GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

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SPOTLIGHT: Is Intensive Outpatient Therapy Better than Massed Outpatient Therapy for Combat-Related PTSD?

Is Intensive Outpatient Therapy Better than Massed Outpatient Therapy for Combat-Related PTSD?

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Massed vs Intensive Outpatient Prolonged Exposure for Combat-Related Posttraumatic Stress Disorder: A Randomized Controlled Trial

Alan LP, Tabatha HB, Edna BF, et al, Massed vs Intensive Outpatient Prolonged Exposure for Combat-Related Posttraumatic Stress Disorder: A Randomized Controlled Trial. *JAMA Netw Open*. 2023; 6(1): e2249422. doi:10.1001/jamanetworkopen.2022.49422.

KEY TAKEAWAY: Both massed and intensive outpatient forms of prolonged exposure therapy are fast and effective for combat-related posttraumatic stress disorder.

STUDY DESIGN: Randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Prolonged exposure (PE) therapy is one of the treatments that have been well studied, showing a significant reduction in combat-related PTSD symptoms. However, 60% of participants continue to meet diagnostic criteria at 6 months follow-up. Intensive outpatient prolonged exposure therapy (IOP) is one of the highest levels of care for PTSD but no previous RCT has evaluated this form of treatment in US military personnel and veterans.

PATIENTS: Deployed veterans and military personnel involved in combat operations

INTERVENTION: IOP prolonged therapy

CONTROL: Massed prolonged therapy

PRIMARY OUTCOME: PTSD symptom severity

Secondary Outcome: PTSD symptom remission

METHODS (BRIEF DESCRIPTION):

- English-speaking members who have experienced at least one deployment-related event and met diagnostic criteria of PTSD and were free from mania, psychosis, substance use, suicidality, or acute psychiatric condition requiring immediate medical attention.
- Participants were randomized to one of the following treatments:
  - Massed prolonged exposure therapy involved 15 therapy sessions of 90 minutes each over three consecutive weeks.
  - Intensive outpatient therapy (IOP-PE) included all the above and an additional 8 treatment augmentations.
- Change in PTSD symptom severity outcome is measured using:
  - Clinician-administered PTSD scale for DSM-5 (CAPS-5): scores range from 0 to 80 with higher scores indicating more severe PTSD.
  - Self-reported PTSD checklist for DSM-5 (PCL-5) at baseline and post-treatment follow-up: scores range from 0 to 80 with higher scores indicating more severe PTSD symptoms.

INTERVENTION (# IN THE GROUP): 117

COMPARISON (# IN THE GROUP): 117

FOLLOW-UP PERIOD: Six months

RESULTS:

Primary Outcome –

- IOP-PE improved PTSD symptom severity from baseline at one month (mean change –14; 95% CI, –16 to –11).
- Massed-PE improved PTSD symptom severity from baseline at one month (mean change –14; 95% CI, –17 to –12).
- Symptom reductions at one month were similar between the two groups.
- IOP- PE reduced PTSD symptom severity (CAPS-5) more than massed-PE at six months (Mean difference 4.4; 95% CI, 0.89–8.0).
  - Utilizing the PCL-5, there was no difference in the reduction of severity of symptoms at six months between the groups.

Secondary Outcome –

- 48% of IOP-PE patients and 62% of massed-PE patients achieved PTSD remission at one month (no statistical measure provided).

LIMITATIONS:

- The patient population may not be a true representation of the entire US population of service members and veterans as they were mostly from Texas.

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Back to Basics: Treatment of Chronic Lower Back Pain

Effect of Medication Optimization vs Cognitive Behavioral Therapy Among U.S. Veterans with Chronic Low Back Pain Receiving Long-Term Opioid Therapy: A Randomized Clinical Trial

Bushey M et al. Effect of Medication Optimization vs Cognitive Behavioral Therapy Among US Veterans with Chronic Low Back Pain Receiving Long-term Opioid Therapy: A Randomized Clinical Trial. *JAMA Netw Open*. 2022;5(11):e2242533. doi:10.1001/jamanetworkopen.2022.42533

KEY TAKEAWAY: Medication optimization of non-opioid pharmaceutical agents significantly reduces pain compared to Cognitive Behavioral Therapy (CBT) in those suffering from chronic low back pain (CBLP). However, medication optimization of non-opioid pharmaceutical agents does not provide a statistically significant change in depressive symptoms.

STUDY DESIGN: Randomized control study

LEVEL OF EVIDENCE: STEP 3 (downgraded due to small sample size)

BRIEF BACKGROUND INFORMATION: Medication optimization of non-opioid pharmaceutical agents and CBT are commonly utilized treatments for (CLBP). Previous studies demonstrated the efficacy of both management plans but have never compared these two treatments to each other. By comparing the effectiveness of medication optimization and CBT in the management of CLBP for patients prescribed long-term opioids, this study provides insight into which protocol may be more beneficial.

