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Para-vertebral intramuscular platelet rich plasma vs. subcutaneous ozone injection for chronic low back pain

Abdullah Ahmed Mohammad[1], Hayder Ghali Wadi Algawwam[2]

[1]Al-Mansoor primary health center, Kirkuk, Iraq
[2]Emergency.it ONG Onlus, Sulaymaniyah, Iraq
Correspondence to Abdullah, Mohammed (e-mail: abdullahmohamaad796@gmail.com)
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Objectives This study aimed to investigate the comparison between para-vertebral intramuscular platelet rich plasma and subcutaneous ozone injection for patients with chronic low back pain (LBP).
Methods This is a retrospective study of 102 patients (68 females and 34 males) with severe chronic LBP treated by subcutaneous ozone (O_3) or para-vertebral intramuscular-platelet rich plasma (PRP) in a private clinic in Kirkuk, Iraq over a 2-year period (July 1, 2016–June 30, 2018). A sample of patient's own blood was used to prepare PRP by a process of two repeated centrifugation. Longevity resources EXT50 Ozone Generator with oxygen tank and CGA870 Oxygen Regulator were used. The response to therapy was graded as excellent, good, fair, and poor.
Results The mean age was 52.5 ± 1.5 years. Two-thirds of patients received PRP and one-third received O_3. Three injections were sufficient to get fair, good, and excellent response in all patients managed with para-vertebral I.M PRP injection, while most of the patients (79.4%) treated with subcutaneous O_3 injection required six injections to get such responses. Although 88.2% of patients had at least one co-morbid condition, no patient experienced a poor response in either group.
Conclusion Although O_3 and PRP are inexpensive therapies, they seem to be safe and effective in palliating chronic LBP pain.
Keywords Back pain, pain management, platelets rich plasma, ozone, Iraq

Introduction

Low back pain (LBP) is one of the most common complaints that make patients see their family physicians. Most Americans (<80%) have LBP some day during their life. 15%–20% of them complain from prolonged pain and 4%–8% experience chronic pain. LBP is considered now as the second most common cause of lost work time after common cold.[1]

LBP is defined as "pain and discomfort localized below costal margin above inferior gluteal fold with or without referred pain in lower limbs." According to USA National Health Institute research standards, chronic LBP (CLBP) is defined as a "persistent back pain for at least half the day for three months duration in the past six months."[2]

Now, more attention is being focused on the diagnostic, therapeutic, and prognostic role of lumbar paravertebral muscles in CLBP.[3] Damage to the ligaments is considered in medical literature as the cause of up to 70% of all cases of LBP. Sacroiliac joint ligament injury is the commonest one; it can refer to pain down the lower limbs to posterior thighs and lateral feet simulating sciatica. An analysis was done on 146 of LBP cases showed that 94% of them had ligaments injury. Another similar survey on 124 cases of CLBP showed that 97% had joint instability as a result of joint ligaments weakness. The sacroiliac ligaments were involved in 75% of cases; lumbosacral ligaments in 54% and 50% of these cases had undergone low back surgery as a cause of intervertebral disc problems.[4] An extensive evaluation using Nuclear Magnetic Resonance showed that more than 76% of apparently normal people have intervertebral disc hernias with or without symptoms; so inflammation more than compression seems to be the cause of LBP.[5]

Ozone (O_3) is a form of oxygen in which three atoms of oxygen bind together instead of two. It was discovered in 1834 by Schoenbein. O3 is considered as an oxidant and disinfectant. O_3 acts by inactivation of infective agents and immune system oxygen metabolism stimulation. It has minimum side effects and has reliable results. O_3 can be used in different ways like subcutaneous (SC), intramuscular (IM), intra-articular (IA), intravenous (IV) injections, rectal insufflations, and topical application as well as ozonated platelet rich plasma (OPRP).[6] IM injection of O_2–O_3 gas mixture in paravertebral muscles has been proved as a successful pain management method in treatment of lumbar spine nerve root compression.[7] In 1988, Verga who is a private O_3 therapist noted a good degree of pain relief in patients complaining from myalgias after he did an infiltration to the trigger points with O_2–O_3, he did the injections of gas mixture in paravertebral muscles (Locus Dolendi) corresponding to the metamer of herniated intervertebral disc. This approach is now commonly used by O_3 and pain management physicians and therapists in Italy which is considered as an indirect approach or in other wards (chemical acupuncture).[5]

Platelet rich plasma (PRP) is a biological agent which gained its attractiveness as an adjuvant treatment for musculoskeletal injuries especially in family medicine and sports medicine as a safe and cheap natural physiological method. It is a fractionated volume of plasma of the own patient's blood which contains a platelet concentrate. It was first used in 1987 in open heart surgery, and then used in dental medicine to get fast wound healing in patients with jaw cancer following jaw reconstruction. PRP is also used by physicians to accelerate healing of bone after spinal injury and soft tissue recovery following plastic surgery. In 2009, PRP gained a very wide popularity when it was reported that two of the Pittsburg Steelers received PRP for their ankle injuries before their triumph at the Super Bowl.[8]

The aim of this study is to compare the efficacy of SC O_3 injection of low back trigger points and lumbar paravertebral intramuscular OPRP injection in the palliation of chronic LBP.

