The Effects of Mirtazapine on Plasma Lipid Profiles in Healthy Subjects

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Background: The novel antidepressant mirtazapine has been linked to elevated random plasma total cholesterol (TC) levels. The purpose of this study was to evaluate in a more controlled and precise approach the putative effects of mirtazapine on plasma lipids.

Method: In a double-blind design, 50 healthy subjects (30 women and 20 men) were randomized to receive either mirtazapine (N = 28) or placebo (N = 22) for a 4-week period. The study was conducted from June 1997 to September 1998. The initial dose for the mirtazapine group was 15 mg daily, which was increased to 30 mg daily at the beginning of the second week. Body weight and plasma lipoprotein profiles, including TC, low-density lipoproteins (LDL), high-density lipoproteins (HDL), and triglycerides, were determined at baseline and at weekly intervals throughout the study period.

Results: At baseline, there were no group differences in any of the measures. There was a statistically significant increase of 2.5% in mean body weight over the course of the study in the mirtazapine group that appeared to reach a plateau at 3 weeks, while no increase was observed in the placebo group. Mirtazapine subjects also showed significantly increased TC at week 4 ($p = .016$) and a transient rise in triglycerides that normalized by week 4. No significant changes in any of the other lipid parameters, including HDL, LDL, and TC/HDL ratios, were observed within either group. Changes in TC were significantly and positively correlated with changes in weight ($p < .01$).

Conclusion: These results suggest that while mirtazapine may be associated with increased TC, it does not increase LDL levels or affect the ratio of TC to HDL.

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Mirtazapine is a novel antidepressant with a unique pharmacologic profile. Mirtazapine blocks presynaptic α_2-noradrenergic autoreceptors, resulting in increased norepinephrine release. In turn, norepinephrine stimulates α_1 receptors on the cell bodies of serotonergic (5-HT) neurons, leading to increased 5-HT neuronal cell firing. Mirtazapine also blocks α_2-adrenergic heteroreceptors on the synaptic terminals of 5-HT neurons, which leads to further increases in 5-HT release. Mirtazapine also acts as an antagonist at 5-HT_2 and 5-HT_3 receptors and histamine (H_2) receptors. Thus, its net effect is enhanced noradrenergic neurotransmission, selective enhancement of 5-HT_1–mediated neurotransmission, and H_2 blockade.[1] Its side effect profile is notable for sedation and increased appetite, as well as the absence of the sexual and gastrointestinal side effects that are commonly seen with selective serotonin reuptake inhibitors (SSRIs).[1]

Mirtazapine has been linked to increased plasma total cholesterol (TC) levels, with a reported average 3% to 4% increase in random TC levels.[2] However, the clinical significance of this association is unclear, since TC levels might be expected to increase with improved appetite, increased caloric intake, and increased weight with remission of symptoms in patients whose symptoms included weight loss. Additionally, the clinical impact of increased TC levels cannot be interpreted without accounting for changes in lipoprotein fractions. The purpose of this study was to evaluate the putative effects of mirtazapine on fasting plasma lipoprotein profiles in healthy subjects. In this way, the actual pharmacologic effects of mirtazapine on

plasma lipids could be distinguished from possible secondary effects that occur as a consequence of clinical improvement in depression-related appetite suppression that occurs in many patients and concurrent changes in caloric intake.

METHOD

The study was approved by the University of North Carolina School of Medicine's Committee on the Protection of Human Subjects. All subjects gave oral and written informed consent after the procedures and possible side effects were explained to them. Fifty healthy subjects (30 women, 20 men) were recruited by newspaper advertisements and posters placed on campus. All subjects underwent careful medical and psychiatric screening, including administration of the Structured Clinical Interview for DSM-IV Axis I Disorders[3] and the Modified Schedule for Affective Disorders and Schizophrenia-Lifetime Version.[4] Subjects were eligible for the study if they had no personal history of psychiatric disorders such as major depression, manic-depressive illness, or schizophrenia or significant history of drug or alcohol abuse and no history in any first-degree relative of psychiatric or serious medical illness, including myocardial infarction prior to 50 years of age. Subjects were excluded if they were pregnant, lactating, ≤ 6 months postpartum, or not using adequate contraception. Exclusion criteria also included a history of cardiac, liver, kidney, or endocrine disease; seizure disorder; a known allergy to mirtazapine; any clinically significant laboratory or physical examination abnormalities; or current nicotine use. Subjects were paid $250 for completion of the study; they received $100 for the first 3 weeks and $150 at the end of the study. The study was conducted from June 1997 to September 1998.

