The Egyptian Journal of Hospital Medicine (April 2021) Vol. 83, Page 1330-1337

Efficacy of Adding Calcitonin to Methylprednisolone in Erector Spinae Plane Block for Thoracic Cancer Pain Management

Medhat Mikhail Messeha, Ghada Fathy Al-Rahmawy,
Esraa Yosri Lotfi Kamel, Mostafa Sayed Ahmed Mohammed Elawady
Department of Anesthesiology and Surgical Intensive Care, Faculty of Medicine, Mansoura University, Egypt
***Corresponding author:** Esraa Yosri Lotfi Kamel, **Mobile:** (+20)1285413623, **E-Mail:** snowwhiteey.ey@gmail.com

ABSTRACT

Background: Pain continues to be a very prevalent symptom too often undertreated in cancer patients at all stages of their disease. It is difficult to manage, and patients often show a poor or limited response to analgesic medications or experience intolerable adverse effects.

Objective: The aim of the current work was to compare the effect of adding calcitonin to methylprednisolone versus methylprednisolone alone to local anesthetic in erector spinae plane block for patient suffering from thoracic cancer pain.

Patients and methods: A double-blind study was conducted from November 2019 until November 2020 at Outpatient Pain Clinic, Oncology Center, Mansoura University (OCMU). This study included thirty patients of both sexes and range of ages (30-70 years), with a history of chronic thoracic cancer pain ≥ 4 on a visual analogue scale (VAS) of 0 – 10 and Chronic pain for at least 3 months prior to study entry. Patients were divided into ywo groups, 15 each, Group (I) (methylprednisolone group) and Group (II) (calcitonin group).

Results: Any post block events like nausea, vomiting, respiratory depression (when SpO2 less than 92%) and pneumothorax were recorded. Consumption of analgesics (tramadol 1 – 1.5 mg / kg when needed) during first three months post procedure was measured. Patients of both groups gained benefits from the techniques. The two groups showed decline in the VAS scores and the total tramadol consumption. Calcitonin group has more prolonged duration of pain relief, significant reduction in pain scores, lower tramadol requirements, tolerable side effects.

Conclusion: Patients received calcitonin added to methylprednisolone and local anesthetics had significant reduction in pain scores, more prolonged duration of pain relief, less rescue analgesia (tramadol) consumed and was more satisfied with the treatment modality as compared to methylprednisolone and local anesthetics treated patients in 3 months follow up periods.

Keywords: Cancer pain, Erector spinae plane block, Visual analogue scale, Methylprednisolone, Calcitonin.

INTRODUCTION

Pain continues to be a very prevalent symptom too often undertreated in cancer patients at all stages of their disease. Pain is present in 59% of all patients undergoing cancer treatment, in 64% with advanced disease, and in 33% of patients after curative treatment [(1)].

Neuropathic pain is a common chronic pain condition with many etiologies, including surgery, trauma, and diseases such as herpes zoster, diabetes, and cancer [(2)].

It is notoriously difficult to manage, and patients often show a poor or limited response to analgesic medications or experience intolerable adverse effects [(3)].

Interventional procedures targeting the central and peripheral nervous system are an alternative but the current evidence for their efficacy is limited. In addition, many of the described techniques (e.g., pulsed radiofrequency, spinal cord stimulation, and intrathecal injection of local anesthetic, steroids, and other medications) are invasive, require specialized expertise, and carry the risk of serious complications [(4)].

The ultrasound-guided erector spinae plane (ESP) is a newly described technique for treating thoracic neuropathic pain [(5)]. It is very easy to be performed and has really low rate of side effects [(6, 7)].

Steroid was added to local anesthetic to achieve prolonged pain relief. However, the risks of repeated injections of steroids are well known, so the presence of the other additive added to the steroid to minimize the need for repetition of the block seems to be crucial. Calcitonin-induced analgesia might be attributed to its effects on prostaglandin and thromboxane synthesis, calcium influx, the cholinergic and serotoninergic systems, B- endorphin release, and a direct action on central nervous system receptors [(8)].

The aim of the study was to compare the effect of adding calcitonin to methylprednisolone versus methylprednisolone alone to local anesthetic in erector spinae plane block for patient suffering from thoracic cancer evaluated by analgesic efficacy and duration.

PATIENTS AND METHODS

This prospective randomized double blind controlled study included a total of 30 patients of both sexes and range of ages (30-70) presented with thoracic cancer pain, attending at outpatient Pain Clinic, Oncology Center, Mansoura University (OCMU). This study was conducted between November 2019 until November 2020. Patients were

Received:18 / /2021
Accepted:15 /3 /2021

interviewed and written informed consents were obtained.

