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O6-Methylguanine-DNA methyltransferase protein expression by immunohistochemistry in brain and non-brain systemic tumours: systematic review and meta-analysis of correlation with methylation-specific polymerase chain reaction.

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Abstract

BACKGROUND: The DNA repair protein O6-Methylguanine-DNA methyltransferase (MGMT) confers resistance to alkylating agents. Several methods have been applied to its analysis, with methylation-specific polymerase chain reaction (MSP) the most commonly used for promoter methylation study, while immunohistochemistry (IHC) has become the most frequently used for the detection of MGMT protein expression. Agreement on the best and most reliable technique for evaluating MGMT status remains unsettled. The aim of this study was to perform a systematic review and meta-analysis of the correlation between IHC and MSP.

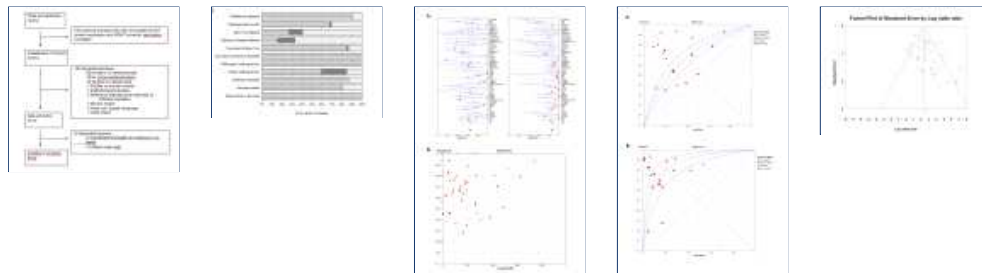
METHODS: A computer-aided search of MEDLINE (1950-October 2009), EBSCO (1966-October 2009) and EMBASE (1974-October 2009) was performed for relevant publications. Studies meeting inclusion criteria were those comparing MGMT protein expression by IHC with MGMT promoter methylation by MSP in the same cohort of patients. Methodological quality was assessed by using the QUADAS and STARD instruments. Previously published guidelines were followed for meta-analysis performance.

RESULTS: Of 254 studies identified as eligible for full-text review, 52 (20.5%) met the inclusion criteria. The review showed that results of MGMT protein expression by IHC are not in close agreement with those obtained with MSP. Moreover, type of tumour (primary brain tumour vs others) was an independent covariate of accuracy estimates in the meta-regression analysis beyond the cut-off value.

CONCLUSIONS: Protein expression assessed by IHC alone fails to reflect the promoter methylation status of MGMT. Thus, in attempts at clinical diagnosis the two methods seem to select different groups of patients and should not be used interchangeably.

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