In a double-blind design, subjects were randomized to receive either mirtazapine (N = 28) or placebo (N = 22) for a 4-week period. Subjects in the mirtazapine group received an initial dose of 15 mg daily, which was increased to 30 mg daily at the beginning of the second week. Blood samples and other measurements were taken at weekly visits. Assays for mirtazapine levels were not performed, but compliance was measured by weekly pill counts and interview. Data were included only for those subjects who completed both baseline and final evaluations and who missed no more than 1 interim evaluation.

Baseline group equivalence was verified by using analysis of variance (ANOVA), controlling for gender. The response variables evaluated were body weight, TC, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), triglycerides, and the ratio of TC to HDL (TC/HDL). Within-subject changes from baseline to endpoint for each treatment group were evaluated using the paired t test, and endpoint group differences were evaluated with analysis of covariance (ANCOVA) on final (week 4) values, controlling for gender and baseline values for each response variable. Also, for completeness, these primary, focused hypothesis tests were supplemented by comprehensive repeated-measures analysis of covariance (RM-ANCOVA) using all timepoints, controlling for baseline values and sex, and corrected for non-sphericity using the Greenhouse-Geisser epsilon method. Frequency comparisons were made using chi-square statistics. Associations between response variables were evaluated using the Pearson correlation, controlling for gender. Results are reported as mean ± SD and were considered significant at $p < .05$; all tests were 2-tailed.

Assays for blood lipoproteins and triglycerides were performed on the same day they were collected by the University of North Carolina Hospitals McClendon Clinical Laboratories according to standard protocol. Cholesterol, HDL, and triglycerides were determined by enzymatic colorimetry. Interassay coefficients of variation values were 1.6 (TC), 3.3 (HDL), and 2.8 (triglycerides). LDL was calculated using the following formula: LDL = TC–(triglycerides/5).

Table 1. Body Weight and Plasma Lipid Values (mean ± SD) at Baseline and Week 4 for Subjects Receiving Placebo or Mirtazapine[a]

	Placebo (N = 22)		Mirtazapine (N = 28)	
Measure	Baseline	Week 4	Baseline	Week 4
Weight, kg	69.6 ± 9.9	69.6 ± 10.2	68.6 ± 10.3	70.3 ± 10.6
TC, mg/dL	164.0 ± 25.4	164.1 ± 29.2	168.2 ± 26.4	175.7 ± 30.3
HDL, mg/dL	52.4 ± 12.1	53.2 ± 13.2	52.8 ± 12.6	54.2 ± 13.8
LDL, mg/dL	92.9 ± 22.9	91.2 ± 23.1	98.3 ± 23.8	101.6 ± 24.0
TG, mg/dL	93.1 ± 57.1	98.8 ± 65.8	86.0 ± 59.3	99.1 ± 68.4
TC/HDL ratio, mg/dL	3.35 ± 0.96	3.31 ± 1.00	3.34 ± 1.00	3.39 ± 1.04

[a]Values adjusted for sex.
Abbreviations: HDL = high-density lipoprotein, LDL = low-density lipoprotein, TC = total cholesterol, TG = triglycerides.

RESULTS

There were 10 men and 12 women in the placebo group, and 10 men and 18 women in the mirtazapine group. The mean age was 27.2 ± 6.2 years for the placebo group and 26.2 ± 8.6 years for the mirtazapine group. The groups did not differ significantly at baseline with regard to sex-adjusted body weight, TC, HDL or LDL cholesterol, triglycerides, or the ratio of TC/HDL cholesterol (Table 1).