Inclusion Criteria: Patients with a history of chronic thoracic cancer pain ≥ 4 on a visual analogue scale (VAS) of 0– 10 and chronic pain for at least 3 months prior to study entry.

Exclusion Criteria: Patients who refuse to participate in the study, patients with bleeding or coagulation disorders, infection at the site of needle entry, psychiatric disorders affecting co-operation of the patient, chest wall deformity and patients with a history of adverse reaction to local anesthetics, steroids, or calcitonin.

The study protocol was explained to all patients. All patients were subjected to history taking, age, height, weight, BMI. Baseline vital parameters were obtained and full medical history was checked. Basic Investigations including complete blood picture, coagulation profile, and liver and renal function tests were checked for any abnormality. General physical and systemic examinations were done. Ten cm Visual Analogue Scale (VAS) for pain assessment was also explained to each patient to be familiar with its use, identifying "0" as no pain and "10" as the worst imaginable pain **(9).** • Basic monitoring with non-invasive arterial blood pressure, electrocardiogram, and pulse oximetry were applied before the procedure, an intravenous catheter (20 G) was inserted in a peripheral line for crystalloid infusion and sedation. Patients were given intravenous midazolam 0.05 mg/kg before the procedure.

Ethical approval and written informed consent:

An approval of the study was obtained from Mansoura University academic and ethical committee.

Randomization: The observer was a senior resident blinded to the randomization who performed all patient assessments and dosages of post procedure analgesics. The interventionist performed the block and was blinded to group assignment or materials used. The randomization was performed using computer – generated randomization software (n indicating the group of the assignment at the time of the first visit to the pain clinic by a chief nurse, who read the number contained in computer – generated randomization software and determined group assignments but did not participate in patients' follow-up. 35 patients were assessed for eligibility. 5 patients were excluded; the remaining 30 patients fulfilling the criteria completed the study. They were randomly allocated into 2 equal groups: **Group I** (control group) (methylprednisolone group) (n=15) received 40 mg methylprednisolone with 10 mL lidocaine 2% using ultrasound at the site of pain and **Group II** (calcitonin group) (n=15) received 40 mg methylprednisolone added to 10 mL of 2% lidocaine plus 50 international units (IU) of calcitonin.

Technique of ultrasound guided erector spinae plane block:

With the patient seated, a scout ultrasound scan using a highfrequency (12–5 MHz) linear transducer probe of MyLabOne / SL3235 ultrasound from Esaote Company was performed to identify and mark the targeted thoracic spine level by counting ribs from above. The skin was strictly sterilized and the transducer was placed in a transverse orientation to identify the spinous process, lamina and transverse process. The tip of the transverse process was centered on the ultrasound screen, and the transducer was rotated 90 degrees into a longitudinal orientation to obtain a Para sagittal view. Depending on the level imaged, 2 or 3 hypo echoic muscle layers could be identified overlying the tip of the transverse processes. From T1 to T5 the erector spinae, rhomboid major and trapezius muscles were visible posterior and superficial to the transverse processes. The rhomboid major muscle has its lower border at the T5 or T6 level, and thus only the erector spinae and trapezius muscles are visible at more caudal levels **(Figure 1)** **(10)**.

