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Impact of concurrent naturalistic pharmacotherapy on psychotherapy of complicated grief

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Abstract

Complicated grief (CG) is a debilitating syndrome that can be reliably identified, but there is a paucity of research examining treatment of CG. A targeted psychotherapy for complicated grief (CGT) was recently shown to be efficacious [Shear, K., Frank, E., Houck, P.R., Reynolds, C.F., 3rd, 2005. Treatment of complicated grief: a randomized controlled trial. Journal of the American Medical Association 293, 2601–2608]. We provide a detailed examination of the association of naturalistic pharmacotherapy use with treatment response and study completion in the psychotherapy study. Patients on an antidepressant medication were more likely to complete a full course of CGT (91% vs. 58% completed), while antidepressant use had no effect on completion rates for the comparator, interpersonal psychotherapy (70% vs. 77%). Our naturalistic data underscore the need for prospective, randomized controlled studies of CG pharmacotherapy and psychotherapy alone and in combination.

Keywords: Treatment; Antidepressant; Benzodiazepine; Complicated grief; Traumatic grief; Prolonged grief

1. Introduction

Complicated grief (CG) is a debilitating syndrome that can be reliably identified. CG is diagnosed when intense grief persists more than 6 months after the loss of a loved one. Symptoms include separation distress (recurrent pangs of painful emotions, with intense yearning and longing for the deceased, and preoccupation with thoughts of the loved one) and traumatic distress (sense of disbelief regarding the death, anger and bitterness, distressing, intrusive thoughts related to the death, and pronounced avoidance of reminders of the painful loss) (Shear et al., 2005).

While CG causes significant distress and impairment (Silverman et al., 2000; Shear et al., 2005), and is associated with excess medical morbidity and suicidality (Prigerson et al., 1997, 1999; Szanto et al., 2006), little is known about its treatment. Pharmacotherapy studies primarily targeting bereavement-related depression found minimal to modest effects of medication on grief (Zygmont et al., 1998; Reynolds et al., 1999; Zisook et al., 2001). Zisook and colleagues treated 22

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individuals who met criteria for a major depressive episode (allowing bereavement) 6–8 weeks after a loss with open-label bupropion, and found significant reduction in depression, with modest though statistically significant concurrent decreases in grief symptoms in this acute period (Zisook et al., 2001). Zygmont and colleagues openly treated 15 individuals with complicated grief 6 to 17 months after a loss with paroxetine (median dose 30 mg/day) for 4 months concurrent with a grief-focused course of psychotherapy and found a similar reduction in grief symptoms as in a historically treated group of 22 individuals who received nortriptyline for bereavement-related depression; however, the study design did not allow separation of paroxetine effects from psychotherapy effects (Zygmont et al., 1998). In the only relevant randomized clinical trial to date, Reynolds and colleagues examined the impact of nortriptyline, interpersonal psychotherapy or the combination on bereavement-related major depressive episodes in 80 patients aged 50 and older, and found that while there were antidepressant effects in this population treated with nortriptyline, neither interpersonal psychotherapy nor nortriptyline led to a significant reduction in grief symptoms (Reynolds et al., 1999), consistent with an earlier open pilot study of nortriptyline in bereavement-related depression that failed to reduce grief intensity (Pasternak et al., 1991).

We therefore developed complicated grief therapy (CGT), which was demonstrated efficacious compared with interpersonal psychotherapy (IPT) in the first randomized controlled trial (RCT) of a treatment for CG (Shear et al., 2005). The active control condition, IPT with a grief focus, followed a standard published manual (Weissman et al., 2000). Briefly, IPT has an introductory phase when symptoms and an interpersonal inventory are reviewed; a middle phase addressing grief symptoms and interpersonal problems (as well as specifically addressing the positive and negative aspects of the patient's relationship with the deceased person), and encouraging participation in satisfying activities and relationships; and a termination phase. CGT similarly followed a manual and consists of an introductory, middle and termination phase. The introductory phase has a greater focuses on psychoeducation about the difference between normal and complicated grief, information about the "dual process" model of adapting to loss including adjustment to loss of the loved one, and an emphasis on personal goals and restoration of life satisfaction. In addition to working directly with personal goals throughout the treatment, the middle phase of CGT included loss-focused elements adapted from exposure therapy techniques, including telling and listening to tapes of the story of the death ("revisiting"), hierarchical exposure to avoided reminders of the loss, direct work with positive and negative memories of the deceased, and an imaginal conversation with the deceased person. CGT and IPT were each 16 sessions in length. In the overall RCT, CGT resulted in a significantly greater proportion of treatment responders than IPT in both the intent to treat (51% CGT vs. 28 IPT, $P=0.02$) and the completers only analyses (66% CGT vs. 32% IPT, $P=0.006$).

Stable medication use was permitted during the psychotherapy study; we previously reported that 45% (43/95) of RCT participants were taking an antidepressant, and initial analyses found non-significant differences in outcome for those on an antidepressant medication (Shear et al., 2005). Given the dearth of information about treatment of CG, we now present detailed secondary analyses of naturalistic pharmacotherapy use and its association with response and completion of CGT and IPT in the trial. To our knowledge, this is the first study to examine the impact of concurrent medication use on two different types of psychotherapy.

2. Methods

Detailed methodology of the parent RCT are available elsewhere (Shear et al., 2005). Briefly, eligible individuals had >6 months of persistent grief with CG their primary clinical problem (as confirmed by an independent evaluator), and scored >30 on the Inventory of Complicated Grief (ICG), a 19-item scale with a total score range of 0 to 76 (Prigerson et al., 1995). Comorbid Axis I psychiatric disorders were diagnosed utilizing the Structured Clinical Interview for DSM-IV (First et al., 1994). Response was defined as a score of 1 or 2 ("very much improved" or "much improved") on the Clinical Global Impression of Improvement Scale (CGI-I: scale range 1 to 7, with 4 = "no change" and 7 = "very much worse" (Guy, 1976)) focused specifically on CG symptoms. Medication for longer than 3 months at a stable dose for >6 weeks was permitted if medication management was transferred to our study pharmacotherapist. Medication could not be increased; although patients were encouraged to maintain stable doses, dose reduction was permitted.

We examined medication use amongst the 95 randomized participants, focusing on its relationship to treatment response and study completion overall and separately for CGT and IPT. Medication history was obtained using study forms and review of written records by our pharmacotherapist (AF). We classified psychiatric medications as follows: antidepressants, benzodiazepines,