Body Weight

Mean sex-adjusted body weights for placebo and mirtazapine groups at baseline and week 4 are shown in Table 1. Mirtazapine-treated subjects experienced small, but statistically significant increases in body weight from

Figure 1. Percentage of Baseline Body Weight Throughout the Study

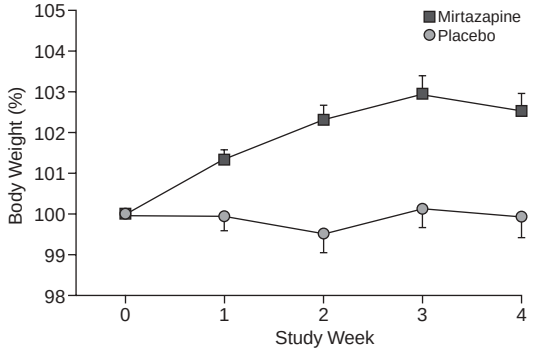
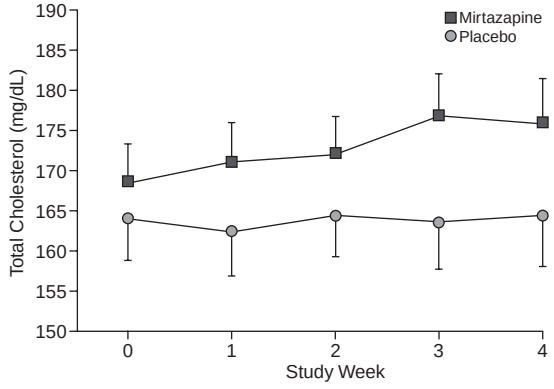


Table 2. Effect of Mirtazapine on Weight at Study Endpoint as a Percentage of Baseline Weight[a]

Effect	F	df	p Value
Group	20.66	1,46	.0001
Time (between groups)	5.41	3,138	.0028
Group by time	3.90	3,138	.0150
Week 1 (between groups)	10.81	1,46	.0019
Week 2 (between groups)	24.19	1,46	.0001
Week 3 (between groups)	19.51	1,46	.0001
Week 4 (between groups)	12.39	1,46	.0010
Time (placebo group)	1.30	3,63	.2840
Time (mirtazapine group)	8.49	3,81	.0002

[a]Repeated-measures analysis of covariance, controlling for sex.

Figure 2. Total Cholesterol Levels Throughout the Study



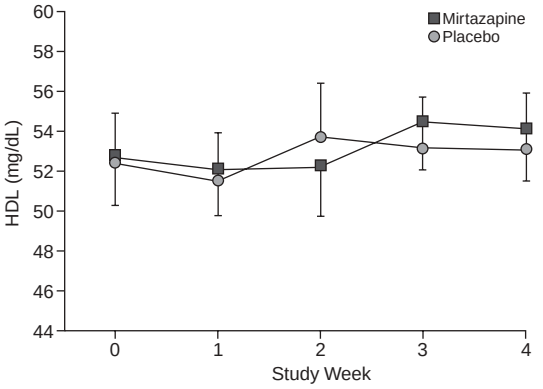
baseline at each study week; no significant changes in body weight were observed among placebo group subjects (Figure 1). At week 4, the mirtazapine group had a mean body weight of 102.5% of their mean baseline weight, compared with 100% for the placebo group (p = .001). At the end of the study, the mean increase for the mirtazapine subjects was 1.64 kg (3.64 lb). The RM-ANCOVA results shown in Table 2 support these primary hypothesis tests.

Table 3. Effect of Mirtazapine on Total Cholesterol Levels[a]

Effect	F	df	p Value
Group	3.67	1,45	.0618
Time (between groups)	1.76	3,135	.1747
Group by time	0.46	3,135	.6505
Week 1 (between groups)	1.12	1,45	.2961
Week 2 (between groups)	0.97	1,45	.3311
Week 3 (between groups)	3.28	1,45	.0770
Week 4 (between groups)	3.26	1,45	.0778
Time (placebo group)	1.43	3,60	.2507
Time (mirtazapine group)	0.65	3,78	.5448

[a]Repeated-measures analysis of covariance, controlling for baseline values and sex.

