CLINICIAN'S TRAUMA UPDATE

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TREATMENT

Challenges persist in developing pharmacological treatment strategies for PTSD

Relatively few medications are effective for treating PTSD. A group of recent studies evaluated commonly prescribed medications as well as novel treatment approaches.

A team led by investigators at the National Center for PTSD and White River Junction VAMC conducted a retrospective analysis of 834 VA patients who received adequate medication treatment (AMT) for PTSD between October 2016 and March 2018. In the 12-week phase of initial AMT, patients showed an improvement of 7-10 points on the PCL-5, with PTSD remission in 0%-11% depending on the medication. Patients taking venlafaxine were more likely to achieve remission than those taking other medications, with a remission rate of 10.9% with venlafaxine, 2.9% with fluoxetine, 0% with paroxetine, 4.7% with sertraline and 1.3% with topiramate. In a 6-month continuation phase, patients receiving AMT were less likely to use acute psychiatric services than those who were not, with no difference between the medications.

In another study, investigators at the Birmingham VAMC led a multisite, randomized, double-blind, placebo-controlled trial of the antidepressant mirtazapine for PTSD. This group found no difference in efficacy, measured by change on the Structured Interview for PTSD, between 39 Veterans randomized to mirtazapine versus 39 Veterans randomized to placebo.

In another multisite study, led by researchers at the Uniformed Services University and Syracuse VAMC, the efficacy of riluzole was tested in a randomized, double-blind, placebo-controlled trial of 74 Veterans with PTSD. Riluzole modulates the glutamate system in the brain, dysfunction of which has been implicated in the pathophysiology of PTSD. No difference in efficacy, measured by change on the CAPS, was found between the groups (riluzole versus placebo), though exploratory analyses suggested that riluzole had a more specific effect on hyperarousal symptoms.

Together, these studies highlight the challenges in developing pharmacological treatment strategies for PTSD: commonly prescribed medications may have efficacy, but this appears to be limited, and novel medication approaches continue to show little promise. However, it is hoped that an improved understanding of the complex pathophysiology of PTSD will continue to identify novel drug targets and that, eventually, a more effective medication treatment strategy for PTSD will emerge.

Read the articles:

https://doi.org/10.4088/JCP.20m13267

Davis, L. L., Pilkinton, P., Lin, C., Parker, P., Estes, S., & Bartolucci, A. (2020). A randomized, placebo-controlled trial of mirtazapine for the treatment of posttraumatic stress disorder in veterans. *Journal of Clinical Psychiatry, 81,* Article 20m13267. PTSDpubs ID: 1560536

http://www.ptsd.va.gov/professional/articles/article-pdf/id1559965.pdf

Shiner, B., Leonard, C. E., Gui, J., Cornelius, S. L., Schnurr, P. P., Hoyt, J. E., . . . Watts, B. V. (2020). Comparing medications for DSM-5 PTSD in routine VA practice. *Journal of Clinical Psychiatry, 81*, Article 20m13244. PTSDpubs ID: 1559965

https://doi.org/10.4088/JCP.20m13233

Spangler, P. T., West, J. C., Dempsey, C. L., Possemato, K., Bartolanzo, D., Aliaga, P., . . . Benedek, D. M. (2020). Randomized controlled trial of riluzole augmentation for posttraumatic stress disorder: Efficacy of a glutamatergic modulator for antidepressant-resistant symptoms. *Journal of Clinical Psychiatry, 81*, Article 20m13233. PTSDpubs ID: 1560381

Take NOTE

Outcomes for unconventional treatments for PTSD

A team led by investigators at Cardiff University carried a systematic review and meta-analyses of non-pharmacological and non-psychological treatments for PTSD, including acupuncture, neurofeedback, transcranial magnetic stimulation, and yoga.