Patients and methods

This is a retrospective study of 102 patients (68 females and 34 males) with severe degree of CLBP (>6 months). The diagnosis was based on clinical and imaging (MRI) features. In this study, the authors used a symptom-based patient-directed questionnaire to assess the outcome after O_3 and PRP therapy. The questionnaire was similar to that described by Bhattacharya et al in their study of thoracic outlet compression but slightly modified. The questionnaire asked patients to grade their perception of symptomatic relief using the terms "Excellent" for complete relief of symptoms, "Good" for relief of most major symptoms, "Fair" for relief of some symptoms, but persistence of others and "Poor" for no improvement .

Pain management was done by lower back paravertebral IM injection of PRP or lower back SC infiltration of O_3 in authors private clinic/Kirkuk/Iraq over 2 years period (July 1, 2016–June 30, 2018).

Under aseptic conditions, 60–80 ml of O_3, 12.5 Gamma concentration were injected subcutaneously at trigger points in low back using G30 needle according to Madrid Declaration of ozone therapy,[9] or low back paravertebral IM PRP injections done by numbing the skin with lidocaine 2% using 30G-needle and then using 23 G-needle for deep intramuscular injection first 0.5 ml lidocaine 2% for each point then 0.5 ml PRP also for each point. Time spacing between PRP and O_3 injection sessions was 1 month and 1 week, respectively.

In patients complaining from chronic low backache and radiculopathy treated with O_3, in addition to low back SC injections, trigger points in lumber area, dermatome and pain radiation course were also injected subcutaneously with O_3.

All patients underwent the aforementioned treatment after failure of conservative medical management such as non-steroidal anti-inflammatory drugs, steroids, and physiotherapy.

All patients with tumor, infection like tuberculosis or osteomyelitis, bleeding tendency, patients on anticoagulants, autoimmune diseases, motor deficiency and G6PD deficiency were excluded from the study.

Choosing the treatment approach whether with PRP or O_3 depended on several points:

- Cost (ozone is cheaper than PRP).
- Patient refuse IM paravertebral injection.
- Patients with contraindication to withdrawal of blood like anemia.

Longevity resources EXT50 Ozone Generator (Fig. 1A) with oxygen tank and CGA870 Oxygen Regulator (Fig. 1B) were used. Preparation of PRP was done by withdrawing an autologous blood from the patient's own vein by a 50-ml syringe. The withdrawn blood was then placed in aseptic tubes, each one filled with 9-ml blood and 1-ml 3.8% sodium citrate as an anticoagulant. The tubes were then placed in Electronic Centrifuge 80-2 (Fig. 1C) at 1500 rpm for 10 min separating the sample into three parts; the upper one made of plasma, the middle (Buffy coat) made of white blood cells while the lower part made of red blood corpuscles. The upper two-thirds of plasma were then discarded while the lower third was transferred to another aseptic tube and placed in a centrifuge again. After 15-min centrifugation at 3000 rpm, the upper half of the sample was discarded while the lower half formed the PRP.

Body mass index of the patients was calculated by the equation: Weight in kg/(Height in m)2 and accordingly, the patients were classified as having a healthy body weight (18.5–24.9), overweight (25–29.9), obesity I (30–34.9), obesity II (35–39.9), and obesity III (≥40).[10]

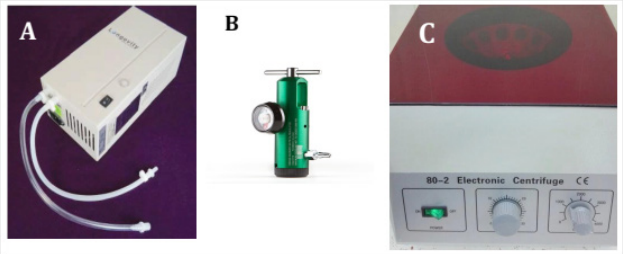

Fig. 1 **(A) Longevity resources EXT50 ozone generator, (B) CGA870 oxygen regulator, (C) 80-2 Electronic Centrifuge.**

Statistical analysis was performed using *z* test for two population proportions.