Figure 3. High-Density Lipoprotein (HDL) Levels Throughout the Study



Total Cholesterol

Mirtazapine-treated subjects showed statistically significant increases in TC at week 3 (p = .027) and week 4 (p = .016) compared with their baseline values, while placebo subjects showed no significant changes at any week (Figure 2). The mean change among mirtazapine-treated subjects was +7.6 mg/dL; placebo subjects showed a mean change of –0.04 mg/dL.

There was no significant difference in mean TC at baseline, but there was a trend toward higher mean TC levels in the mirtazapine group compared with the placebo group at study endpoint (p = .076) (Table 1). These indications of group differences at weeks 3 and 4 were reflected in the RM-ANCOVA, but the endpoint trend was not supported by the group-by-time interaction result shown in Table 3.

Changes in weight were linearly associated with changes in total cholesterol. After controlling for sex, the overall Pearson correlations were as follows: at week 3, r = 0.45, p = .001 (within groups, mirtazapine: r = 0.42, p = .03; placebo: r = 0.35, p = .12); at week 4, r = 0.38, p = .008 (within groups, mirtazapine: r = 0.25, p = .22; placebo: r = 0.45, p = .04).

Figure 4. Low-Density Lipoprotein (LDL) Levels Throughout the Study

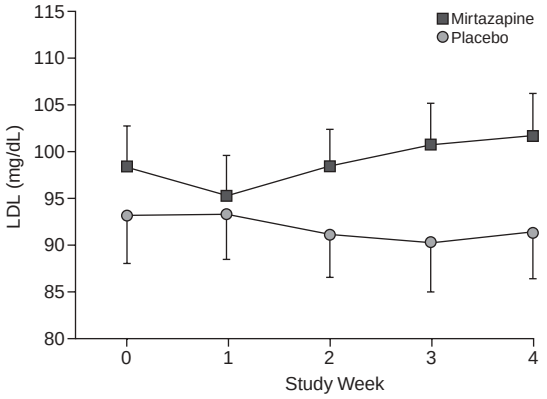


Table 4. Effect of Mirtazapine on High-Density Lipoprotein Cholesterol Levels[a]

Effect	F	df	p Value
Group	0.00	1,45	.9697
Time (between groups)	0.85	3,135	.4622
Group by time	1.24	3,135	.2971
Week 1 (between groups)	0.11	1,45	.7406
Week 2 (between groups)	0.79	1,45	.3794
Week 3 (between groups)	0.22	1,45	.6400
Week 4 (between groups)	0.40	1,45	.5303
Time (placebo group)	0.14	3,60	.9146
Time (mirtazapine group)	1.42	3,78	.2437

[a]Repeated-measures analysis of covariance, controlling for baseline values and sex.

Table 5. Effect of Mirtazapine on Low-Density Lipoprotein Cholesterol Levels[a]

Effect	F	df	p Value
Group	1.33	1,45	.2553
Time (between groups)	0.32	3,135	.7806
Group by time	1.53	3,135	.2148
Week 1 (between groups)	0.48	1,45	.4922
Week 2 (between groups)	0.51	1,45	.4777
Week 3 (between groups)	2.48	1,45	.1220
Week 4 (between groups)	3.22	1,45	.0796
Time (placebo group)	0.27	3,60	.8147
Time (mirtazapine group)	0.15	3,78	.8926

[a]Repeated-measures analysis of covariance, controlling for baseline values and sex.

Figure 5. Triglyceride Levels Throughout the Study

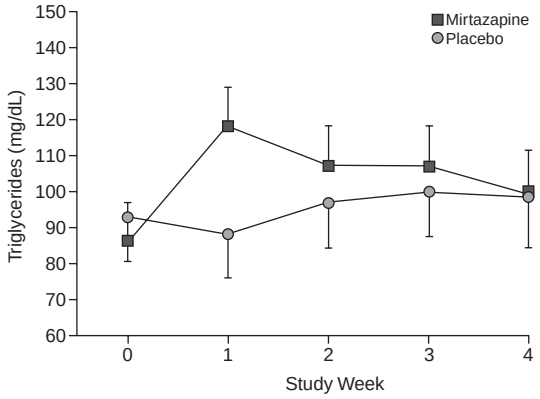


Table 6. Effect of Mirtazapine on Triglyceride Levels[a]