Read the article: https://doi.org/10.1080/20008198.2020.1795361

Bisson, J. I., van Gelderen, M., Roberts, N. P., & Lewis, C. (2020). Non-pharmacological and non-psychological approaches to the treatment of PTSD: Results of a systematic review and meta-analyses. *European Journal of Psychotraumatology, 11,* Article 1795361. PTSDpubs ID: 1559470

Predicting outcomes in psychotherapy for PTSD

Investigators at Cardiff University conducted a systematic review of factors associated with outcomes in 126 RCTs of psychotherapies for PTSD.

Read the article: https://doi.org/10.1080/20008198.2020.1774240

Barawi, K. S., Lewis, C., Simon, N., & Bisson, J. I. (2020). A systematic review of factors associated with outcome of psychological treatments for post-traumatic stress disorder. *European Journal of Psychotraumatology, 11,* Article 1774240. PTSDpubs ID: 1559483

Writing-based therapies for PTSD

A team led by investigators at Australian National University carried out a systematic review and meta-analysis of 13 RCTs of exposure-based writing therapies for full and subthreshold PTSD.

Read the article: https://doi.org/10.1002/jts.22596

Dawson, R. L., Calear, A. L., McCallum, S. M., McKenna, S., Nixon, R. D. V., & O'Kearney, R. (2020). Exposure-based writing therapies for subthreshold and clinical posttraumatic stress disorder: A systematic review and meta-analysis. *Journal of Traumatic Stress*. Advance online publication. PTSDpubs ID: 1559988

CPT followed by behavioral activation shows promise for comorbid PTSD and depression

Although depression is a common comorbidity of PTSD that may affect treatment engagement or outcomes, few studies have examined treatments specifically targeting both conditions. Investigators from Flinders University examined a sequential approach to treating comorbid PTSD and major depressive disorder (MDD) using CPT and behavioral activation (BA), an evidence-based treatment for MDD. Fifty-two community patients (92% women) with PTSD and MDD were randomized to receive CPT alone (n = 18), BA followed by CPT (BA/CPT, n = 17), or CPT followed by BA (CPT/BA, n = 14). CPT-alone included 12 60-minute sessions with 3 optional sessions; the combined treatments contained 5 BA sessions and 10 CPT sessions, with the last 4 CPT sessions extended to 90 minutes to cover the full protocol content. All groups showed large pre-post reductions in PTSD (d = 1.7-2.9) and depression (d = 1.0-1.7), with the largest reductions in both symptoms in the CPT/BA group. At 3-month follow-up, 49% of patients in the CPT/BA group no longer met diagnostic criteria for both PTSD and MDD compared to 18% in CPT-alone and 11% in BA/CPT. Additionally, fewer patients dropped out of CPT/BA (29%) than CPT-alone (56%) and BA/CPT (53%). Although the small sample size of this study limits generalizability, the findings suggest that adding BA after a course of CPT is optimal for treating comorbid PTSD/MDD.

Read the article: https://doi.org/10.1016/j.janxdis.2020.102324

Angelakis, S., Weber, N., & Nixon, R. D. V. (2020). Comorbid posttraumatic stress disorder and major depressive disorder: The usefulness of a sequential treatment approach within a randomised design. *Journal of Anxiety Disorders, 76*, Article 102324. PTSDpubs ID: 1560706

Treatment gains maintained following intensive outpatient program for PTSD

Intensive delivery of EBPs for PTSD is increasingly used in clinical practice, but are treatment gains maintained over time? Investigators from Rush University Medical Center examined outcomes up to 12 months following a 3-week CPT-based intensive outpatient program (IOP) for PTSD. A sample of 209 Veterans with PTSD (63% male) completed the program, which included 13-14 daily sessions each of individual CPT, group CPT, mindfulness-based stress reduction, yoga, and psychoeducation. Veterans completed self-report assessments at posttreatment and at 3-, 6-, and 12- month follow-up. Overall, there were large improvements in self-reported PTSD (d = 1.3) and depression (d = 1.2) from pre-treatment to 12-month follow up. There was a slight symptom increase between posttreatment and 3-months, but no further changes in symptoms between the 3- and 12-month follow-ups. Most participants who completed the follow-up assessments (>85%) reported seeing a mental health provider after the IOP; surprisingly, this did not predict better long-term outcome, which may have been due to limited statistical power. The study was limited by relatively low participation in follow-up (37% at 12-months), so results may not generalize to the larger sample. However, these findings provide preliminary evidence that intensive treatments can provide lasting results for many.