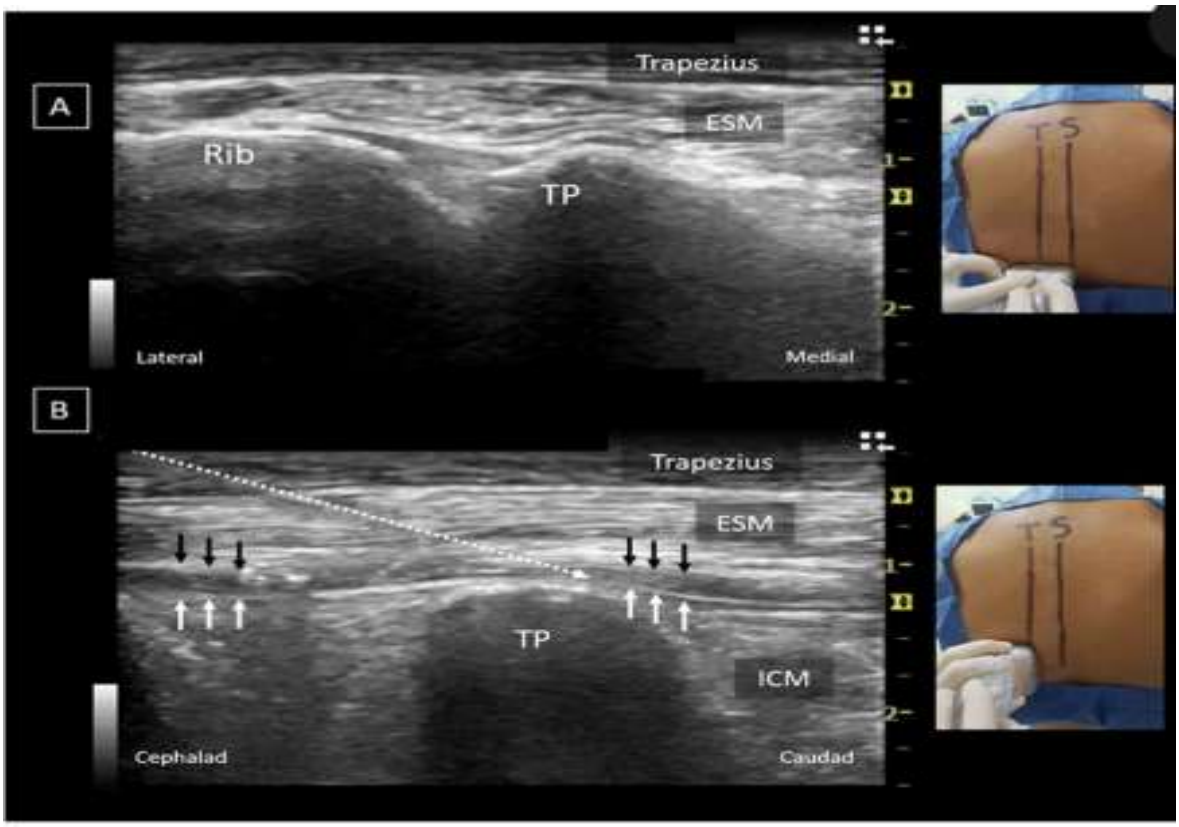

Figure (1): Sonoanatomy and technique of the erector spinae plane (ESP) block. (A) The probe is placed lateral to the spinous processes (line S) to obtain a transverse view of tip of transverse process (TP) and rib with overlying trapezius and erector spinae muscle (ESM). (B) The probe is rotated into a longitudinal orientation to obtain a parasagittal view of the tips of the TPs (line T), and the block needle (dotted arrow) is advanced in a cephalo-caudad direction to contact the TP. Correct needle tip position is identified by linear spread of local anesthetic (solid arrows) deep to ESM and superficial to the TP and intercostal muscle (ICM) [(10)].

An 8-cm 22-gauge block needle was inserted in-plane to the ultrasound beam in a cephalic-to-caudal direction. It was visualized as hyper echoic line. The tip of the needle was placed into the facial plane on the deep aspect of erector spinae muscle between the posterior fascia of erector spinae and the tip of the targeted transverse process. Correct tip position was confirmed by injection of 0.5 mL of 2% lidocaine and visualization of linear fluid spread deep to the erector spinae muscle **(Figure 2) [(10)].**

