Title A systematic review of combination and high-dose atypical antipsychotic therapy in patients with schizophrenia

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Reference CADTH Optimal Use Report, Issue 1b, December 2011.
ISSN: 1927-0127. Available From: http://www.cadth.ca/media/pdf/H0503_AAP_science-report_e.pdf

Aim

To identify and appraise clinical evidence pertaining to the use of atypical antipsychotics (AAPs), combination therapy and high-dose treatment strategies in adolescents and adults with schizophrenia.

Conclusions and results

No clinically significant improvements were found favouring combination or high-dose AAP treatment strategies when compared with standard-dose monotherapy. In terms of safety, no clinically significant differences were evident between combination or high-dose therapy in comparison with standard-dose monotherapy, with the exception of clozapine combination therapy where patients experienced more serious adverse events compared with clozapine monotherapy. However, the safety evidence was considered inconclusive, due to the sparsity of data for key harms-related outcomes.

Recommendations

Recommendations on the use of AAP combination and high-dose treatment strategies in adolescents and adults with schizophrenia are available separately from: http://www.cadth.ca/media/pdf/H0503_AAP_rec-report_e.pdf. CADTH's expert review committee recommended that combination or high-dose AAP treatment strategies should not be used for patients with inadequate response to standard dose AAP monotherapy. Standard-dose clozapine was recommended instead.

Methods

English or French language RCTs related to the use of AAP combination therapy or high-dose treatment strategies in adolescents and adults with treatment-resistant schizophrenia were selected from bibliographic databases, websites of relevant agencies and associations, and other specialized databases.

Two reviewers independently selected trials based on predefined inclusion criteria and assessed study quality using the SIGN-50 checklist for RCTs. Meta-analyses were performed using a random effects model, where appropriate and subgroup analyses were performed, where possible.

Further research/reviews required

Longer-term studies of sufficient size and

methodological quality are required to determine whether combination or high-dose treatment strategies have clinical value in treatment-resistant patients with schizophrenia.

Written by

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