



Safety considerations regarding Methotrexate off-label use in tubal ectopic pregnancy

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Dear Editor,

We carefully read the comment of Dardalas et al. regarding our article recently published in *Archives of Gynecology and Obstetrics* [1]. In their letter, the authors aimed to underline the safety considerations surrounding Methotrexate (MTX) off-label use in tubal ectopic pregnancy. Indeed, several life-threatening or fatal conditions associated with MTX therapy have been published.

MTX toxicity is correlated with total dose administered. While multidose protocol is associated with increased side effects compared to surgical approach [2], data focusing on single dose MTX therapy are more conflicting [3, 4]. In the vast majority of cases, adverse events are not severe and transient. They mainly comprise abdominal pain, nausea, anorexia, spotting and elevation of liver enzymes [5]. In contrast, single dose MTX protocol displays the advantage of avoiding inherent risks of surgery and general anesthesia [5]. Furthermore, MTX treatment is cost effective in comparison with surgery, particularly in low active presentations of tubal ectopic pregnancy [6, 7]. Hence intramuscular administration of MTX has been recommended for the management of clinically stable patients with non ruptured ectopic pregnancy by both American and French guidelines (Level A) since it is considered a safe and effective treatment [6, 7].

However, we completely agree with Dardalas et al. regarding the potentially severe side effects of MTX therapy, although their occurrence is low. Such consideration highlights the need for an adequate counseling before treatment initiation. Practitioners should provide patients with detailed information regarding follow-up modalities, failure rate, potential adverse events and de novo symptoms requiring immediate medical evaluation. In our department, such information is systematically provided so the ultimate choice in treatment modalities always originates from a shared making-decision approach.

Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest.

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