PATIENTS: Veterans with CLBP on long-term opioids

INTERVENTION: Psychologist-delivered CBT

CONTROL: Nurse case manager (NCM)-delivered medication optimization

PRIMARY OUTCOME: Pain

Secondary Outcome: Treatment response, disability, pain catastrophizing, alcohol use, opioid misuse, general health and function, depressive and anxiety symptoms

METHODS (BRIEF DESCRIPTION):

- Inclusion Criteria: Veterans 18 years old or older, with CLBP for at least six months of moderate severity (≥5 on 10-point scale) and ≥3 opioid prescriptions of any dosage ≥28 days during the prior 12 months.
- Patients were randomized into two treatment arms:
  - Medical optimization: NCMs delivered algorithm-based analgesic treatment along with opioid management to patients in eight treatment sessions over six months.
  - CBT: Patients received psychologist-led CBT with eight, 45-minute face-to-face or virtual sessions over six months.
- Treatment efficacy was measured by the Brief Pain Inventory (BPI): A validated measure that rates past-week pain severity and pain interference (0– 10 with higher scores representing worse pain; MCID=1).
  - A variety of questionnaires were utilized to measure secondary outcomes.

INTERVENTION (# IN THE GROUP): 130

COMPARISON (# IN THE GROUP): 131

FOLLOW-UP PERIOD: 12 months

RESULTS:

Primary Outcome –

- At the end of treatment, there was no statistically significant difference in pain between CBT and medication optimization (between-group difference –0.46; 95% CI, –0.94 to 0.11).
- At 12 months, patients in the medical optimization group had greater improvements in pain compared to patients in the CBT group (between-group difference –0.54; 95% CI, –1.2 to –0.31).

Secondary Outcome –

- At six and 12 months, there was no statistically significant difference between the two treatment arms in the following attributes: pain-related disability, pain catastrophizing, alcohol use disorders or hazardous drinking, opioid misuse, general health, social function, vitality, depression, or anxiety.

LIMITATIONS:

- There were a small number of participants enrolled in the study thus decreasing the power of the study.
- Generalizability of the study is decreased due to the focus of the study on the veteran population (mostly older males).

- This study was limited by using a two-group design without the use of a “standard care” group, thus inhibiting a true assessment of CBT intervention.
- The length of the study was only 12 months, whereas participants had chronic back pain for 22 years on average. A longer duration of intervention may have a different impact on outcomes compared to this study.

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The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the US Army Medical Department, the Army at large, or the Department of Defense.

Treatment of Glenohumeral Osteoarthritis: Is Endogenous Superior to Exogenous?

Efficacy of Ultrasound-Guided Glenohumeral Joint Injections of Leukocyte-Poor Platelet-Rich Plasma Versus Hyaluronic Acid in the Treatment of Glenohumeral Osteoarthritis: A Randomized, Double-Blind Controlled Trial

Kirschner JS, Cheng J, Creighton A, et al. Efficacy of Ultrasound-Guided Glenohumeral Joint Injections of Leukocyte-Poor Platelet-Rich Plasma Versus Hyaluronic Acid in the Treatment of Glenohumeral Osteoarthritis: A Randomized, Double-Blind Controlled Trial. *Clin J Sport Med*. 2022;32(6):558-566. doi:10.1097/JSM.0000000000001029

KEY TAKEAWAY: A single injection of platelet-rich plasma (PRP) or hyaluronic acid (HA) similarly improves pain and function in patients with glenohumeral osteoarthritis.

STUDY DESIGN: Double-blind randomized controlled trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to small sample size)

BRIEF BACKGROUND INFORMATION: Multiple therapies exist for osteoarthritis (OA) including modified activity, physical therapy, NSAIDs, and corticosteroid injections. If these conservative measures fail in an elderly population, shoulder arthroplasty is recommended; however, arthroplasty has not been as efficacious in patients younger than 50 years old. There has been a recent emergence of HA and PRP injections as treatment options.

PATIENTS: Patients with glenohumeral OA

INTERVENTION: HA injection

CONTROL: PRP injection

PRIMARY OUTCOME: Shoulder pain and disability

Secondary Outcome: Functional shoulder assessment, sleep quality, general well-being

METHODS (BRIEF DESCRIPTION):

- Patients met criteria including >18 years old with identified glenohumeral OA on imaging, >5/10 rating on a pain scale, three months of failure of conservative management trials, and transient relief after anesthetic injection into joint space.
- Patients were randomized between HA and PRP injections.
- Patients, physicians, and outcome assessors were blinded to treatment modality.
- 6 mL of either PRP or HA was injected by a trained physician under ultrasound guidance.
- Patients were assessed based on Shoulder Pain and Disability Index (SPADI), where higher scores indicate greater pain.
- Functional assessments of the shoulder were scored with the American Shoulder and Elbow Surgeons Society-Standardized Shoulder Assessment Form (ASES).
- Sleep quality and general well-being were assessed with an average Numerical Rating Scale (NRS), with higher scores indicating better responses.
- Outcomes were assessed at baseline and again at one, two, three, six, and 12 months post-injection.

