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Effectiveness of ketamine in chronic low back pain patients

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Abstract

Background: To evaluate effectiveness of ketamine in chronic low back pain patients. **Methodology:** Sixty patients of chronic low back pain of both genders were divided into 2 groups of 30 each. Group I patients were given 25 mg ketamine and group II patients were given 50 mg ketamine as adjunct to 40 mg triamcinolone in total 6 ml volume given epidurally. Pain was recorded using visual analogue scale (VAS). Side-effects were recorded. **Results:** The mean age in group I was 47.2 years and in group II was 48.4 years. The mean weight was 68.3 Kgs in group I and 65.2 kgs in group II. The mean height was 158.2 cm in group I and 154.6 cm in group II. A non- significant difference was observed (P> 0.05). The mean VAS at baseline in group I was 76.3 and in group II was 83.4. At 2 weeks, in group I was 47.2 and in group II was 55.6. At 4 weeks in group I was 45.6 and in group II was 43.7. At 8 weeks in group I was 39.8 and 34.0. At 12 weeks was 34.5 in group I and 33.2 in group II. The difference was non-significant (P> 0.05). Nausea was seen in 4 in group I and 2 in group II. Hallucinations was seen in 8 in group I and 12 in group II. Hypertension was seen in 1 in group I and 4 in group II and tachycardia was seen in 2 in group I and 6 in group II. A significant difference was observed (P< 0.05). **Conclusion:** Ketamine in dosage of 50 mg is effective as compared to 25 mg in chronic low back pain patients.

Keywords: Chronic low back pain, Ketamine, side effects.

INTRODUCTION

Cardiovascular-related deaths are the leading cause of death in the last decades, there has been a growing number of patients being diagnosed with some form of chronic pain. The treatment of chronic pain is based on a trial and error approach with antidepressants, anti-epileptics and opioids as drugs of first choice.[1] Irrespective of treatment, efficacy is limited with just 30–40% of patients showing adequate to good pain relief. The remaining population either displays no effect or responds poorly. Chronic low back pain (LBP), a multifactorial and multidimensional problem with both sensory and emotional components, is challenging to manage.[2] It is one of the leading causes of chronic pain. The most frequent cause of LBP is intervertebral disc pathology, ranging from a ligamental tear to disc degeneration, herniation, protrusion and extrusion. Epidural steroid injection (ESI) acts by multiple mechanisms like anti-inflammatory, antinociceptive, decreased capillary permeability and reduced intra-neuronal oedema.[3]

Based on recent concepts of pain, during inflammation there is an increase in glutamate and aspartate; its role in central sensitization and wind up has been known.[4] Wind up can magnify responses of dorsal horn neurons up to 20- fold in magnitude and duration. NMDA receptor antagonists prevent induction and maintenance of the central sensitization process which is usually manifested as a post injury reduction of pain threshold and hypersensitivity of the withdrawal reflexes.[5] Ketamine is an NMDA receptor antagonist which has potent anesthetic and analgesic effects. Ketamine has been used in pain medicine in recent years with increasing frequency along with multiple publications.6 Considering this, we performed present study to assess the effectiveness of ketamine in chronic low back pain patients.

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METHODS

A sum total of sixty patients of chronic low back pain of both genders were selected. All were informed regarding the study and their written consent was obtained. Ethical clearance was obtained before starting the study.

Demographic profile of patients was recorded. Patients were divided into 2 groups of 30 each. Group I patients were given 25 mg ketamine and Group II patients were given 50 mg ketamine as adjunct to 40 mg triamcinolone in total 6 ml volume given epidurally. Pain was recorded using visual analogue scale (VAS). Side-effects were recorded. The results were compiled and subjected for statistical analysis using Mann Whitney U test. P value less than 0.05 was set significant.

RESULTS

Table 1: Patients distribution.

Parameters	Group I	Group II	P value
Age (years)	47.2	48.4	0.82
Weight (Kgs)	68.3	65.2	0.90
Height (cm)	158.2	154.6	0.64

The mean age in group I was 47.2 years and in group II was 48.4 years. The mean weight was 68.3 Kgs in group I and 65.2 kgs in group II. The mean height was 158.2 cm in group I and 154.6 cm in group II. A non- significant difference was observed (P> 0.05) [Table 1].

Table 1: Comparison of VAS in different interval in both groups

Duration	Group I	Group II	P value
Baseline	76.3	83.4	0.02
2 weeks	47.2	55.6	0.05
4 weeks	45.6	43.7	0.83
8 weeks	39.8	34.0	0.92
12 weeks	34.5	33.2	0.87

The mean VAS at baseline in group I was 76.3 and in group II was 83.4. At 2 weeks, in group I was 47.2 and in group II was 55.6. At 4 weeks in group I was 45.6 and in group II was 43.7. At 8 weeks in group I was 39.8 and 34.0. At 12 weeks was 34.5 in group I and 33.2 in group II. The difference was non- significant (P> 0.05) [Table 2].