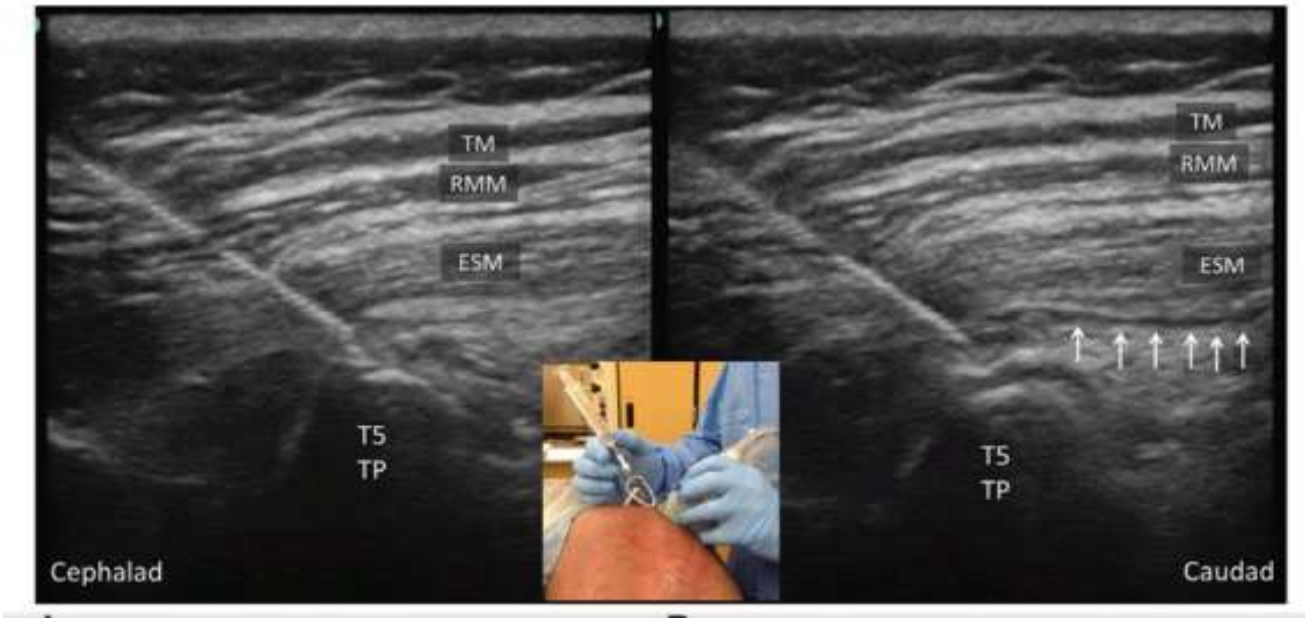

Figure (2): Needle insertion and local anesthetic injection. (The ultrasound-guided ESP block performed deep to the erector spinae muscle (ESM), The probe is in a longitudinal orientation over the tip of the T5 transverse process (TP) and the block needle is advanced in a cephalad-to-caudad direction through the trapezius (TM), rhomboid major (RMM), and ESM to gently contact the TP. Injection into the interfascial plane deep to ESM produces a visible linear pattern of fluid spread (arrows) beneath the ESM) [(10)].

The reduction of systolic blood pressure more than 20% of the basal value or MAP < 60 mmHg was considered hypotension and treated with 250 ml fluid bolus; but if there was no response or MAP was still below 60 mmHg, 5 mg ephedrine was given in boluses. The reduction of heart rate below 50 beats/min was considered bradycardia and was treated by atropine 0.01mg/kg. Signs of potential pleural puncture and pneumothorax were suspected if there were desaturation or diminished air entry following the block and were confirmed by auscultation and chest x-ray.

Evaluation of the erector spinae plane block:

The followings were recorded:

- Onset of the block: was assessed by VAS and perception of paresthesia as 0 (no paresthesia), mild (1–3 points), moderate (4–7 points), severe (8–10 points) based on patient's expression on VAS graded from 0 (no paresthesia) to 10 (maximum intolerable paresthesia) **(11).**
- VAS: range from 0 to 10 (where 0 means no pain and 10 means the worst possible pain) at the onset of the block(T1), 30minutes (T2), 1h (T3) , 24h (T4) , 1week (T5) , 2 weeks (T6) , 4 weeks (T7),8weeks (T8),12weeks (T9) after ESP block. • HR, MAP and SPO2 values were recorded before injection and after 5min, 10 min, 15min, 30 min and 1hour after block.
- Any post block events like nausea, vomiting, respiratory depression (when SpO2 less than 92%) and pneumothorax were recorded. PONV was treated with IV metoclopramide 10 mg.
- Consumption of analgesics (tramadol 1 – 1.5 mg / kg when needed) during first three months post procedure.

Sample size calculation:

After performing a pilot study, the mean ±SD of duration of the erector spinae plane block in decreasing of VAS below 3 in the steroid group was 28.55±7.32 day. Assuming α error 0.05 and β error 0.2 (power = 80%), we needed 13 cases in each group to increase the duration of the ESP block 30%. Allowing 10% drop out, 15 cases were needed in each group.

Statistical analysis

Statistical Package for Social Science (SPSS) IBM program version 26 was used to analyze the recorded data. Any change or difference establishing probability (P) less than 0.05 was remarked statistically significant at 95% confidence interval. Kolmogorov–Smirnov test was used to test the normality of data distribution. For comparison between groups, Qualitative data were tested by Chi-square test. Quantitative parametric variables were tested by unpaired Student-t test, Quantitative non-parametric variables were tested by Mann–Whitney test and The Wilcoxon signed rank test. Data description was in the form of mean ± standard deviation (SD) for quantitative data, and in the form median and range for qualitative data. P value < 0.05 was considered significant.

