**Efficacy of Agomelatine on Major Depressive Disorder and Sleep**

**: A meta-analytic study**

**Running title:** Agomelatine in the treatment of major depressive disorder and sleep

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**Objective:**  Agomelatine is a novel antidepressant, a combination of antagonist activity at 5HT2C receptors and agonist activity at melatonergic MT1/MT2 receptors. To systematically review efficacy studies of agomelatine in the treatment of depression and sleep.

**Design:** Systematic review and meta-analysis.

**Data sources:** Literature search (Pubmed, Medline), and Cochrane Central Register of Controlled Trials.

**Eligibility criteria:** Double blind randomized placebo and comparator controlled trials of agomelatine in depression with standard depression rating scales.

**Data synthesis:** Studies were pooled by using a fixed effects model for comparisons with placebo and comparator antidepressant. The primary efficacy measure (change in rating scale score) was summarized with standardized mean difference (SMD; a measure of effect size) and secondary outcome measures with sleep evaluation. All results were presented with 95% confidence intervals. Statistical heterogeneity was explored by visual inspection of funnel plots and by the I2 statistic. Moderators of effect were explored by meta-regression.

**Results** We identified 11 trials with 3,537 participants meeting inclusion criteria. All studies used the 17 item Hamilton depression rating scale (score 0-50). Agomelatine was significantly more effective than placebo with Effect Sizes(Ess) of -0.697 (95% confidence interval -0.811 to -0.583, p<0.001). Compared with other antidepressants, agomelatine showed more efficacy although not significant (ESs: -0.254, −0.587 to 0.080, p=0.136). In addition, six of these trials (2,090 patients) evaluated sleep with the Leeds Sleep Evaluation Questionnaire (LSEQ) or polysomnography. Meta-analyses revealed that improvement in subjective sleep (LSEQ) was associated with agmelatine (Ess: -0.510 on quality of sleep score, -0.072 on sleep awakening score, -0.241 on integrity of behavior score, respectively).

**Conclusions** Agomelatine is an effective antidepressant with similar efficacy to standard antidepressants. Furthermore, agomelatine showed greater efficacy in improving subjective sleep than other antidepressants in MDD patients.

**Keywords:** Agomelatine, major depressive disorder and sleep.