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**P-308 Spontaneous reports of menstrual cycle disorders after mRNA Covid-19 vaccine**

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**Study question:** Does the mRNA Covid-19 vaccine have an influence on the ovulatory process and menstrual disorders?

**Summary answer:** Menstrual disorders were more frequently reported in women aged 25 to 45 years, mainly amenorrhoea and increased cycle length, and were often not severe.

**What is known already:** Menstrual disorders can be due to several factors, including stress, especially during a pandemic or sometimes during a vaccination. However, the SARS-CoV-2 spike protein is able to interact with the human ACE2 receptor, which is widely expressed in the ovaries, uterus, vagina, and hypothalamic pituitary axis. Accumulating evidence now suggests that

2019-nCoV/ACE2 may interfere with the female reproductive functions, leading to menstrual disorder. The role of this spike protein is also to trigger an immune response, used in particular for mRNA vaccines. The aim of this study is to describe the side effects on menstrual cycles after mRNA Covid-19 vaccine.

**Study design, size, duration:** This is a descriptive analysis of adverse events affecting the menstrual cycle reported to a regional pharmacovigilance center between May 2021 and January 2022. A case-by-case review was performed to collect variables characterizing the patient and the reactions.

**Participants/materials, setting, methods:** Patients upper 11 years and under 60 years with mRNA Covid-19 vaccine suspected, were enrolled. Medical Dictionary for Drug Regulatory Activities (MedDRA) was used to identify cases of menstrual disorders. Reactions related to the following System Organ Classes from MedDRA were extracted: amenorrhoea, disorder of menstrual cycle, dysmenorrhoea, long menstrual cycle, menorrhoea, menometrorrhagia, metrorrhagia. Seriousness was defined, according to the WHO, as the occurrence of death, lifethreatening, hospitalisation, requirement of consultation.

**Main results and the role of chance:** Side effects with mRNA Covid-19 vaccine concerned women in 67.8% (N = 1306) of cases, between 12 and 59 years old. 5.1% (N = 67) were related to the menstrual cycle. Serious cases 53.7% (N = 36) were no more frequent than in the whole women 50.1% (N = 654). Menstrual disorders were more represented in the 25-45 age group 64.2% (N = 43) vs 12-24 age group 14.9% (N = 10) and over 45 age group 20.9% (N = 14) p = 0.001. Menstrual disorders not recovered at the time of reporting accounted for 38.9% (N = 26). For the all studied population, amenorrhoea or increased cycle length were more frequent 53.8% (n = 36) vs increased duration of menstruation or menorrhagia 26.8 % (N = 18) or increased frequency of menstruation metrorrhagia/menometrorrhagia 22.4% (N = 13) p < 0.001. Long cycles or amenorrhoea were most represented in the 12-24 age group 90% (N = 9) p < 0.0001 and 25-45 age group 62.7% (N = 27) p < 0.1 vs dysmenorrhoea, menorrhoea, metrorrhagia, menometrorrhagia. The difference was not significative in women over 45 years old 35.7% (N = 5). Finally amenorrhoea and long cycles were less often reported with severity 22.2% (N = 8) than other menstrual side effect (dysmenorrhoea, menorrhoea, menometrorrhagia, metrorrhagia) 45.2% (N = 14), p < 0.1.

**Limitations, reasons for caution:** The most important limitation relies on the spontaneous reporting. Underreporting is estimated to about 90%. It was probably not the case for side effect due to the Covid-19 vaccination. Furthermore, serious cases are more likely to be reported than mild or minor cases resulting in a possible reporting bias.

**Wider implications of the findings:** The cases reported reflect the experience of clinicians who were asked about cycle disturbances after covid-19 vaccination (V. Male BMJ 2021). We observed more frequent changes in cycle length but not in menstrual length, as reported by A. Edelman (Obstet Gynecol 2022). Fertility may be punctually affected by Covid-19 vaccination.

**Trial registration number:** Analyzing anonymous data, being retrospective and non-interventional, the approval of an Ethics committee was not necessary according to the Good Clinical Practice in pharmacovigilance.