RESULTS

The study was performed on 30 patients, 26 females and 4 males, whose ages ranged from 30 to 70 years, and with a history of chronic thoracic cancer pain ≥ 4 on a visual analogue scale (VAS) of 0–10 and Chronic pain for at least 3 months prior to study (each group 15 patient) divided to Group (I) (methylprednisolone group) and Group (II) (calcitonin group).

Regarding the results of this study, patients of both groups gained benefits from the techniques. The two groups showed decline in the VAS scores and the total tramadol consumption. Patients in the two studied groups were comparable with respect to the demographic data (age, sex, weight, height, BMI) (Table 1).

There was no statistical difference between the distributions of types of malignancy in both groups (Table 2).

There was no statistically significant difference (p-value > 0.05) between groups regarding mean arterial blood pressure MAP) (Table 3).

According to the VAS, calcitonin group showed statistically significant lower VAS values after 1, 2 and 3 months as compared to methylprednisolone group. Furthermore, calcitonin group showed significant decrease in VAS compared to basal at all assessment interval while methylprednisolone group showed only significant decrease in VAS compared to basal at 30 min, one hour, one day, one week and two weeks (Table 4).

According to patient requirements of tramadol, calcitonin group showed statistically significant lower tramadol requirements after one and two months as compared to methylprednisolone group. Furthermore, methylprednisolone group showed significant decrease in tramadol dose compared to basal at one week, two weeks and one month while calcitonin group showed significant decrease in VAS compared to basal at one week, two weeks and one month and two months (Table 5).

The first analgesic request was longer in calcitonin group with a statistical significance. There was no statistical difference between the incidence of nausea, vomiting and hypotension in both groups (Table 6).

No other complications related to the injection or severe adverse events were observed during the 3-month follow-up period.

Table (1): Demographic data, Data are expressed as mean ± SD or number (%)

Variables		Methylprednisolone group (N=15)	Calcitonin group (N =15)	P value
Age (years)		47.8 ± 5.8	50.5 ± 11	0.422
sex	**Male**	1 (6.7 %)	3 (20 %)	0.598
	Female	14 (93.3 %)	12(80 %)	
Weight (kg)		73.8 ± 9.4	71.8 ± 11.2	0.505
Height (cm)		168 ± 5	172 ± 4.8	0.055
BMI (kg/m^2)		26.15 ± 3.9	24.45 ± 4.7	0.296

Kg kilogram, **cm** centimeter, **Kg/m^2** kilogram per meter square, **BMI** = Body mass index
P probability, **P value** is considered significant if < 0.05

Table (2): Different types of thoracic malignancy in groups. Data are expressed as number (%)

Type	Methylprednisolone group (N=15)	Calcitonin group (N =15)	P value
Breast cancer	11 (73.3%)	10 (66.7%)	0.337
chondrosarcoma	3 (20%)	1 (6.7%)	
osteosarcoma	1 (6.7%)	2 (13.3%)	
Ewing sarcoma	0 (0%)	2 (13.3%)	

P probability **P value** is considered significant if < 0.05

Table (3): Mean blood pressure changes before and after injection in both groups, Data are expressed as mean ± SD

Time	Methylprednisolone group (N=30)	Calcitonin group (N =30)	P value
Before injection	79 ± 10	79 ± 7	0.833
5 minutes	77 ± 11	78 ± 8	0.833
10 minutes	78 ± 11	78 ± 8	0.965
15 minutes	78 ± 11	78 ± 8	0.899
30 minutes	78 ± 12	79 ± 9	0.899
60 minutes	78 ± 11	79 ± 9	0.932

P probability **P value** is considered significant if < 0.05

Table (4): Basal and follow-up values of the VAS score of the studied groups. Data are expressed as median

Time		Methylprednisolone group (N=15)	Calcitonin group (N =15)	P value
Before injection		6 (5 – 8)	6 (5 – 8)	0.778
After	30 min	3 (2 – 5) *	3 (2 – 4) *	0.441
	1 hour	3 (1 – 4) *	2 (1 – 3) *	0.171
	1 day	2 (1 – 3) *	2 (1 – 2) *	0.123
	1 week	2 (1 – 3) *	2 (1 – 4) *	0.539
	2 weeks	3 (2 – 6) *	3 (2 – 5) *	0.555
	4weeks	6 (4 – 7)	4 (3 – 5) *	0.000**
	8weeks	6 (5 – 8)	5 (3 – 6) *	0.000**
	12weeks	7 (6 – 8)	6 (4 – 6) *	0.000**

P probability & P value is considered significant if < 0.05
****** refer to the presence of statistical significance between groups
* refers to the presence of statistical significance between basal VAS and the VAS at the time of assessment.