Effect	F	df	p Value
Group	4.16	1,45	.0474
Time (between groups)	0.39	3,135	.7155
Group by time	1.79	3,135	.1640
Week 1 (between groups)	9.31	1,45	.0038
Week 2 (between groups)	1.93	1,45	.1714
Week 3 (between groups)	0.92	1,45	.3432
Week 4 (between groups)	0.12	1,45	.7268
Time (placebo group)	0.02	3,60	.9642
Time (mirtazapine group)	1.37	3,78	.2595

[a]Repeated-measures analysis of covariance, controlling for baseline values and sex.

HDL and LDL Cholesterol

The mirtazapine group demonstrated a trend toward increased HDL levels at week 3 (p = .15) that diminished at week 4 (p = .20), while no changes were observed for the placebo group (Figure 3). No significant changes in LDL levels were noted at study endpoint (Figure 4). Sex-adjusted mean baseline and week 4 HDL and LDL levels for both groups are found in Table 1. These nonsignificant findings were supported by the RM-ANCOVA results shown in Tables 4 and 5.

Triglycerides

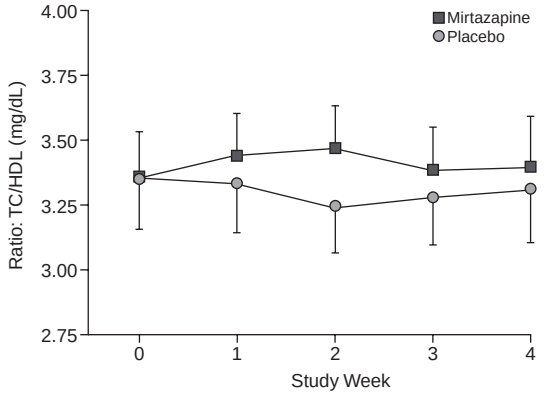
The mirtazapine group exhibited a transient increase in triglyceride levels compared with baseline, which were significantly increased at week 1 (p = .003), week 2 (p = .005), and week 3 (p = .02), but not at week 4 (p = .155) (Figure 5). No significant changes were noted in the placebo group. These nonsignificant findings were supported by the RM-ANCOVA results shown in Table 6.

Changes in weight were linearly associated with changes in triglycerides; after controlling for gender, the overall Pearson correlations were as follows: at week 3, r = 0.35, p = .01; at week 4, r = 0.26, p = .07. These correlations were relatively homogeneous across groups at each of these timepoints.

TC/HDL Ratio

Neither mirtazapine nor placebo group subjects showed any significant change in the ratio of TC/HDL cholesterol over time (Figure 6). No subject in either group demonstrated a rise in their TC/HDL ratio that would indicate an increased risk of cardiovascular disease (defined as 4.4 for women, 5.0 for men). No significant between-group differences were observed at week 4 in

Figure 6. TC/HDL Ratio Throughout the Study



Abbreviations: HDL = high-density lipoprotein, TC = total cholesterol.

Table 7. Effect of Mirtazapine on TC/HDL Ratio[a]

Effect	F	df	p Value
Group	2.26	1,45	.1395
Time (between groups)	0.62	3,135	.5589
Group by time	0.74	3,135	.4950
Week 1 (between groups)	0.60	1,45	.4423
Week 2 (between groups)	4.23	1,45	.0454
Week 3 (between groups)	0.74	1,45	.3935
Week 4 (between groups)	0.10	1,45	.7590
Time (placebo group)	0.58	3,60	.5421
Time (mirtazapine group)	0.61	3,78	.6003

[a]Repeated-measures analysis of covariance, controlling for baseline values and sex.
Abbreviations: HDL = high-density lipoprotein, TC = total cholesterol.

the TC/HDL ratio (Table 1). These nonsignificant findings were supported by the RM-ANCOVA results shown in Table 7.

