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Integrity of Uterine Arteries: A Key for Pregnancy after Fibroid Embolization

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Summary

Particles used today to occlude uterine arteries in fibroids management cannot guarantee a full anatomical and functional recovery of these arteries as they should for women willing to conceive. New resorbable materials could constitute a serious alternative.

Text

Uterine fibroid embolization (UFE) consists of blocking the blood flow of uterine arteries (UA) with small particles to generate an ischemic necrosis of the fibroids (leiomyomas) present in uterus. UFE has been offered initially to a majority of women over the age of 40 at the time of treatment, i.e. to a population of women generally not interested in future pregnancy. UFE is now commonly proposed as an organ preserving treatment to a population of younger women willing to conceive.

In this context, a serious concern is the fate of the UA after embolization. Their anatomical integrity and functional preservation is of crucial importance for future pregnancy, since their number and diameter shall drastically increase to supply nutrients and oxygen for foetal and placental growth and any reduction of flow during pregnancy may be pejorative. Intra-uterine growth retardation is clearly linked to a reduction of UA flow, for example after hypogastric artery ligation [1,2] or after UFE [3,4].

The particles used for embolization are mostly non degradable materials which generate a chronic inflammation and vessel damage. The UA recanalization rate is limited to 50% to 77% 6 months after embolization with poly (vinyl-alcohol) particles [5,6]. These particles act as durable obstacle in the UA, disturbing the physiological variations of their diameter that occur during the hormonal cycle and pregnancy. This may explain the cases of smallness for age observed in animal and human. In animal, a high rate of low weight at birth (80%) was observed after complete and bilateral embolization of uterine arteries with poly (vinyl-alcohol) particles [7]. It was clearly related to chronic inflammation, fibrosis and stenosis of the uterine arteries [8] which durably impair the uterine arteries to adapt their flow to the foetal growth. In human, the percentage of newborns that are small for gestational age varies according to authors, 22% in Pron et al. [9] study, 14% in Kim et al. [4] study and 7% in Goldberg et al. [10], probably due to less extensive embolization than in animal.

Resorbable embolization particles made from gelatin sponge have been used as an alternative to non degradable particles. The clinical results are similar to those of non degradable particles [11]. However gelatin particles are not devoid of disadvantages. Their degradation lasts from 3 weeks to 4 months and is accompanied by a chronic inflammatory response, and possible generation of arterial aneurisms on the site of arterial remodeling [12,13]. The UA recanalization estimated 4 months after embolization by magnetic resonance angiography is present in 88% arteries but the percentage of diameter recovery is unknown [14]. The fertility after embolization with gelatin has not been evaluated, either in animal or in human.

To prevent the deleterious effects inherent to all these non degradable and degradable particles, a short-life occlusive agent could be proposed. It could play its role as a flow blocker during a time duration sufficient to yield a tumor ischemia, leading to a tumor necrosis, and thereafter degrade quickly without leaving any inflammation or stenosis of the UA. Unfortunately, the minimal time of occlusion required for getting a fibroid necrosis is not well defined. Lichtinger observed by laparoscopy

that a bilateral UA transient clamp during 26min (min-max 10-59min) resulted in a complete blanching of the uterus, which was reversible at clamp opening [15]. A temporary uterine arteries occlusion varying from 5 to 7 hours has been proposed as a surgical alternative to UFE [16-18]. From these data, we can hypothesize that the minimal duration for achieving a non reversible ischemia should be comprised between one hour and 7 hours.

The first results obtained in animal with embolization microspheres which degrade in vitro and in vivo in 24 hours [19] vs a non degradable microspheres as control are promising [20]. On the angiographic control at one week, there was a complete recanalization of UA; the arterial flow and uterine parenchymography was similar to pre-embolization [20]. There was no structural alteration of the arterial wall, no residual microsphere and no inflammation. There was similar degree of uterus necrosis in myometrium and endometrium after embolization with resorbable microspheres and non degradable control. Conversely, with non degradable control, there were arterial blood flow reductions and defects of parenchymography and an inflammatory reaction.

These results suggest that the duration of arterial occlusion obtained with a particle which degrades within 24H would be sufficient to achieve both an ischemic necrosis of fibroids and a full recanalization of UA [20]. The efficacy of these degradable particles on fibroid necrosis and UA recanalization shall now be estimated with clinical trials.

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