Table (5): Basal and follow up of analgesic requirements (tramadol dose mg / day) in both groups.

Time		Methylprednisolone group (N=15)	Calcitonin group (N =15)	P value
Before injection		200 ± 107	250 ± 102	0.092
At	1 week	3.3 ± 13*	0 *	0.5
	2 weeks	20 ± 32 *	3.3 ± 13*	0.072
	4 weeks	157 ± 101 *	20 ± 41*	0.000**
	8 weeks	187 ± 91	83± 75*	0.002**
	12 weeks	187 ± 119	197 ± 131	0.357

P probability & **P value** is considered significant if < 0.05
****** refer to the presence of statistical significance between groups
* refers to the presence of statistical significance between basal tramadol requirements and the tramadol requirements at the time of assessment.

Table (6): First analgesic request after the technique, nausea, vomiting and hypotension in both groups.

	Methylprednisolone group (N=15)	Calcitonin group (N =15)	P value
First analgesic request	24 ± 10 day	64 ± 33 day	0.000**
Nausea & vomiting	3 (20 %)	5 (33.3 %)	0.409
hypotension	4 (26.7 %)	2 (13.3 %)	0.361

P probability **P value** is considered significant if < 0.05

****** refer to the presence of statistical significance between groups.

DISCUSSION

Local anesthetics act through sympathetic blockade and vasodilatation, so increasing blood supply, and inhibit neural sensitization and neurotransmitters release. Steroid was added to local anesthetic to achieve prolonged pain relief. It is well-established in chronic pain management, and it can potentially contribute to analgesia through a combination of anti-inflammatory effects, suppression of ectopic discharges from damaged nerves, and modulation of conduction in normal nerves **(12).**

However, the risks of repeated injections of steroids are well known, so the presence of the other additive added to the steroid to minimize the need for repetition of the block seems to be crucial. Calcitonin is a polypeptide hormone regulating the metabolism of calcium in the body. For many years calcitonin has been used to maintain and improve bone mineral density and to reduce the fracture rate. Many studies showed that calcitonin had analgesic role in several painful circumstances **(13).**

To the best of our knowledge, this first controlled trial to compare the efficacy of adding calcitonin to local anesthetic and methylprednisolone versus methylprednisolone alone in erector spinae plane block for patients suffering from thoracic cancer pain.

Regarding the results of this study, patients of both groups gained benefits from the techniques. The two groups showed decline in the VAS scores and the total tramadol consumption in comparison to pre-enrollment values. The current results as regards VAS score can be explained by blocking of the dorsal and ventral rami of the spinal nerves by ESPB **(14).**

As regards **demographic data (**in terms of age, sex, weight, height, BMI**) and type of cancer** there was no statistically significant difference between both groups (P>0.05).

The study included different types of thoracic malignancy such as breast cancer, chondrosarcoma, osteosarcoma, and Ewing sarcoma. There was no significant difference between their distributions in both groups.

Our study revealed that **(calcitonin group) (Group II)** has statistically significant lower VAS values after 1, 2 and 3 months as compared to methylprednisolone group. The median for VAS scores for calcitonin group was 4&5&6 at 1&2&3 months respectively while the median for VAS scores for methylprednisolone group was 6&6&7 at 1&2&3 months respectively.

In agreement with the present study, **Elsheikh and Amr** **(15)** in their prospective Randomized double blind clinical trial. Comparing the effect of adding calcitonin to local anesthetic and methylprednisolone using a modified coronoid approach in management of trigeminal neuralgia pain involving the mandibular and/or maxillary branches founded that a significantly longer duration of effective pain relief was noticed in **group (II)** (calcitonin) compared with **group (I) (**methylprednisolone) (VAS ≤ 3) was noticed in group 2 (34.7 ± 14.2 weeks) compared with group 1 (16.2 ± 12.7 weeks), (P < 0.0004). Four patients did not need repeated blocks in **group (I)** versus 15 in **group (II)**.

This finding is mostly due to the effect of calcitonin on prostaglandin and thromboxane synthesis, calcium influx, the cholinergic and serotoninergic systems, B- endorphin release, and a direct action on central nervous system receptors **(8).**

On the other hand, data indicated that calcitonin is no better than placebo or acetaminophen irrespective of administration mode or outcomes evaluated, according to **Eskola *et al.* (16), Streifler *et al.* (17), Onel *et al.* (18)**; it seemed that if IM calcitonin had some benefits in cases having LSS.