DISCUSSION

Unfavorable serum lipoprotein levels, particularly high LDL and TC/HDL ratios, are widely accepted as a risk factor for coronary heart disease and arteriosclerosis. Conversely, HDL levels are inversely correlated with coronary heart disease risk. Diet, exercise, and medications can have an effect on lipoprotein levels. Given that antidepressants are widely prescribed by psychiatrists, as well as primary care physicians, examination of the effect of these drugs on plasma lipoprotein profiles is important.

According to Organon, Inc., product information, during premarketing controlled studies, mirtazapine was associated with increases of nonfasting TC of greater than or equal to 20% above the upper limits of normal in 15% of patients treated with mirtazapine compared with 7% treated with placebo.[5] Increases of nonfasting triglycerides of greater than or equal to 500 mg/dL were observed in 6% of mirtazapine-treated patients compared with 3% of the placebo group.[5] However, the clinical meaning of random (nonfasting) total cholesterol and triglyceride levels is not clear. Much more important are the deleterious effects of increased LDL balanced with the protective effects in HDL.

In our study, at the endpoint (week 4), we found modest but statistically significant increases in mean body weight and mean fasting total cholesterol over baseline in mirtazapine-treated subjects, while no significant changes were observed in subjects receiving placebo. At week 4, no significant changes from baseline were observed for triglycerides, HDL, LDL, or the more clinically sensitive TC/HDL ratio in either group.

No between-group differences were noted at baseline or study endpoint, although in the original (ANCOVA) analysis there was a trend toward higher TC levels in the mirtazapine group compared with the placebo group. The subsequent RM-ANCOVA analyses generally supported those of the ANCOVA, except in one instance: the finding of a trend ($p = .076$) toward an endpoint (week 4) group difference in TC was not found by its closest analog in the repeated-measures analysis, the group-by-time interaction (cf. Table 3, $p = .65$). The most probable explanation for this discrepancy is that the 2 analyses tested somewhat different hypotheses: the original analysis focused on the week 4 endpoint outcome, while the RM-ANCOVA generalized over weeks 1 through 4, testing whether the pattern of changes over time differed between groups.

Few studies have examined the relationship between cholesterol levels and antidepressant therapy. Yeragani et al.[6] noted increased TC/HDL ratios following treatment with imipramine. A study of 60 outpatients with major depressive disorder treated with bupropion or imipramine showed no change in weight or TC with bupropion but increases in both parameters with imipramine.[7] Pollock et al.,[8] in an open-label study of nortriptyline in 26 depressed patients over 60 years of age, found significant increases in very low-density lipoproteins and triglycerides, but no changes in HDL, LDL, or TC levels.

A literature review by Andrews and Nemeroff[9] found that, in general, SSRIs do not significantly alter serum cholesterol. However, there was some evidence of increased serum cholesterol levels associated with venlafaxine therapy. In a study by Maes et al.,[10] depressed men who had low HDL were treated with 5 weeks of antidepressant therapy consisting of trazodone, trazodone and pindolol, or trazodone and fluoxetine. No changes were reported in HDL, TC/HDL ratio, TC, or other lipid variables.

There is some evidence that SSRIs may have a favorable effect on lipid levels. In a study of 16 obese diabetic patients randomly assigned to fluoxetine or placebo, O'Kane et al.[11] found significant median weight loss and

a fall in triglycerides, but no change in serum cholesterol levels associated with fluoxetine. De Zwaan and Nutzinger[12] examined 40 obese women undergoing 13 weeks of behavioral treatment for weight reduction. The subjects were randomly assigned to receive fluvoxamine or placebo. Despite no differences in weight loss between the 2 groups, those given fluvoxamine had a significantly larger decrease in TC and those with initially elevated cholesterol levels (> 200 mg/dL) had a significantly larger reduction.

There have been interesting findings suggesting that low cholesterol might be a risk factor for depression and suicidality.[13–15] Primary prevention trials designed to lower serum cholesterol levels by diet, drugs, or both have found that these measures, designed to reduce mortality from cardiac disease, have resulted in an increased number of deaths due to suicide. Morgan et al.[16] found that depression was 3 times more common in elderly subjects with lowered cholesterol, while Golier et al.[14] found that men with lower TC levels were twice as likely to have made a medically serious suicide attempt. Furthermore, Muldoon et al.[15] found significantly lower TC, LDL, and HDL and higher triglyceride in hospitalized patients with affective disorder compared with healthy controls.

