INTERPHASE FISH SERVES AS A USEFUL ADJUNCT IN NON-VIABLE PRODUCTS OF CONCEPTION

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ABSTRACT

Cytogenetic analysis of Products of Conception (POC) is a useful tool for detection of chromosomal abnormalities that cause intrauterine fetal demise and spontaneous abortion (SAB). Low cellular viability and contamination during tissue collection frequently hamper the culture process with consequent failure to yield results. In recent years, fluorescence in situ hybridization (FISH) studies on interphase cells have served as a useful adjunct in investigating non-viable POC tissues. It is known that early SAB frequently contain numeric abnormalities. Monosomy X, triploidy, and trisomies of 13, 16, 18, 21, and 22 are common in SABs. Each of these abnormalities can be detected by FISH. Upon receipt of the POC specimen, our laboratory protocol includes making touch preparations from fetal tissue for further use, if required. On specimens that have failed to yield cytogenetic results, we perform interphase FISH testing using centromeric or locus specific probes for chromosomes 13, 18, 21, X and Y and in first trimester pregnancy losses we include probes for 16 and 22. In the past three years, our laboratory has received 530 POC specimens. Cytogenetic results were available on 414 cases (78%; 414/530) with 116 being abnormal (22%; 116/530). Fetal tissue touch preparations were available on 91 of the 116 cases that failed to yield cytogenetic results. FISH studies were successfully performed on 85 specimens and 17 of these were abnormal. Upon combining the cytogenetic and FISH results, a total of 133 (25%; 133/530) cases were abnormal by either method, an increase of 3% in abnormality detection. A more precise tissue selection and CGH microarray on fetal tissues may further improve the determination of other possible causes for SABs.

METHODS

Standard FISH procedures were used on fixed touch preparations prepared from SAB tissues before culture initiation. Interphase FISH testing was performed using centromeric or locus specific probes for chromosomes 13,18,21,X and Y, and in first trimester pregnancy losses we included probes for 16 and 22.

RESULTS (2003-2005)

- 530 Total POCs Received for cytogenetic analysis.
- 116 Failed by cytogenetics (21.89% failure rate).
- 91 of those failed were analyzed using FISH.
- 85 of those analyzed using FISH were successful.
- Reduced number failed to 31 cases (5.85% failure).
- 17 Cases analyzed using FISH were abnormal.

CONCLUSION

Our results show that FISH is a useful addition to cytogenetic studies of POCs facilitating analysis and abnormality detection. The abnormality rate significantly increased when FISH analysis was added. Significance was tested using statistical analysis by a paired proportions t-test with a significance level of 0.05.

FISH studies increased our abnormality rate, however additional measures would also be beneficial at increasing the abnormality rate. Additional methods include specific tissue selection, careful dissection, and CGH microarray. Careful dissection of POCs should be done to separate the villi tissue from the placental tissue and fetal tissue. The tissue types should be set up separately to help ensure growth of specific tissue types and to aid in analysis of these tissues. CGH-microarray on fetal tissues may further improve the determination of other possible causes for SABs. CGH-microarray can detect more abnormalities beyond the common aneuploidies. Array CGH can pick up many unbalanced chromosome abnormalities and should further be tested to see if it significantly increases the laboratory’s abnormality rate.

REFERENCES