According to patient requirements of tramadol, **group (II)** showed statistically significant lower tramadol requirements after one (20 ± 41 versus 157 ± 101, p value < 0.001) and two months (87± 71 versus 177 ± 98, p value = 0.013) as compared to methylprednisolone group. This result is supported by the results of **Elsheikh and Amr** **(15)** in adding calcitonin to trans laminar epidural steroid in degenerative lumbar spinal canal stenosis whom founded that analgesic consumption was comparable in both groups at 2 and 4 weeks after injection (P > 0.05). It was significantly less in **Group II** from the second month onward (P < 0.0001).

Also, **Elsheikh and Amr** **(15)** in their study comparing the effect of adding calcitonin to local anesthetic and methylprednisolone using a modified coronoid approach in management of trigeminal neuralgia pain founded that carbamazepine requirements significantly decreased in **group (II)** versus **group (1**) at the second, third, sixth, and eighth assessment times. Meanwhile, pregabalin requirements significantly decreased in the same group at the third, fifth, sixth, and seventh assessment times. The values were comparable through other assessments.

The first analgesic request was longer in **group (II) (54 ± 30 day** versus **24 ± 10 day**) with a

statistical significance (p value < 0.001) and this was in agreement with the results of **Elsheikh and Amr [15].**

Takayama *et al.* [19] postulated that the descending serotonergic system is involved in the analgesic effect of calcitonin in post-menopausal states by modifying the expression of serotonin receptors at the central terminals of C afferents. Meanwhile, another study **Ito *et al.* [8]** revealed the presence of a calcitonin receptor-mediated system which might regulate the excitability of primary afferents by activation of calcitonin-induced signals via the calcitonin receptors to control the sodium channel in the dorsal root ganglia neurons. Moreover, this system is silent under normal conditions but becomes active following nerve injury.

Regarding to hemodynamics parameters, the current study showed that the patients had no variations in blood pressure or heart rate after the administration of calcitonin. These findings correlate with **Gabopoulou *et al.* [20].** This is in accordance with **Foster [21] and Azria [22]** who state that this hormone has a vasoregulatory action.

There was no statistical difference between the incidence of nausea, vomiting and hypotension in both groups. No other complications related to the injection or severe adverse events were observed during the 3-month follow-up period in both groups.

Similarly **Terashima *et al.* [23]** reported that there was no serious side effects of calcitonin were observed.

In contrast to the current study, **Elsheikh and Amr [15]** in their study, Effect of Adding Calcitonin to Trans laminar Epidural Steroid in Degenerative Lumbar Spinal canal stenosis founded that transient diuresis for 24 hours was the most common adverse event in the calcitonin group, occurring in approximately 25% of the procedures performed. Nausea was reported in 12 patients. Three patients suffered from persistent vomiting lasting up to 48 hours. They had a good response to antiemetic. Some consideration must be given regarding these side effects. They should be thoroughly evaluated in further studies. However, there were no reported side effects in the steroid group.

In addition, **Ashraf *et al.* [24]** reported that calcitonin may induce significant cancerous effects if administrated by oral or nasal routs for long periods but not after short-term therapy and with a low dose injected calcitonin.

CONCLUSION

It could be concluded that patients received calcitonin added to methylprednisolone and local anesthetics had significant reduction in pain scores, more prolonged duration of pain relief, less rescue analgesia (tramadol) consumed and was more satisfied with the treatment modality as compared to methylprednisolone and local anesthetics treated patients in a 3 months follow up periods.