Maes et al.[10] reported significantly lower HDL, TC, and TC/HDL ratio values in subjects with major depressive disorder compared with healthy controls. Furthermore, they found significantly lower serum HDL levels in depressed men who had made a serious suicide attempt. These findings suggested an impairment of reverse cholesterol transport from body tissues to the liver in this group of patients.

There is additional evidence that alterations in lipid metabolism may be related to depression. Studies have shown altered omega-3/omega-6 polyunsaturated fatty acid (PUFA) ratios in depressed patients, as well as lowered omega-3 PUFAs in serum phospholipids and cholesteryl esters.[10,17]

Since there is a known association between weight gain and increased lipid levels, it is reasonable to assume that antidepressants that increase body weight might also be associated with increases in TC, LDL, and triglyceride levels. Andrews and Nemeroff[9] found tricyclic antidepressants, particularly amitriptyline, to be associated with weight gain. Othmer et al.[7] found both a 6% weight gain and a 10% gain in mean serum cholesterol in patients treated with amitriptyline compared with those treated with bupropion. There appears to be variation in the pattern of weight gain associated with different antidepressants. Goodnick et al.[18] did a meta-analysis of 4 U.S. studies comparing subjects receiving mirtazapine, amitriptyline, and placebo. For the subjects receiving mirtazapine who had gained weight, 75% of the increase occurred in the first 4 weeks of treatment with no increase from week 5 to 6. Also, subjects with a body mass index (BMI) greater than 30 gained less weight than those whose BMI was less than 30. Those subjects treated with amitriptyline had a linear increase throughout the study and gained weight at all BMI levels.

In this study, both body weight and total cholesterol increased significantly in healthy subjects treated with mirtazapine. Weight gain appeared to level off between weeks 3 and 4. It would be clinically useful to know whether body weight would increase or continue to level off with long-term mirtazapine exposure. If weight continued to rise with long-term treatment, then it would be prudent to use mirtazapine cautiously in patients predisposed to obesity or who have risk factors for obesity-related diseases such as hypertension, cardiovascular disease, or diabetes mellitus. Additionally, for those patients with atypical symptoms associated with depression (hypersomnia, hyperphagia, and weight gain), mirtazapine may not be the appropriate choice for initial treatment. However, conclusive data regarding long-term weight changes or weight changes associated with higher doses of mirtazapine are not yet available.

In this study, since compliance was measured by interview and pill count rather than measurement of mirtazapine levels, it is possible that the mirtazapine-treated subjects failed to report missed doses secondary to unpleasant side effects such as sedation or fear of weight gain. If this were the case, effects of mirtazapine on weight and cholesterol may be underestimated in our study.

The nonsignificant rise in HDL from baseline to week 4 in the mirtazapine group probably explains the lack of significant change in the TC/HDL ratio. The known association of increased caloric intake with these lipid measures may account for the significant linear correlations between increased body weight and both TC and triglycerides.

The meaning of the increased TC levels in depressed subjects treated with mirtazapine is unclear. As reviewed above, there are substantial data suggesting that low levels of TC and HDL cholesterol are associated with depression and that this may be secondary to altered cholesterol reverse transport. Studies examining the effects of dietary supplementation with essential fatty acids on mood as well as plasma lipoprotein levels in depressed subjects could be valuable in clarifying this relationship. Could treatment with mirtazapine potentiate normalization of cholesterol metabolism, or is increased TC more simply explained by increased caloric intake and weight gain? Unfortunately, our dietary intake data were not reliable and thus we were unable to determine if the changes in lipid levels were associated with increased intake of calories and/or fat. Furthermore, the effects of mirtazapine on body weight and plasma lipids in hypercholesterolemic subjects were not addressed in our study.