INTERVENTION (# IN THE GROUP): 36

COMPARISON (# IN THE GROUP): 34

FOLLOW-UP PERIOD: 12 months

RESULTS:

Primary Outcome –

- HA injections improved pain and disability from baseline to 12 months, but not differently than PRP (mean SPADI score decrease of 16 vs 14, respectively; $P<.05$).

Secondary Outcome –

- Patient function (ASES scores) improved in both the HA group and the PRP group (40 vs 55, respectively; $P<.05$).
- Pain outcomes (NRS scores) improved in both the HA group and PRP group (6 vs 4, respectively; $P<.05$).
- Sleep quality and well-being were unchanged in both HA and PRP groups.

LIMITATIONS:

- The study had a small sample size of 70, thus limiting the power of the study.
- 10 patients underwent surgical intervention but were still included in the final analysis which may have altered the results.
- Most patients had severe OA, limiting generalizability to patients with milder disease.

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Understanding Patient Predispositions in Developing Post-COVID Musculoskeletal Pain

Prevalence and Risk Factors of Musculoskeletal Pain Symptoms as Long-Term Post-COVID Sequelae in Hospitalized COVID-19 Survivors: A Multicenter Study

Fernández-de-Las-Peñas C, de-la-Llave-Rincón AI, Ortega-Santiago R, et al. Prevalence and risk factors of musculoskeletal pain symptoms as long-term post-COVID sequelae in hospitalized COVID-19 survivors: a multicenter study. *Pain*. 2022; Publish Ahead of Print (9). doi: 10.1097/j.pain.0000000000002564.

KEY TAKEAWAY: Chronic musculoskeletal (MSK) disease/pain and the number of hospitalization days during admission are key risk factors associated with developing post-COVID musculoskeletal pain. Additionally, headaches and female sex were secondary risk factors found to contribute to a patient's likelihood of developing post-COVID MSK pain.

STUDY DESIGN: Cohort study

LEVEL OF EVIDENCE: STEP 4 (downgraded due to lack of generalizability)

BRIEF BACKGROUND INFORMATION: As COVID-19 research continues to develop, it is clear the disease affects multiple organ systems, including the MSK system. The purpose of this study is to understand the prevalence of MSK complications post-COVID and understand potential risk factors that would predispose individuals to MSK complications.

PATIENTS: Survivors of COVID hospitalization

INTERVENTION: Not applicable

CONTROL: Not applicable

PRIMARY OUTCOME: MSK pain post-COVID

Secondary Outcome: Risk factors that predispose patients to develop post-COVID MSK pain

METHODS (BRIEF DESCRIPTION):

- Patients were included from five urban hospitals in Madrid, Spain, where information on sex, height, weight, age, COVID-19-associated symptoms, and pre-existing comorbidities was collected.
- A total of 1,969 individuals (46.4% women; average age 61 years old with a standard deviation of 16 years) were included. Specific comorbidities were not listed in the study.
- During a phone interview, patients were asked to quantify and qualify MSK pain through a questionnaire that was developed by a multidisciplinary research team in accordance with the International Association for the Study of Pain. The questionnaire qualified pain based on character, duration, and absence of comorbidities.
- Once data was collected, it was presented as means with paired t-test.

INTERVENTION (# IN THE GROUP): Not applicable

COMPARISON (# IN THE GROUP): Not applicable

FOLLOW-UP PERIOD: Eight months

RESULTS:

Primary Outcome –

- At the time of the evaluation, 887 (45.1%) patients reported musculoskeletal post-COVID pain symptoms.

Secondary Outcome –

- Risk factors for developing post-COVID MSK pain were identified and included the following:
  - Female sex (OR 1.3; 95% CI, 1.1–1.7)
  - History of musculoskeletal pain (OR 1.6; 95% CI, 1.3–1.9)
  - Presence of myalgia with COVID (OR 1.6; 95% CI, 1.2–2.1)
  - Headache with COVID (OR 1.9; 95% CI, 1.3–2.6)
  - Days at hospital (OR 1.01; 95% CI, 1.004–1.02)

LIMITATIONS:

- The limitations of this study did affect overall outcomes in terms of generality since it was only applicable to hospitalized COVID patients.
- The study did not account for ethnic/cultural differences.
- For anxiety and depression, evaluations were scored differently for the Spanish population for unknown reasons. This detail can result in data that may not be comparable with data from other countries.
- Inflammatory labs were not collected to understand if there were already previous underlying musculoskeletal inflammatory or autoimmune diseases prior to getting COVID.

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