Commentary

Has Kisspeptin found a place to be a biomarker in the differentiation of viability of early pregnancy-a short commentary

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Since the discovery of kisspeptins its role in reproduction was studied initially in rodent models [reviewed in ref 1]. Recently role of Kisspeptins(Kp) have started getting studied in relation to viability of pregnancy. Kisspeptins(Kp) are peptides which are products of the KISS1 gene that is located on the chromosome 1q32q41.It encodes a peptide having 145 amino acids named kisspeptin. This peptide can get further hydrolyzed into a number of truncated fragments; kisspeptin 54(Kp54/metastin with 54 amino acids), kisspeptin 14(14 amino acids) and Kp13 and Kp10 with 13and 10 amino acids respectively.[1,2] Initially kisspeptin 54 got named metastin since it was isolated in metastatic tissues though both are synonymous fragments encoded by the same gene that encodes the larger peptide which then further gets broken into smaller fragments by enzymes. Then Jayasena et al.[3] started studying them in human reproduction in hypothalamic amenorrhea initially. In previous studies it has been found that levels of Kp increase as the pregnancy develops and there is significant but weak correlation ($r=0.46; p<0.005$) between Kp54 and progesterone(P) levels.[4] LH also gets increased with kisspeptin administration.[5] Importance of LH and HCG to corpus luteum function is also well established. It is well known that using HCG in the luteal phase improves corpus luteum(CL) function and outcome in women with unexplained recurrent loss.[6] Now kp-54 has been emerging as a biomarker for the discrimination of viable pregnancy from cases of spontaneous abortion in view of its potential regulatory role in trophoblast function and placentation.[7,8]

Though the performance of Kp as a plasma biomarker for discriminating spontaneous abortion and intrauterine pregnancy (IUP) had been shown in the late first trimester by the team of Jayasena et al.[8] its role in early 1st trimester as a biomarker had not been examined. Jayasena et al.[8] examined Kp54 as a biomarker between viable pregnancy and miscarriage using an in house developed radioimmunoassay in their laboratory and measured plasma Kp drawn at the initial prenatal visit. They studied 993 asymptomatic women at the time of their initial prenatal visit at a mean gestation age of 11.2+-2weeks. They found that a single measurement of HCG and plasma Kp at the initial prenatal visit were both able to discriminate between viable and nonviable pregnancies but plasma Kp was more predictive. Though earlier Wu et al.[9] studied the correlation of Kp and progesterone induced blocking factor (PIBF) In recurrent spontaneous abortion(RSA) and found Kp, GPR54 and PIBF expressions were reduced in both syncytiotrophoblast and cytotrophoblast in RSA significantly along with decrease in Kp, PIBF, PR expression in deciduas of RSA group as compared to control. Thus conluding reduced Kp and PIBF expressions in trophoblast and deciduas were associated with RSA although role of Kp as a biomarker had not been considered.

Recently Sullivan –Pykel et al.[10] utilized the same hormones namely Kp and HCG to differentiate between viable pregnancy or IUP in patients presenting with bleeding per vaginum, abdominal pain, cramps along with USG evidence of spontaneous abortion (SAB) i.e. either gestation sac with no pole, or small pole or fetal pole with no cardiac activity between 6-10weeks gestation age. They found a significant positive correlation with HCG in SAB but not in IUP. Further they gave evidence that it is serum which is more ideal for checking the Kp54 levels having desired stability than plasma for this purpose. The authors further indicated the need for carrying out a phase 4 study, which is a prospective cohort study.[10] This has started another controversy as proposed by Savaris RF, that is once it is decided that there is serum Kp level of 0.2ng/ml, there is 80% chance of having a miscarriage in the next 10weeks ,how does one counsel these patients -i.e. telling that there is only a 20%chance of having a normal pregnancy which has been known for several years .Then measuring Kp would instead create more complications as patient might be happy to know that at least there is 5%chance of getting a newborn.[11]

Still one needs to carry out the further studies to get the reliability of the test of using Kp as a biomarker for viability in the early first trimester. Another point to be considered is that the prognosis of same pregnancy where S Kp is 0.19 will vary with the history, like a patient presenting with bleeding and pelvic pain in contrast to an asymptomatic patient .Chances of getting a SAB may be much higher in the early history and one might need to postpone certain prenatal tests which here get replaced by Kp, and in latter case normal prenatal care can start. Future phase 4 studies need to address these questions before Kp gets established as a reliable biomarker of viability of pregnancy.

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Conflict of interest

The authors declare that there is no conflict of interest.

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