Results

There were 102 patients (68 females and 34 males) with a female: male ratio of 2:1. The age ranged between 24 and 86 years with a mean of 52.5 ± 1.5. Fig. 2 displays the age and sex distribution of the studied patients.

Most of the patients were in the 5th–7th decades of life (*n* = 62, 60.8%).

Most of the female patients were housewives (*n* = 59, 86.8%) while most males were free workers and government employees (*n* = 33, 97%).

Table 1 shows the co-morbidities encountered in the studied patients.

The top co-morbid condition was obesity as most of the patients (*n* = 86, 84.3%) were either overweight or obese. Hypertension ranked second. Thirty-five patients (34.3%) had hypertension either alone or in combination of other conditions while eighteen patients (17.6%) had diabetes mellitus either alone or in combination of other conditions.

Fig. 4 shows that two-thirds of patients (*n*: 68, 66.7%) were treated by PRP injection while (*n*: 34, 33.3%) one-third treated with O_3.

Fig. 5 shows different degrees of response versus numbers of paravertebral IM PRP injection, three injections were sufficient to get fair, good, and excellent response in all patients

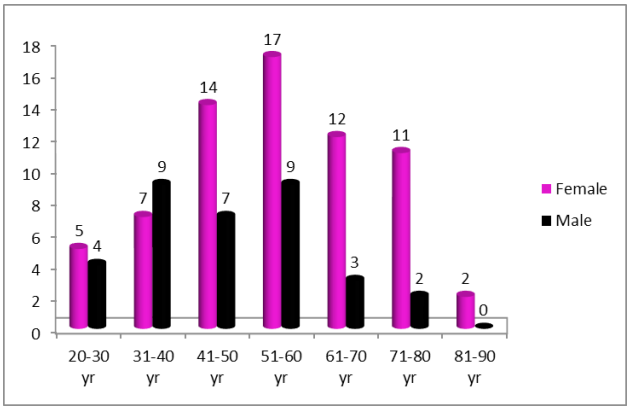

Fig. 2 **Patients age and sex distribution.**

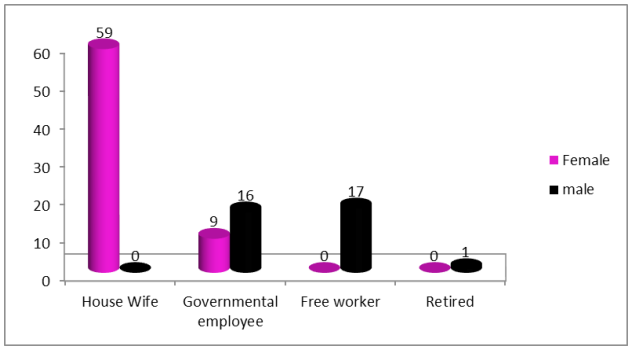

Fig. 3 **Patients job distribution.**

Table 1. **The co-morbid conditions**

Co-morbidity	Sex		Total
	Females	Males	
Overweight or obese	60	26	86
HT	18	4	22
DM & HT	8	2	10
DM	3	2	5
DM, HT & CAD	2	0	2
HT & Asthma	1	0	1
DM, HT & Asthma	1	0	1
CAD	1	0	1
Gall Stones	1	0	1

DM: diabetes mellitus, HT: hypertension, CAD: coronary artery disease.

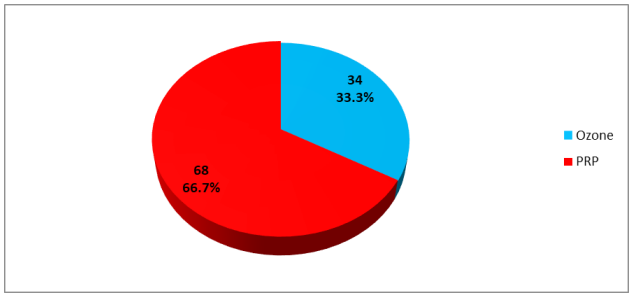

Fig. 4 **Distribution of patients treated with Ozone and PRP.**

(n = 68, 100%) treated with PRP, there was statistically significant difference between the two groups (p<0.01)

Fig. 6 shows different degrees of response versus numbers of SC lower back O_3 injection, most of the patients (n = 27, 79.4%) required six injections to get good and excellent response, there was statistically significant difference between the two groups (p<0.01).