Table 3: Assessment of complications

Complications	Group I	Group II	P value
Nausea	4	2	0.04
Hallucinations	8	12	0.01
Hypertension	1	4	0.02
Tachycardia	2	6	0.03

Nausea was seen in 4 in group I and 2 in group II. Hallucinations was seen in 8 in group I and 12 in group II. Hypertension was seen in 1 in group I and 4 in group II and tachycardia was seen in 2 in group I and 6 in group II. A significant difference was observed (P< 0.05) [Table 3].

DISCUSSION

In chronic pains, neuropathic aspect occurs due to NMDA receptor sensitisation at pre-synaptic site resulting in increased glutamate release and its phosphorylation at the post-synaptic site, manifesting as wind up phenomenon.[7] Based on this concept, ketamine, an NMDA receptor antagonist with mild opioid receptor action as well as local anaesthetic properties, has been used in a wide range of doses through epidural and intrathecal routes for acute postoperative and chronic neuropathic pain conditions. There is no single effective drug dose recommended in the above-said trials.[8]

Ketamine is commonly used as an analgesic in emergency medicine and as an adjuvant drug in the perioperative setting. In addition, it is used as a third-line adjuvant drug for opioid-resistant pain in palliative care and for intractable chronic noncancer pain.[9] More recently, ketamine is increasingly being used to treat major depression and other mood disorders.[10] Ketamine was first synthesized in the early 1960s as a safer alternative to phencyclidine. In 1965 its anaesthetic properties were identified. Ketamine is a dissociative anaesthetic that produces profound analgesia and amnesia.[11] Its use in contemporary anaesthesia is limited given the occurrence of a variety of side effects, most importantly the induction of a psychedelic state causing agitation, hallucinations and panic attacks. Although these side effects may be prevented or treated and the availability of alternatives has limited the use of ketamine in anaesthesia.[12] Considering this, we performed present study to assess the effectiveness of ketamine in chronic low back pain patients.

Our results showed that the mean age in group I was 47.2 years and in group II was 48.4 years. The mean weight was 68.3 Kgs in group I and 65.2 kgs in group II. The mean height was 158.2 cm in group I and 154.6 cm in group II. Sigtermans et al.[13] evaluated if the N-methyl-D-aspartate receptor antagonist S(+)-ketamine improves pain in CRPS-1 patients. Sixty CRPS-1 patients (48 females) with severe pain participated in a double-blind randomized placebo-controlled parallel-group trial. Patients were given a 4.2-day intravenous infusion of low-dose ketamine (n=30) or placebo (n=30) using an individualized stepwise tailoring of dosage based on effect (pain relief) and side effects (nausea/vomiting/psychomimetic effects). The primary outcome of the study was the pain score (numerical rating score: 0-10) during the 12-week study period. The median (range) disease duration of the patients was 7.4 (0.1-31.9) years. At the end of infusion, the ketamine dose was 22.2+/-2.0 mg/h/70 kg. Pain scores over the 12-week study period in patients receiving ketamine were significantly lower than those in patients receiving placebo (P<0.001). The lowest pain score was at the end of week 1: ketamine 2.68+/-0.51, placebo 5.45+/-0.48. In week 12, significance in pain relief between groups was lost (P=0.07). Treatment did not cause functional improvement. Patients receiving ketamine more often experienced mild to moderate psychomimetic side effects during drug infusion (76% versus 18%, P<0.001). Treatment with ketamine was safe with psychomimetic side effects that were acceptable to most patients.

Our results showed that the mean VAS at baseline in group I was 76.3 and in group II was 83.4. At 2 weeks, in group I was 47.2 and in group II was 55.6. At 4 weeks in group I was 45.6 and in group II was 43.7. At 8 weeks in group I was 39.8 and 34.0. At 12 weeks was 34.5 in group I and 33.2 in group II. Amr et al.[14] determined the safety and efficacy of adding a multi-day low dose ketamine infusion to oral gabapentin for treating chronic pain related to post spinal cord injury. Forty patients diagnosed with neuropathic pain secondary to spinal cord injury were randomized into 2 equal groups. Group I received an 80 mg intravenous ketamine infusion diluted in 500 cc normal saline over a 5 hour period daily for one week and 300 mg of gabapentin 3 times daily. Group II received a placebo infusion and 300 mg of gabapentin 3 times daily (continued) after 300 mg of gabapentin 3 times daily. Using the visual analogue scale, pain was assessed prior to treatment, daily following ketamine or placebo infusions for 7 days, and then weekly for one month after infusion termination. Side effects, specifically those related to ketamine or gabapentin, were reported. Both groups demonstrated significantly reduced pain scores compared with pre-treatment values (P < 0.05). Group I showed significant pain score improvements over Group II at all measurements

(P < 0.0001) during infusion and 2 weeks after infusion termination. There was no statistical difference between the groups at 3 weeks and 4 weeks after infusion termination (P = 0.54 and P = 0.25 respectively). Both drugs were tolerated by all patients; no side effects required intervention.

