Title Genetic Test for Fragile X Syndrome – January 2002

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Aim

To assess the safety and effectiveness of nucleic acid amplification for fragile X testing and under what circumstances public funding should be supported for the procedure.

Conclusions and results

Safety: An extensive literature search did not identify any studies reporting adverse events associated with i) testing individuals suspected of having fragile X syndrome, or ii) cascade testing of relatives of affected individuals. Similarly, no adverse events specific to prenatal diagnosis of fragile X (ie, amniocentesis or chrionic villus sampling) were identified in the literature, although the potential adverse events of these procedures are well documented.

Effectiveness: Evidence of the accuracy of the tests from the published literature indicates that cytogenetic testing is not as accurate as molecular techniques (ie, PCR and Southern blot) in detecting the fragile X full mutation. With regard to a fragile X premutation, cytogenetic testing was unable to detect such a mutation. The sensitivity of cytogenetic testing varied across studies, although specificity was consistently high with few false positive results reported. Studies comparing PCR to Southern blot reported high sensitivity and specificity. It should be noted, however, that PCR may not reliably amplify full mutations, and Southern blot is usually necessary to reliably demonstrate a full mutation.

Cost effectiveness: A cascade testing program is estimated to cost up to $4 million annually, and would result in a cost per initial case detected of between $14 000 and $28 000.

Recommendations

Public funding should be supported for Nucleic Acid Amplification (NAA) in those with specific clinical features of Fragile X (A) syndrome, including intellectual disabilities and in first and second degree relatives of individuals with Fragile X (A) mutation and Southern blot where the results of NAA testing are inconclusive.

Methods

MSAC conducted a systematic review of the biomedical literature (Cochrane Library, EBM-Reviews-ACP Journal Club, MEDLINE, PreMedline, Current Contents, Biological Abstracts and PsychINFO) from commencement to June 2001. The above sources were searched for cross-sectional studies which evaluated the diagnostic characteristics of at least two tests (PCR, Southern blot or cytogenetic test) for the diagnosis of fragile X (full or premutation).

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