Fig. 7 shows that (n: 60, 88.2%) of patients treated with PRP and (n: 28, 82.4%) of patients treated with O_3 had had at least one co-morbid condition.

Fig. 8 shows different degrees of response to paravertebral IM injection of PRP in lower chronic backache in presence and absence of co-morbidity. Sixty (88.2%) of all patients treated with PRP and showed either fair, good, or excellent response

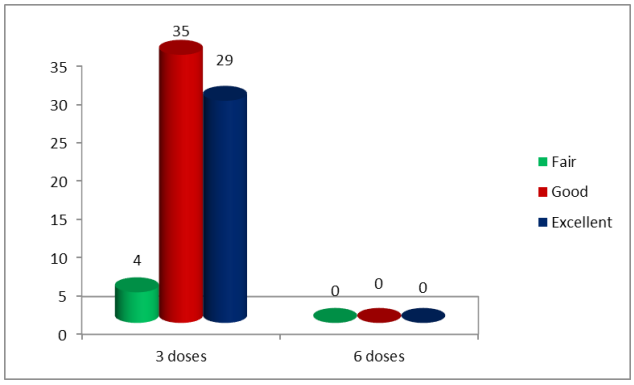

Fig. 5 **Degrees of response with 3 and 6 doses of PRP injections.**

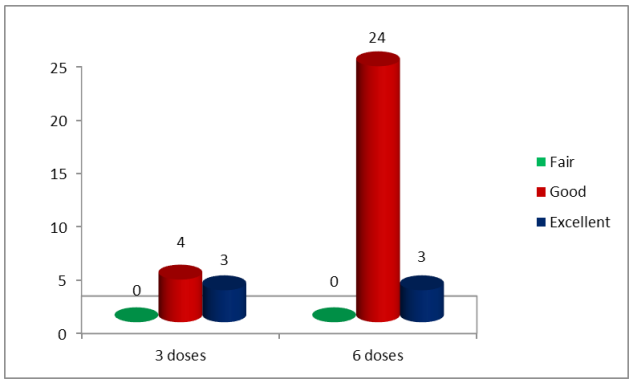

Fig. 6 **Shows degrees of response with 3 and 6 doses of Ozone injections**

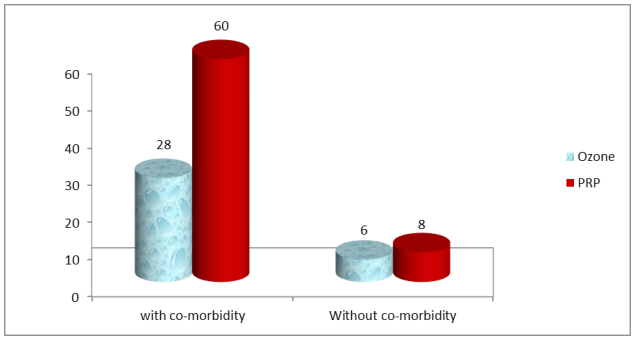

Fig. 7 **Effect of different co-morbidities on response of patients treated with Ozone and PRP injections.**

had had at least one co-morbid condition; there was statistically significant difference between the two groups (p<0.01).

Fig. 9 shows different degrees of response to low back SC O_3 injection in lower chronic backache in presence and absence of co-morbidity. (n = 28, 82.4%) from all patients treated with ozone and showed either fair, good, or excellent response had at least one co-morbid condition, there was statistically significant difference between the two groups (p<0.01).

Discussion

As regards to LBP, it is a very troubling symptom that can affect up to 80% of the world's population. Fortunately, in many cases, conservative physical therapies can resolve the problem. Summarizing, the use of O_3 to treat back pain is worth trying

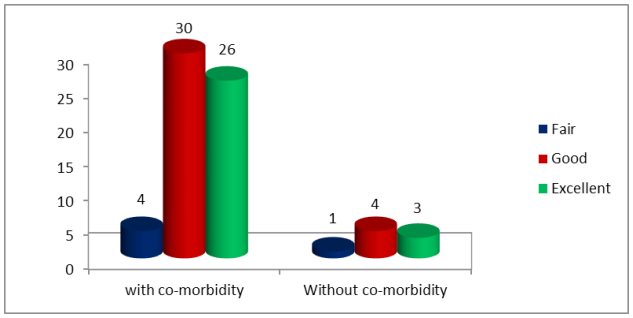

Fig. 8 **Degrees of response of patients with or without a co-morbidity in patients treated with PRP.**

