



## Editorial

## Medical abortion



One study<sup>1</sup> has reported that the rate of unintended or incidental pregnancy in the United States declined substantially between 2008 and 2011, but unintended pregnancies were most prevalent among women and girls who were poor or women who were cohabiting. In the same study, the percentage of unintended pregnancies that ended in abortion remained stable during this period (40% in 2008 and 42% in 2011); however, the rate of unintended pregnancies that ended in birth declined from 27/1000 in 2008 to 22/1000 in 2011 in women and girls aged 15–44 years.<sup>1</sup> However, unintended pregnancy is still the major contributor to abortion.<sup>2</sup>

Since the 1960s, abortion through vacuum aspiration or dilatation and curettage has been the method used to successfully terminate an early pregnancy. The risks of surgery and anesthesia for women undergoing an abortion, and the shortage of providers that offer comprehensive abortion care services are always concerning.<sup>3,4</sup> A recent report from the United States showed that approximately 16.1 million abortion procedures were conducted from 1998 to 2010 and resulted in the deaths of 108 women, which is an overall mortality rate of 0.7 deaths/100,000 procedures. The mortality rate per 100,000 procedures increased with gestational age from 0.3 deaths for procedures performed at  $\leq 8$  gestational weeks to 6.7 for procedures performed at  $\geq 18$  gestational weeks. It is important to show that most abortion-related deaths at  $\leq 13$  gestational weeks were associated with anesthesia complications and infection.<sup>5</sup> All of these studies suggest that alternative therapy is always welcome, including medical abortion, for early pregnancy termination to minimize the need of more invasive procedures such as surgery.<sup>6–9</sup> The combination of misoprostol, a prostaglandin analog that has a strong uterotonic effect, and mifepristone (RU-486, a selective progesterone receptor modulator), creates a potent antiprogesterone effect for pregnancy. This treatment is used to block the progesterone receptors (PR) and glucocorticoid receptors. It may also sensitize the uterine myometrium to prostaglandins, decrease the contractility threshold of the uterus, and ripen the cervix, thereby facilitating abortion.<sup>6,9</sup> This combination treatment of misoprostol and mifepristone is more effective than single agents<sup>9,10</sup>; therefore, Dr. Jiang's study in this issue of the *Journal of Chinese Medical Association* also used the combination therapy for medical abortion.

Jiang et al<sup>11</sup> investigated 63 pregnant primiparous women, aged 18–30 years with a gestational period of 35–49 days, who visited the Second Affiliated Hospital of Wenzhou Medical University (Zhejiang, China) between March 2009 and April 2011. The authors attempted to compare the expression of estrogen receptors (ERs), PRs, insulin-growth factor-1 (IGF-1), and vascular endothelial growth factor (VEGF) in the chorionic villi between incomplete and complete abortions.<sup>11</sup> Their study showed no statistically significant difference in IGF-1 and VEGF messenger RNA (mRNA) expression, although the authors claimed that immunohistochemical staining of VEGF and IGF-1 was relatively stronger in the incomplete abortion group than in the complete abortion group, and achieved statistical significance.<sup>11</sup>

However, there are many aspects of their study that remain unclear, and thus are worthy of further discussion. First, their study indicated that up to 54% (34/63) of pregnant women had an incomplete medical abortion.<sup>11</sup> This finding suggests that the successful abortion rate in Jiang's report was very low. For example, a study by Li et al<sup>6</sup> enrolled 242 women with unintended pregnancies of  $\leq 49$  days of gestational. After treatment by medical abortion, the complete abortion rate was 92.6%.<sup>6</sup> On comparing the results of the Li et al<sup>6</sup> study and Jiang et al's<sup>11</sup> study, we found a significant difference, including the prescription route and dosage of the drugs, which was emphasized in our previous comment, after modifying the original description: "Overcoming the barriers of treatment—a better route and a better outcome."<sup>8</sup> Dr Li used 200 mg mifepristone orally, followed by the immediate intravaginal placement of 600  $\mu\text{g}$  misoprostol<sup>6</sup>; Dr Jiang used 50 mg mifepristone orally, followed by 25 mg of oral mifepristone every 12 hours at home (for a total dose of 150 mg mifepristone), and finally 600  $\mu\text{g}$  oral misoprostol in the management of the same criteria of a similar study population.<sup>11</sup> This protocol contributed to successful abortion rates of 92.6%<sup>6</sup> and 54%.<sup>11</sup> The sublingual and vaginal routes of misoprostol administration resulted in a shorter abortion duration, compared with the oral route.<sup>6</sup> In addition, the vaginal administration of misoprostol (600  $\mu\text{g}$ ) appears to generate fewer adverse effects without interfering with the efficacy of medical abortion for early pregnancy. Furthermore, patient compliance may be questionable in Jiang's study. It is

reasonable to suppose that these patients may not obey the clinician's recommendation to take the medication.

Second, the mean induction to abortion interval was approximately 6 hours in Li's study,<sup>6</sup> but the interval for collection of a sample in Dr Jiang's study<sup>11</sup> was only 4 hours. Therefore, it is highly possible that the sample in Jiang's study was not adequately collected, partly because of the need for a longer duration to induce abortion and partly because of the reduced amount or absence of chorionic villi collected in their experimental protocol.<sup>11</sup>

Third, a significant discrepancy of data presented by reverse transcriptase polymerase chain reaction (i.e., mRNA expression) and immunohistochemical analysis (i.e., protein expression) is noted in Jiang's study.<sup>11</sup> The cause of this discrepancy in the expression of mRNA level (factory) and protein level (product) was unknown, since Dr. Jiang's study showed the down-regulated mRNA levels but increased expression of protein levels (IGF-1 and VEGF). It is unusual, because most studies often showed the similar trend for increasing expression of both mRNA and protein or decreasing expression of both.<sup>12,13</sup> Are there any unknown truncated forms of these targets? In fact, the typical example of a truncated protein is p53, which is often an overexpression of a function-lost protein when *p53* genes are mutated.<sup>14</sup> However, in our limited knowledge, we did not find any truncated form of either IGF-1 or VEGF.

It is noteworthy that women who want to avoid surgery seem to value the option of a medical abortion and tend to be satisfied, regardless of the regimen used.<sup>9</sup> Dr Jiang's study showed that more than one-half of the patients' pregnancies were ended by an incomplete abortion.<sup>11</sup> We believe that this was also true in their study in which nearly one-half of the patients were unsatisfied with their method.

Furthermore, what is the value of testing the expression of IGF-1 and VEGF of chorionic villi? Could physicians reverse or change the treatment strategy on knowing that a patient has increased expression of IGF-1 or VEGF before prescribing or performing this procedure? In fact, a clinician cannot perform such a preabortion test because specimens would be needed to test for the aforementioned genes, which requires a "procedure" to obtain them. It is impossible to know the expression of IGF-1 and VEGF in the chorionic villi before the induction of a medical abortion. Therefore, we do not believe that the authors could provide any new information to predict the success of the inducing medical abortion by mifepristone and misoprostol, even though the authors claimed this.<sup>11</sup>

### Conflicts of interest

The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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