-term pregnancy with Implanon\(^\text{®}\) in situ by Drs Cooling and Paul that appeared in the July 2006 issue of the Journal.

I had a similar experience when I fitted an Implanon in a patient who, in retrospect, was probably about 4 months pregnant. She gave a history of regular periods and was bleeding when I fitted it. She had not had unprotected sexual intercourse at all need in her history.

The patient then had amenorrhea for several months and presented to her general practitioner with abdominal swelling and weight gain. She was obviously in advanced pregnancy (perhaps not the world’s brightest!).

She was 36 weeks pregnant and the hospital contacted me to see if the Implanon should be removed. I could not see any reason for doing so at such a late stage. The patient delivered without problem and chose not to breastfeed. She at least now has effective contraception for a few years!

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References


Full-term pregnancy with Implanon\(^\text{®}\) in situ

I read with interest the letter in the July 2006 issue of the Journal regarding a successful full-term pregnancy with Implanon\(^\text{®}\) in situ. I too have a patient who presented in similar circumstances and is continuing her pregnancy with the Implanon\(^\text{®}\) as she would wish to use this method of contraception following her confinement.

After discussion with the patient and colleagues, it seemed that to leave the Implanon in place was an option. Time will reveal the outcome in due course.

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References


Full-term pregnancy with Implanon\(^\text{®}\) in situ

The case of the full-term pregnancy with Implanon\(^\text{®}\) in situ reported by Drs Cooling and Pauli in a recent issue of this Journal\(^1\) raises several interesting issues.

First, influence of pregnancy on Implanon. As stated by the authors, the rate of release of the progestogen from the implant is likely to be altered in pregnancy. Also, the effects of the progestogen (both in terms of intended action and side effects) are likely to be overwhelmed by the massive increase in the placental production of progestogens.

Second, influence of Implanon on pregnancy. The authors correctly state that “progestogens in pregnancy have not been linked with fetal abnormality”\(^2\) but applies only to low-dose progestogen. High doses (>10 mg per day of norethisterone or equivalent) has been associated with masculinisation of the female fetus and hypospadias of the male fetus.\(^3\) It is accepted that the dose of progestogen released by Implanon is low at 40 µg per day.

Liquid-based cytology

Arabinda Saha and Kathryn Snee

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