Read the article: https://doi.org/10.1080/20008198.2020.1789324

Held, P., Zalta, A. K., Smith, D. L., Bagley, J. M., Steigerwald, V. L., Boley, R. A., . . . Pollack, M. H. (2020). Maintenance of treatment gains up to 12-months following a three-week cognitive processing therapy-based intensive PTSD treatment programme for veterans. *European Journal of Psychotraumatology, 11*, Article 1789324. PTSDpubs ID: 1559473

Effectiveness of service dogs as PTSD intervention remains unclear

Investigators at Purdue University previously found that Veterans and Service members who received service dogs had greater reductions in PTSD symptoms since applying for their dogs than participants on a waitlist for dogs (see the February 2018 *CTU-Online*). Because the investigators had used the PCL for DSM-IV, they recently sought to examine the effects associated with service dogs on PTSD symptoms assessed with the PCL-5. Participants (N = 186, 74.2% male) had applied for a service dog through a nonprofit that required documentation of PTSD diagnosis by a healthcare provider. The dogs were trained for tasks such as interrupting nightmares and flashbacks. Assignment to a dog was not randomized. Instead, investigators compared PCL-5 scores between 112 participants who had already received a dog (sometime between 2 weeks and 7 years prior) and 74 participants on a waitlist (n = 74). The average PCL-5 score was 14.5 points lower in the service dog group (d = -1.0) after statistical adjustment for demographic factors, but remained above the threshold for clinically significant symptoms (M = 44.3). The results of this cross-sectional comparison are challenging to interpret because of the lack of randomization. Forthcoming results from a VHA-sponsored RCT comparing the impact of service dogs versus emotional support dogs for Veterans with PTSD will be able to provide more definitive information about the effects of service dogs on PTSD.

Read the article: https://doi.org/10.1002/jts.22587

Jensen, C. L., Rodriguez, K. E., & O'Haire, M. E. (2020). Service dogs for veterans and military members with posttraumatic stress disorder: Replication with the PTSD Checklist for DSM-5. *Journal of Traumatic Stress*. Advance online publication. PTSDpubs ID: 1559750

High psychotherapy initiation but low retention among women Veterans with PTSD

Engaging Veterans in therapy is an ongoing challenge (see the April 2019 *CTU-Online*). Women Veterans may face unique barriers to seeking care in largely male-dominated VHA environments. A team led by investigators at Palo Alto University examined data from a nationally representative sample of women Veterans to identify factors associated with their psychotherapy initiation and retention. Participants included 986 women who used VHA primary care and reported interest in mental health services on a treatment preferences survey conducted in 2012. All participants had at least one outpatient visit with a PTSD diagnostic code in the year prior to the study. The investigators linked survey responses to VHA records of participants' outpatient mental health services use in the preceding year. Most women (79.1%) initiated psychotherapy, but only 41.7% of these attended at least 8 sessions, considered a minimally adequate dose. Military sexual trauma histories and comorbid mental health diagnoses were associated with higher session attendance. Receiving treatment that matched a Veteran's preferences (e.g., working with a female provider or in group settings) was also linked to higher retention. In contrast, Veterans who identified as parents attended fewer sessions. These findings suggest the importance of patient-centered care and collaborative decision-making to retain women Veterans in psychotherapy. Addressing specific needs of parents may also be key to enhancing engagement.

