

given ½ h before the completion of the surgery. At the end, residual neuromuscular block was reversed with neostigmine and atropine. Tracheal extubation was performed based on the standard criteria for extubation.

WI was performed by the primary surgeon who was blinded to the group assignment. After the closure of the fascia, for patients allocated in both groups, the surgeon was asked to infiltrate the wound with a 50 mm in length, 18-gauge needle. The infiltration was performed along the incision with separate injections, with the needle being inserted every 3 cm, at a 45° angle to the skin.

After having completely recovered in postanesthesia care unit, patients were transferred to the Gynecology Ward, where they were observed by the anesthesiologist, who was blinded to the group assignment, for 24 h. Total duration of the study was 24 h from the time of extubation. Pain score was assessed by VAS (0 = no pain and 100 = worst pain). Pain scores were recorded immediately after extubation (taken as 0 h) and after 1, 3, 6, and 24 h later, at rest and after cough, while sedation score was observed at the same hours.

Postoperative analgesia was provided with an IV-PCA pump with 0.5 mg/ml of morphine. The device was set to deliver a 1 mg bolus of morphine IV, with a lock-out period of 7 min, a 4 h limit of 24 mg morphine, and without a continuous background infusion. All patients were given humidified oxygen on nasal cannula with a flow rate of 2–4 l/min for 24 h.

The accumulated data were analyzed using Student's *t*-test, two-way ANOVA (followed by Bonferroni correction), or Mann–Whitney U-test, where appropriate. Differences with $P < 0.05$ were considered as statistically significant.

RESULTS

Study groups were comparable for baseline characteristics (age, gender, weight, and height) and also for type and duration of surgery [Table 1]. Forty-six patients finished the study procedures, while 14 were excluded from the study. Of the latter, ten were excluded because the surgeon decided to proceed with a vertical midline incision, and four of them either needed reoperation or did not comply with the criteria of our study [Figure 1].

The mean value of the 24 h total morphine consumption was significantly lower in the IM group as compared with

the WI group (-27.2% ; 11.33 ± 8.30 vs. 15.56 ± 9.69 mg, as mean \pm SD, respectively). Moreover, the morphine consumption was consistently, but not significantly, lower in the IM group as compared to the WI group, at all examined time points (1 h: -29.3% ; 3 h: -8.9% ; 6 h: -19.3% ; 24 h: -40.1%).

The VAS pain scores after cough [Figure 2] and at rest [Figure 3] demonstrated no significant differences between the two study groups. However, the median sedation scores achieved after the IM administration of pethidine were consistently lower than those after the administration of the drug through WI [Figure 4]. However, only at 6 hrs after the operation did the WI group exhibited a statistically significant higher sedation score ($p < 0,05$), compared to the one reported for the IM group [Figure 4].

Finally, it should be noted that a similar number of patients developed nausea and vomiting in the gynecology ward and that all patients recovered well and were discharged, without any complications or wound infections (28% vs. 48%, 16% vs. 5% in WI group and IM group, respectively).

DISCUSSION

This study investigates the analgesic effects of a meticulous surgical site infiltration technique with pethidine in patients undergoing TAH through a Pfannenstiel incision. According to pethidine pharmacokinetic principles, IM injection was considered to have a duration of action of at least 4–6 h. Our results indicate that compared to IM administration, postincisional subfascial wound infusion of pethidine does not provide better postoperative analgesia or decreased morphine consumption and lower pain scores in a statistically significant manner as reported in previous studies in relevant literature. One of the strengths of our study is that we included a well-recognized multimodal regimen, such as acetaminophen and parecoxib, in combination with an opioid with well-proven local anesthetic properties.^[8,10,21]

Local infiltrative analgesia with local anesthetics is an established method of providing postoperative analgesia. It is suggested that the mechanism involved blocks the transmission of pain due to activation of voltage-dependent sodium channels,^[9] and furthermore, sensitization of nociceptive receptors reduces the release of inflammatory mediators causing pain.^[24,25] A recent study has shown the efficacy of WI during total abdominal hysterectomies, reducing the opioid requirements during the first postoperative 24 h,^[26] and another one^[27] has confirmed its suggested mechanism in abdominal surgeries using a neuroanatomical approach. Moreover, Jabalameli *et al.* found that subcutaneous administration of pethidine or tramadol, compared to bupivacaine, had an opioid-sparing effect after cesarean section.^[28] Söderlund *et al.* featured pethidine as an effective alternative to local anesthetics during intra-articular administration in joint-knee surgery, and these results were consistent with a previous study of Ekblom *et al.* evaluating pain in arthroscopies comparing prilocaïne to pethidine.^[18,29] Moreover, apart from the efficacy

