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420 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 3 Table 3.15 Reported associations between antidepressants and increased prolactin. Drug/group Prospective studies Case reports/series Agomelatine No mention of prolactin changes in clinical trials8 Melatonin itself may inhibit prolactin production9 None Bupropion Single doses of up to 100mg seem not to affect prolactin10 May decrease prolactin11 None Monoamine oxidase inhibitors Small mean changes observed with phenelzine11 and tranylcypromine12 Very occasional reports of increased prolactin11 Mirtazapine Strong evidence that mirtazapine has no effect on prolactin13 Occasional reports of galactorrhoea14 and gynaecomastia15 SNRIs Clear association observed between venlafaxine and duloxetine and prolactin elevation16–18 Galactorrhoea reported with venlafaxine19,20 and duloxetine.21,22 Duloxetine-linked hyperprolactinaemia has been treated with aripiprazole.16 SSRIs Prospective studies generally show no change in prolactin.23–25 Some evidence from prescription event monitoring that SSRIs are associated with higher risk of non--puerperal lactation.26 In a French study, 1.6% of adverse event reports for SSRIs were of hyperprolactinaemia.3 Galactorrhoea reported with fluoxetine,6,27 paroxetine,28–30 sertraline31 and fluvoxamine30 Euprolactinaemic galactorrhoea and amenorrhoea32 reported with escitalopram33 and fluvoxamine34 Hyperprolactinaemia reported with sertraline7,35 Tricyclics Small mean changes seen in some studies11,36,37 but no changes in others11,38 Symptomatic hyperprolactinaemia reported with imipramine,33 dosulepin39 and clomipramine40,41 Galactorrhoea reported with nortriptyline42 and when trazodone was added to citalopram43 Raised prolactin may be linked to response to amitriptyline36,44 Vortioxetine No mention of prolactin changes in clinical trials45 None One review suggests ‘probable relation between vortioxetine and galactorrhoea’46 Antidepressants and hyperprolactinaemia Prolactin release is controlled by endogenous dopamine but is also indirectly modulated by serotonin via stimulation of 5HT1C and 5HT2 receptors.1,2 Long-standing increased plasma prolactin (with or without symptoms) is very occasionally seen with antidepressant use.3 Where antidepressant-induced hyperprolactinaemia does occur, rises in prolactin are usually small and short-lived,4 so symptoms are very rare. There is no association between SSRI use and breast cancer.5 Routine monitoring of prolactin is not recommended but where symptoms suggest the possibility of hyperprolactinaemia then measurement of plasma prolactin is essential. Where symptomatic hyperprolactinaemia is confirmed, a switch to mirtazapine is recommended (see below), although there is also evidence that switching to an alternative SSRI can resolve symptoms.6,7 Some details of associations between antidepressants and increased prolactin are given in Table 3.15.

Revision #1
Created 2026-01-04 20:15:45 UTC by Omar Ayman
Updated 2026-01-04 20:15:45 UTC by Omar Ayman