Read the article: http://www.ptsd.va.gov/professional/articles/article-pdf/id1556646.pdf

Farmer, C. C., Rossi, F. S., Michael, E. M., & Kimerling, R. (2020). Psychotherapy utilization, preferences, and retention among women veterans with post-traumatic stress disorder. *Women's Health Issues, 30*, 366-373. PTSDpubs ID: 1556646

Proof-of-concept open trial of ketamine-enhanced PE

Using medications to promote mechanisms of action of EBPs for PTSD could enhance the effectiveness of EBPs. In a proof-of-concept pilot study, investigators from the Minneapolis VA Health Care System examined the effect of PE combined with intravenous ketamine on PTSD symptoms in 10 Veterans. Ketamine has been shown to rapidly reduce depressive symptoms, which are associated with poorer response to PTSD treatment, and to enhance extinction learning, a key mechanism of PE. In this uncontrolled trial, Veterans participated in 10 weekly PE sessions, with administration of intravenous ketamine 24 hours prior to the first three sessions. From pre- to post-treatment, there were improvements in PTSD symptoms on both the CAPS-5 (d = 1.2) and PCL-5 (d = 1.8), as well as depressive symptoms measured with the MADRAS (d = 1.4). After controlling for reductions in depression, the change in PCL-5 was retained, but the CAPS-5 change was no longer significant, suggesting that interviewer-assessed changes in PTSD symptoms were explained by changes in depression. Well-powered randomized trials with active control conditions will be needed to isolate the additive effect of ketamine on PE outcomes.

Read the article: http://www.ptsd.va.gov/professional/articles/article-pdf/id1561134.pdf

Shiroma, P. R., Thuras, P., Wels, J., Erbes, C., Kehle-Forbes, S., & Polusny, M. (2020). A proof-of-concept study of subanesthetic intravenous ketamine combined with prolonged exposure therapy among veterans with posttraumatic stress disorder. *Journal of Clinical Psychiatry, 81*, Article 20l13406. PTSDpubs ID: 1561134

Take NOTE
THE COVID-19 PANDEMIC

VHA's response to Veterans' mental health needs during the pandemic

A team led by investigators at the National Center for PTSD review how VHA expanded its use of telemental health care delivery to ensure treatment access for Veterans during the COVID-19 pandemic.

Read the article: http://www.ptsd.va.gov/professional/articles/article-pdf/id1560361.pdf

Rosen, C. S., Morland, L. A., Glassman, L. H., Marx, B. P., Weaver, K., Smith, C. A., . . . Schnurr, P. P. (2020). Virtual mental health care in the Veterans Health Administration's immediate response to coronavirus disease-19. *American Psychologist*. Advance online publication. PTSDpubs ID: 1560361

Delivering intensive treatment for PTSD during the COVID-19 pandemic

Investigators at Rush University detail how they adapted their 2-week, CPT-based IOP for PTSD to be delivered by telehealth. They also describe two case studies of successful treatment.

Read the article: https://doi.org/10.1016/j.cbpra.2020.09.002

Held, P., Klassen, B. J., Coleman, J. A., Thompson, K., Rydberg, T. S., & Van Horn, R. (2020). Delivering intensive PTSD treatment virtually: The development of a 2-week intensive cognitive processing therapy–based program in response to COVID-19. *Cognitive and Behavioral Practice*. Advance online publication PTSDpubs ID: 1560783

Virtual training in Written Exposure Therapy

A team led by investigators at the National Center for PTSD describe a fully virtual facilitated learning collaborative in Written Exposure Therapy and present data on program and patient outcomes.

Read the article: http://www.ptsd.va.gov/professional/articles/article-pdf/id1559248.pdf

Worley, C. B., LoSavio, S. T., Aajmain, S., Rosen, C., Wiltsey Stirman, S., & Sloan, D. M. (2020). Training during a pandemic: Successes, challenges, and practical guidance from a virtual facilitated learning collaborative training program for written exposure therapy. *Journal of Traumatic Stress, 33*, 634-642. PTSDpubs ID: 1559248

Veterans Health Administration

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