

Mirena[®] and ectopic pregnancies

Introduction

Mirena[®] is an intrauterine system containing levonorgestrel 52mg. The initial release of levonorgestrel is about 20 micrograms/24 hours. Mirena[®] has been approved for the Dutch market since 21-02-1996 and is indicated for “*contraception, idiopathic menorrhagia and protection from endometrial hyperplasia during estrogen replacement therapy*”.

This report provides an overview of ectopic pregnancies associated with the use of Mirena[®] in the Netherlands.

Reports

Until March 3, 2008, the Netherlands Pharmacovigilance Centre Lareb received 31 reports of ectopic pregnancies in association with Mirena[®]. Of these reports, 20 were submitted by the marketing authorisation holder of Mirena[®].

The patient's age was known in 25 cases; mean age was 28.5 years (SD 7.6 years). The latency was reported in 26 cases; mean latency was 20.6 month after insertion (SD 15.9 months, with a range from 1.5 to 48 months).

In 18 cases the outcome was reported as recovered/recovering. In 13 of these 18 cases it is known that the patient underwent a tubectomy. In one patient it is known that the Mirena[®] IUD was removed and replaced by a copper IUD. For three patients who underwent a tubectomy the outcome is reported as unknown.

For one patient with an ectopic pregnancy in the abdominal cavity, it is mentioned that she will be followed by a gynaecologist.

In two of the reports an IUD dislocation was mentioned (for one report the IUD was located at the omentum). For four cases it was reported that an ultrasound scan verified that the Mirena[®] IUD was correctly in situ.

Other sources of information

SmPC

In March 2008, the only information about pregnancies in section 4.8 of the SmPC of Mirena[®] is the following: “*Should a pregnancy occur during the use of Mirena[®] then it is advisable to remove the IUD by pulling the threads because this lowers the risk of an infection or miscarriage. The chance of a miscarriage is 50% in these cases; while possibly the chance of a septic abortion is also increased.*” [1] On September 22, 2008, the Dutch SmPC has been updated and ectopic pregnancies are now included in sections 4.4 and 4.8. [2]

Literature

In the literature case-reports about ectopic pregnancies associated with the use of a levonorgestrel releasing intrauterine system can be found [3,4]. In these cases a previous ectopic pregnancy is not mentioned [3,4].

In 2004 a study was undertaken to evaluate the pregnancy rate with the levonorgestrel intrauterine system (LNG IUS) and to analyse the outcome of

pregnancies with the LNG IUS *in situ* in regular use. Pregnancy with the LNG IUS *in situ* was rare. Ectopic pregnancies constituted 53% of all pregnancies [5].

Databases

On February 20, 2008, the Lareb database contained 31 reports with the preferred term ectopic pregnancies on Mirena[®]. Ectopic pregnancy is disproportionately associated with this IUD. On April 24th, the Eudravigilance database contained 438 reports of ectopic pregnancies occurring in users of the Mirena[®] IUD. Age ranged from 20 to 46 years the mean age was 33.5 years. Age was not specified in 114 cases.

Conclusion

Lareb received 31 reports of ectopic pregnancies of patients using a Mirena[®] UID. For only two of these patients a prior ectopic pregnancy was reported. In 15 cases it was reported that the patient underwent a tubectomy.

References

1. Dutch SmPC Mirena[®]. (version date: 19-2-2007, access date: 4-3-2007)
2. Dutch SmPC Mirena[®]. (version date: 22-9-2008, access date: 30-10-2008) <http://db.cbg-meb.nl/IB-teksten/h16681.pdf>.
3. Ojutiku D, Cutner A, Rymer J. Ectopic pregnancy with levonorgestrel releasing intrauterine system. Br J Fam Plann 1998;24(2):85-6.
4. Abu JI, Wandless GM, Emembolu JO. Ectopic pregnancy in the levonorgestrel releasing intrauterinesystem (LNG-IUS) user: atypical presentation. J Obstet Gynaecol 2002;22(5):567-8.
5. Backman T, Rauramo I, Huhtala S, Koskenvuo M. Pregnancy during the use of levonorgestrel intrauterine system. Am J Obstet Gynecol 2004;190(1):50-4.

This signal has been raised on June 2008. It is possible that in the meantime other information became available. For the latest information please refer to the website of the MEB www.cbg-meb.nl/cbg/en/default.htm or the responsible marketing authorization holder(s).