Women with mechanical heart valves require anticoagulation during pregnancy in order to prevent thromboembolic events, but each drug regimen risks harming either the mother or fetus. Now, a new meta-analysis published online this week in the Journal of the American College of Cardiology may help clinicians navigate that balancing act.

For the pregnant women, treatment with a vitamin K antagonist (VKA) offers the lowest risk of adverse outcomes, researchers found. But for the fetus, the lowest risk is seen with low-molecular-weight heparin (LMWH). Yet dose appears to matter: fetal risk is similar between LMWH and warfarin, provided that the VKA's dose is no greater than 5 mg daily.

"A considerable number of women in childbearing age undergoing a valve replacement require mechanical prosthetic heart valves because of their superior durability and hemodynamic characteristics, and therefore require lifelong anticoagulation," Uri Elkayam, MD (University of Southern California, Los Angeles), writes in an editorial accompanying the paper. "Because of the hypercoagulable state of pregnancy, there is an increased risk of valve thrombosis.

"The search for a safe and effective [anticoagulation] regimen has been challenging because both oral anticoagulants [VKAs] and heparins may be associated with important maternal and fetal complications," he says.

For their meta-analysis, investigators led by Zachary L. Steinberg, MD (University of Washington School of Medicine, Seattle), and colleagues included a total of 800 pregnancies from 18 publications.

Maternal risk—a composite of death, thromboembolism, and valve failure—was lower with a VKA taken throughout the pregnancy versus with LMWH throughout, LMWH for the first trimester followed by a VKA, or unfractionated heparin (UFH) for the first trimester followed by a VKA. Fetal risk, on the other hand, was lowest with LMWH throughout pregnancy.

Estimated Risk of Adverse Events

	VKA	LMWH	LMWH+VKA
Maternal	5%	16%	16%
Fetal	39%	13%	23%

Warfarin at a daily dose of 5 mg or less, though, was no more risky to the fetus than LMWH.

"Our results support the American College of Cardiology and American Heart Association guidelines for the management of patients with valvular heart disease, which recommend the use of low-dose warfarin in women who are able to maintain therapeutic INRs (Class IIa) over the use of either first-trimester LMWH or UFH use (Class IIb)," Steinberg et al conclude, adding that prospective randomized studies and large registries are needed to validate their findings.

In his editorial, Elkayam stresses that this and another recent meta-analysis, though informative, are based on data from "a considerable number of single-center series of small sample sizes, limited by incomplete reporting of quality of [anticoagulation], reporting bias, or the lack of control groups or head-to-head comparisons between the different . . . regimens."

Yet, there are some lessons to be had, he suggests.

"Because of the high risk to the fetus, a VKA throughout pregnancy seems advisable only in women with old-generation [prosthetic heart valves] in the mitral position or when other optional therapies are not available," he says. Moreover, Elkayam adds, "the results clearly suggest that the detrimental effect of a VKA on fetal outcome is not limited to the first trimester." VKA use during pregnancy has previously been tied to intracranial bleeding, abnormalities of the central nervous system, minor neurologic dysfunction, and lower IQ, he reports.

"Despite the Class I recommendations by both the American and European guidelines for the use of a VKA during the second and third trimesters, there is a need to clearly inform women about the risk-benefit ratio associated with this approach," he concludes.

At his institution, the University of Southern California, LMWH throughout pregnancy is the preferred strategy. According to Elkayam, the protocol includes patient education, close monitoring, more consistent therapeutic levels, and other factors “designed to maximize efficacy and prevent complications.”

Sources

- Steinberg ZL, Dominguez-Islas CP, Otto CM, et al. Maternal and fetal outcomes of anticoagulation in pregnant women with mechanical heart valves. J Am Coll Cardiol. 2017;69:2681-2691.
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Disclosures

- Steinberg and Elkayam report no relevant conflicts of interest.