Novel approach to depression in ischemic heart disease: attenuation of autonomic dysfunction lowers depression scores

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Introduction: Depression in ischemic heart disease (IHD) is associated with increased mortality, and autonomic nervous system dysfunction (ANSD) may link the two conditions. Regulatory functions of the autonomic nervous system with respect to IHD risk factors include heart rate, blood pressure, serum cholesterol, and glycated hemoglobin. While painful sensitivity to pressure (Pressure-Pain Sensitivity, PPS) at the sternum rises with increased depression in IHD, reduction of elevated PPS reflects lower depression scores, lower ANSD, and lower mortality rates in IHD. Beta-adrenoreceptor blockade (BB) inhibits the anti-depressive effect associated with reduced PPS measures as well as the efferent sympathetic autonomic activity.

Purpose: We tested the hypothesis that lowering of elevated PPS measures is associated with restored autonomic regulation of depression, measured as the association between baseline depression scores and subsequent lowering of the depression score. We determined whether autonomic regulation in depression is associated with non-pharmacological reduction of elevated PPS measures.

Methods: In a randomized controlled intervention trial of IHD that included 213 individuals with elevated PPS, 20% of participants had elevated Major Depression Inventory scores (MDIS). We compared subjects with previously defined minimum reduction of at least 15 PPS units (PPS reverters) with subjects without this effect (PPS non-reverters), as well as non-users with users of BB. We recorded linear regressions of depression score changes as the dependent variable versus baseline depression scores as the independent variable. We compared active and control treatments by dividing participants into three pre-study defined groups of no depression (MDIS < 15), incipient depression (15 < MDIS < 20), and manifest depression (MDIS > 20).

Results: For reverters (N=72) compared to non-reverters (N=93), the mean anti-depressive effect increased in favor of reverters by a rate of 0.3 MDI units (95% CI 0.10–0.5, P=0.004) per unit increase in baseline MDIS. Comparing BB non-users (N=97) with BB users (N=67), the rate in favor of BB non-users was 0.4 units (95% CI 0.2-0.6, P=0.0002). In combination, comparing reverting non-users of BB (N=27) to non-reverting BB users (N=52), the rate in favor of the former group was 0.7 MDI (95% CI 0.4-0.9, P<0.00001). For reverting BB non-users, Cohen’s effect size reached 1.5. For the comparison of active and control groups for the three levels of MDIS, the trend was significant at P=0.04.

Conclusions: In patients with IHD, depression is associated with disruption of specific sympathetic beta-adrenergic regulatory functions of the autonomic nervous system. The findings imply that lowering of elevated PPS measures is associated with enhanced autonomic regulation of depression scores, and with marked clinical effect in individuals with elevated depression scores, but with no effect in BB users.