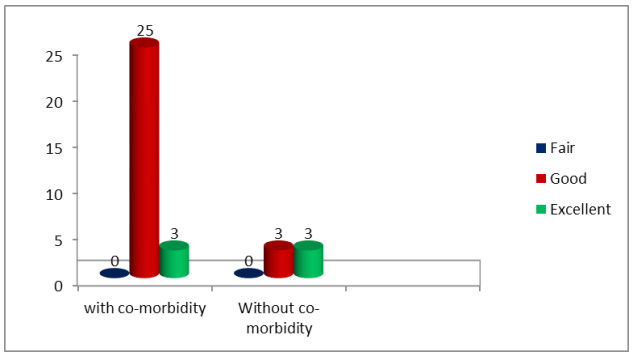

Fig. 9 **Degrees of response of patients with or without a co-morbidity in patients treated with Ozone.**

before surgical intervention. It is becoming widely used worldwide due to its effectiveness, low cost, and safety.[11]

With the wide use of neural prolotherapy, it seems that shifting of focus to the SC nerves as a source of pathology looks to be promising. These SC nerves in a pathological state that can lead to extensive neurogenic inflammation and severe pain.[12] From this point of view, the use of SC O_3 and paravertebral intramuscular PRP in the treatment of CLBP was introduced.

In recent years, PRP injections have gained considerable attention as a treatment method for musculoskeletal conditions due to their safety and ability to potentially improve soft tissue healing. Tissue regeneration in musculoskeletal conditions is achieved by injecting PRP percutaneously. PRP has been effectively used for the treatment of rotator cuff tears, osteoarthritis of the knee, ulnar collateral ligament tears, lateral epicondylitis, hamstring injuries, and Achilles tendinopathy. Yet, there are limited data about its effectiveness in the treatment of LBP.[13]

In this study, most of the patients were in the 5th–7th decades of life, 68 females and 34 males. These findings are similar to the study of Hauser & Hauser4 in which there were 92 females (63%) and 53 males (37%) with an average age of 57.

In this study, about one-third of patients (n = 34, 33.3%) were treated with O_3. Application routes may trigger local, regional, and/or or systemic effects. Muscle pains of different etiologies, especially those related to lactic acid build up and subsequent decrease of local pH, are relieved with O_3. Spinal pains, such as cervical pain and LBP (with or without sciatic pain) are treated with intradiscal, regional SC, paravertebral supralaminar muscular and rectal insuflation O_3 therapy, and by muscle or venous self-hemotherapy.[14]

Follow-up for all patients result and degree of response was done for at least 6 months after the last injection of both PRP and O_3.

Two-thirds of patients (n = 68, 66.7%) were treated by PRP paravertebral muscle injection. This technique was described by many researchers using prolotherapy, dye, and lidocaine.[15–16]

In our study, patients achieved good to excellent pain relief after multiple O_3 injections.[3–6] However, Noci[17] patients could achieve almost total pain relief within 1–2 weeks of injecting the painful area with ozone. The pain relief is attributed to the interaction of O_3 with pain mediators as well as stimulation of antinociceptive apparatus in a way similar to serotonin and endogenous opioids.

In PRP group, 64 patients (94%) achieved good or exellent responses. This success rate was slightly higher than that obtained by Cameron and Thielen[8] who reported 87% success rate in treatment of spinal disc herniation. The healing potential of PRP is attributed in part to its growth factors including Platelet-Derived Growth Factor, Transforming Growth Factor-β1, Insulin-Like Growth Factor, and Vascular Endothelial Growth Factor. These growth factors are associated with repair processes of the central nervous system.[1]

In a pilot study performed on 10 patients in 2016 by Bhatia and Chopra, PRP injections were shown to improve pain.[13] Platelet concentrates had an analgesic effect. This phenomenon was explained by the presence of large amount of serotonin released from the dense granules of the activated concentrated platelets at the injection site.[18] Overall, the improvement of pain, disability, success rate, and patient satisfaction were statistically significant and reached their maximum between 12 and 18 months, then remained stable throughout the follow-up period.[19]

In a summary, the results of this study indicate that paravertebral IM PRP and low back SC O_3 injections is an effective, safe, and cheap treatment method for chronic LBP. All patients treated with PRP (100%) required only three sessions of injections to get fair, good, and excellent response while 79.4% from patients treated with O_3 required six sessions of injections to get good and excellent response. High success rate was attained even with the bad characteristics of patients; being elderly, obese, having severe pain and 85.2% of patients have co-morbidites. The use of PRP and O_3 in CLBP should be encouraged as it may save the patient using costly drugs with adverse effects. Obesity should always be considered as it is the top co-morbidity in CLBP.

Conflict of Interest

None.

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