CONCLUSION

To our knowledge, this is the first controlled study to date that shows the modest, but statistically significant, effect of mirtazapine on mean increases in body weight and fasting TC in healthy subjects. However, there were no significant differences in LDL or the more clinically meaningful measure, the TC/HDL ratio. There was also a trend toward increased levels of HDL and a significant positive association between change in TC and triglycerides with change in weight. Although it appears that no changes occurred in the clinically sensitive TC/HDL index, it would be prudent for clinicians to monitor weight and lipoprotein levels in those mirtazapine-treated patients who are at high risk for hyperlipidemia or coronary artery disease.

Drug names: amitriptyline (Elavil and others), bupropion (Wellbutrin and others), fluoxetine (Prozac and others), fluvoxamine (Luvox and others), imipramine (Tofranil and others), mirtazapine (Remeron and others), nortriptyline (Aventyl, Pamelor, and others), pindolol (Visken and others), trazodone (Desyrel and others), venlafaxine (Effexor).

REFERENCES

1. Golden RN, Dawkins K, Nicholas L, et al. Trazodone, nefazodone, bupropion, and mirtazapine. In: Nemeroff C, Schatzberg A, eds. Textbook of Psychopharmacology. 2nd ed. Washington, DC: American Psychiatric Press; 1998:251–270
2. Davis R, Wilde MI. Mirtazapine: a review of its pharmacology and therapeutic potential in the management of major depression. CNS Drugs 1996;5:389–402
3. First MB, Spitzer RL, Gibbon M, et al. Structured Clinical Interview for DSM-IV-TR Axis I Disorders-Non-Patient Edition (SCID-I/NP, 11/2002 revision). New York, NY: Biometrics Research, New York State Psychiatric Institute; 2002
4. Spitzer RL, Endicott J. The Schedule for Affective Disorders and Schizophrenia. 3rd ed. New York, NY: New York State Psychiatric Institute; 1978
5. Remeron [package insert]. West Orange, NJ: Organon Inc; 1998
6. Yeragani VK, Pohl R, Balon R, et al. Increased serum total cholesterol to HDL-cholesterol ratio after imipramine. Psychiatry Res 1990;32: 207–209
7. Othmer E, Othmer SC, Stern WC, et al. Long-term efficacy and safety of bupropion. J Clin Psychiatry 1983;44:153–156
8. Pollock BG, Perel JM, Paradis CF, et al. Metabolic and physiologic consequences of nortriptyline treatment in the elderly. Psychopharmacol Bull 1994;30:145–150
9. Andrews JM, Nemeroff CB. Contemporary management of depression. Am J Med 1994;97:24S–32S
10. Maes M, Smith R, Christophe A, et al. Lower serum high-density lipoprotein cholesterol (HDL-C) in major depression and in depressed men with serious suicidal attempts: relationship with immune-inflammatory markers. Acta Psychiatr Scand 1997;95:212–221
11. O'Kane M, Wiles PG, Wales JK. Fluoxetine in the treatment of obese type 2 diabetic patients. Diabet Med 1994;11:105–111
12. de Zwaan M, Nutzinger DO. Effect of fluvoxamine on total serum cholesterol levels during weight reduction. J Clin Psychiatry 1996; 57:346–348
13. Sullivan PF, Joyce PR, Bulik CM, et al. Total cholesterol and suicidality in depression. Biol Psychiatry 1994;37:472–477
14. Golier JA, Marzuk PM, Leon AC, et al. Low serum cholesterol level and attempted suicide. Am J Psychiatry 1995;152:419–423
15. Muldoon MF, Rossouw JE, Manuck SB, et al. Low or lowered cholesterol and risk of death from suicide and trauma. Metabolism 1993; 42(9 suppl 1):45–46
16. Morgan RE, Palinkas LA, Barrett-Connor EL, et al. Plasma cholesterol and depressive symptoms in older men. Lancet 1993;341:75–79
17. Hibbeln JR, Salem N Jr. Dietary polyunsaturated fatty acids and depression: when cholesterol does not satisfy. Am J Clin Nutr 1995;62:1–9
18. Goodnick P, Kremer C, Wingard P. Weight change during mirtazapine therapy. Primary Psychiatry 1999;5:103–108