Our results showed that nausea was seen in 4 in group I and 2 in group II. Hallucinations was seen in 8 in group I and 12 in group II. Hypertension was seen in 1 in group I and 4 in group II and tachycardia was seen in 2 in group I and 6 in group II. Schwartzman et al.[15] evaluated the effectiveness of intravenous ketamine in the treatment of CRPS. Before treatment, after informed consent was obtained, each subject was randomized into a ketamine or a placebo infusion group. Study subjects were evaluated for at least 2 weeks prior to treatment and for 3 months following treatment. All subjects were infused intravenously with normal saline with or without ketamine for 4 hours (25 ml/h) daily for 10 days. The maximum ketamine infusion rate was 0.35 mg/kg/h, not to exceed 25 mg/h over a 4 h period. Subjects in both the ketamine and placebo groups were administered clonidine and versed. This study showed that intravenous ketamine administered in an outpatient setting resulted in statistically significant reductions in many pain parameters. It also showed that subjects in our placebo group demonstrated no treatment effect in any parameter.

CONCLUSION

Ketamine in dosage of 50 mg is effective as compared to 25 mg in chronic low back pain patients.

REFERENCES

1. Patel, Ghandhi R, Shah A, Bhatt M, Suther A. Comparative study of bupivacaine vs bupivacaine and ketamine (intrathecally) during intraoperative and postoperative analgesia in non PIH cesarean section. Natl J Med Res 2011;1:71-5.
2. Manchikanti L, Pampati V, Boswell MV, Smith HS, Hirsch JA. Analysis of the growth of epidural injections and costs in the Medicare population: A comparative evaluation of 1997, 2002, and 2006 data. Pain Physician 2010;13:199-212.
3. Stoelting RK, Hillier SC. Local anesthetics. In: Brown B, Murphy F, editors. Pharmacology & Physiology in Anesthetic Practice. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2006. p. 90-9.
4. Park CH, Lee SH, Kim BI. Comparison of the effectiveness of lumbar transforaminal epidural injection with particulate and nonparticulate corticosteroids in lumbar radiating pain. Pain Med 2010;11:1654-8.
5. Dualé C, Sibaud F, Guastella V, Vallet L, Gimbert YA, Taheri H, Filaire M, Schoeffler P, Dubray C. Perioperative ketamine does not prevent chronic pain after thoracotomy. Eur J Pain. 2009;13:497–505.
6. Bell RF, Dahl JB, Moore RA, Kalso E. Perioperative ketamine for acute postoperative pain. Cochrane Database Syst Rev. 2006;(1) CD004603.
7. Bell RF, Eccleston C, Kalso E. Ketamine as adjuvant to opioids for cancer pain. A qualitative systematic review. J Pain Symptom Manage. 2003;26:867–875.
8. Juni A, Klein G, Kest B. Morphine hyperalgesia in mice is unrelated to opioid activity, analgesia, or tolerance: evidence for multiple diverse hyperalgesic systems. Brain Res. 2006;1070:35–44.
9. Juni A, Klein G, Pintar JE, Kest B. Nociception increases during opioid infusion in opioid receptor triple knock-out mice. Neuroscience. 2007;147:439–444.
10. Van Dorp E, Kest B, Kowalczyk WJ, Morariu AM, Waxman AR, Arout CA, Dahan A, Sarton E. Morphine-6β-glucuronide rapidly increases pain sensitivity independently of opioid receptor activity in mice and humans. Anesthesiology. 2009;110:1356–1363.
11. Berman RM, Cappiello A, Anand A, Oren DA, Heninger GR, Charney DS, Krystal JH. Antidepressant effects of ketamine in depressed patients. Biol Psychiatry. 2000;47:351–354.
12. Zarate CA, Singh JB, Carlson PJ, Brutsche NE, Ameli R, Luckenbaugh DA, Charney DS, Manji HK. A randomized trial of an N-methyl-D-aspartate antagonist in treatment-resistant major depression. Arch Gen Psychiatry. 2006;63:856–864.
13. Sigtermans MJ, van Hilten JJ, Bauer MCR, Arbous MS, Marinus J, Sarton EY, Dahan A. Ketamine produces effective and long-term pain relief in patients with Complex Regional Pain Syndrome Type 1. Pain. 2009;145:304–311.
14. Amr YM. Multi-day low dose ketamine infusion as adjuvant to oral gabapentin in spinal cord injury related chronic pain: A prospective, randomized, double blind trial. Pain Physician. 2010;13:245–249.
15. Schwartzman RJ, Alexander GM, Grothusen JR, Paylor T, Reichenberger E, Perreault M. Outpatient intravenous ketamine for the treatment of complex regional pain syndrome: a double-blind placebo controlled study. Pain. 2009;147:107–115.