REFERENCES

1. **van den Beuken-Van Everdingen M, De Rijke J, Kessels A *et al.* (2016):** Update on prevalence of pain in patients with cancer: systematic review and meta-analysis. Pain Symptom Manage, 18: 1070-1090.
2. **Bouhassira D, Lantéri-Minet M, Attal N *et al.* (2008):** Prevalence of chronic pain with neuropathic characteristics in the general population. Pain, 136: 380-387.
3. **Attal N, Bouhassira D (2015):** Pharmacotherapy of neuropathic pain: which drugs, which treatment algorithms? Pain, 156: 104-114.
4. **Dworkin R, O'connor A, Kent J *et al.* (2013):** Interventional management of neuropathic pain: NeuPSIG recommendations. Pain, 154: 2249-2261.
5. **Ramos J, Peng P, Forero M (2018):** Long-term continuous erector spinae plane block for palliative pain control in a patient with pleural mesothelioma. Canadian Journal of Anesthesia, 65: 852-853.
6. **Forero M, Rajarathinam M, Adhikary S *et al.* (2018):** Erector spinae plane block for the management of chronic shoulder pain: a case report. Canadian Journal of Anesthesia, 65: 288-293.
7. **Fusco P, Scimia P, Luciani A *et al.* (2017):** Could the new ultrasound-guided erector spinae plane block be a valid alternative to paravertebral block in chronic chest pain syndromes? Minerva anestesiologica, 83: 1112-1113.
8. **Ito A, Takeda M, Yoshimura T *et al.* (2012):** Anti-Hyperalgesic Effects of Calcitonin on Neuropathic Pain Interacting with its Peripheral Receptors. Molecular Pain, 8: 1744-8069-8-42.
9. **Hawker G, Mian S, Kendzerska T *et al.* (2011):** Measures of adult pain: Visual analog scale for pain (vas pain), numeric rating scale for pain (nrs pain), mcgill pain questionnaire (mpq), short-form mcgill pain questionnaire (sf-mpq), chronic pain grade scale (cpgs), short form-36 bodily pain scale (sf-36 bps), and measure of intermittent and constant osteoarthritis pain (icoap). Arthritis Care Research, 63: 240-252.
10. **Forero M, Rajarathinam M, Adhikary S *et al.* (2017):** Erector spinae plane (ESP) block in the management of post thoracotomy pain syndrome: A case series. Scandinavian Journal of Pain, 17: 325–329.
11. **Sihoe A, Lee T, Wan I *et al.* (2006):** The use of gabapentin for post-operative and post-traumatic pain in thoracic surgery patients. European Journal of Cardio-Thoracic Surgery, 29: 795-799.
12. **Macmahon P, Eustace S, Kavanagh E (2009):** Injectable corticosteroid and local anesthetic preparations: a review for radiologists. Radiology, 252: 647-661.
13. **Yazdani J, Khiavi R, Ghavimi M *et al.* (2019):** Calcitonin as an analgesic agent: review of mechanisms of action and clinical applications. Rev Bras Anestesiol., 69: 594-604.
14. **Chin K, Adhikary S, Sarwani N *et al.* (2017):** The analgesic efficacy of pre-operative bilateral erector spinae plane (ESP) blocks in patients having ventral hernia repair. Anasethesia, 72: 452-460.

15. **Elsheikh N, Amr Y (2016):** Calcitonin as an additive to local anesthetic and steroid injection using a modified coronoid approach in trigeminal neuralgia. Pain Physician, 19: 457-464.
16. **Eskola A, Alaranta H, Pohjolainen T *et al.* (1989):** Calcitonin treatment in lumbar spinal stenosis: clinical observations. Calcified Tissue International, 45: 372-374.
17. **Streifler J, Hering R, Gadoth N (1989):** Calcitonin for pseudoclaudication in lumbar spinal stenosis. Journal of neurology, neurosurgery. Psychiatry, 52: 543-548.
18. **Onel D, Sari H, Dönmez C (1993):** Lumbar spinal stenosis: clinical/radiologic therapeutic evaluation in 145 patients. Conservative treatment or surgical intervention? Spine, 18: 291-298.
19. **Takayama B, Kikuchi S, Konno S *et al.* (2008):** An immunohistochemical study of the antinociceptive effect of calcitonin in ovariectomized rats. BMC Musculoskelet Disord., 15:164-169.
20. **Gabopoulou Z, Vadalouca A, Velmachou K *et al.* (2002):** Epidural calcitonin: does it provide better postoperative analgesia? An analysis of the haemodynamic, endocrine, and nociceptive responses of salmon calcitonin and opioids in epidural anesthesia for hip arthroplasty surgery. Pain Practice, 2: 326-331.
21. **Foster G (1968):** Calcitonin (thyrocalcitonin). N Engl J Med., 279:349–360.
22. **Azria M (1989):** The Calcitonins. Physiology and Pharmacology Karger 1989: Basel; New York: Karger, Pp. 67–130.
23. **Terashima Y, Takebayashi T, Jimbo S *et al.* (2019):** Analgesic effects of calcitonin on radicular pain in male rats. Journal of Pain Research, 12: 223-228.
24. **Ashraf A, Khodadadi M, Sadraei A *et al.* (2015):** The efficacy of intramuscular calcitonin injection in the management of lumbar spinal stenosis. Asian Spine Journal, 9: 75-82.