Table 1: Demographic data, duration, and type of surgery in the performed study

	WI group (n=25)	IM group (n=21)	t-test comparison (P)
Age (years)	42.4 (7.9)	46.2 (10.2)	>0.05
Weight (kg)	70.8 (11.5)	67.3 (8.4)	>0.05
Height (cm)	166.4 (7.7)	161.9 (8.4)	>0.05
Duration of the operation (h: min)	1:27 (0:28)	1:49 (0:45)	>0.05

WI: Wound infiltration, IM: Intramuscular

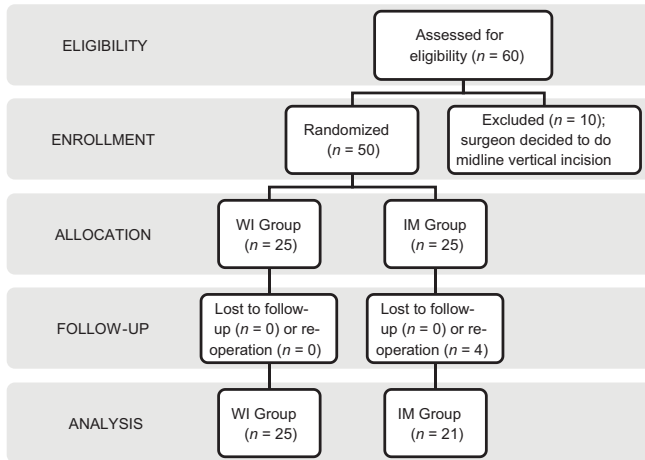


Figure 1: Flowchart of the recruitment procedure followed, where patients in the wound infiltration group received pethidine intrafascially (0.5 mg/kg in a 15 ml saline syringe and a simultaneous intramuscular injection of 2.5 ml of normal saline), whereas the intramuscular group received an intramuscular injection of pethidine (0.5 mg/kg intragluteally in a solution of 2.5 ml and a simultaneous injection of 15 ml of normal saline intrafascially)

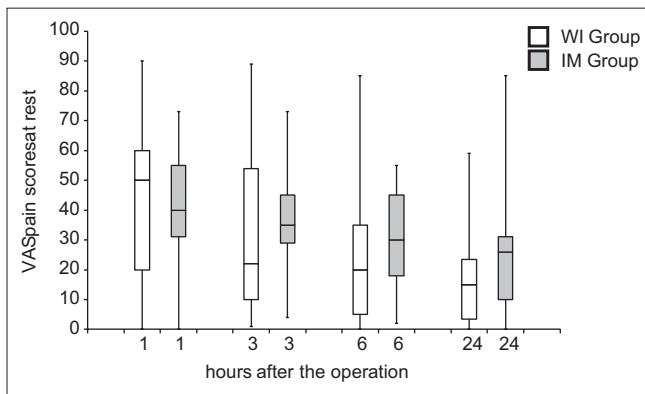


Figure 3: Box plots with visual analog scale pain scores at rest over the 24 h postoperative period after arrival in the gynecology ward. Data are presented as median visual analog scale with 25th to 75th percentiles (box) and range (whiskers)

of pethidine during IV regional anesthesia,^[13,30] more recent studies demonstrate its usefulness, as a sole agent, in achieving a successful transversus abdominis block during laparoscopic cholecystectomy.^[31]

The outcomes of this study are not in consequence with previous research on the local analgesic efficacy of pethidine. It has been analyzed that reduced pain scores could be attributed to its analgesic effects, mostly by systemic absorption and interaction with peripheral opioid receptors, whereas the duration of its analgesic effect up to 24 h could only be explained due to its local anesthetic properties.^[31,32] Moreover, there are several studies evaluating the local analgesic efficacy of pethidine, especially in achieving peripheral blocks. Onutu *et al.* showed that WI analgesia using pethidine exerts a postoperative analgesic effect in patients undergoing total hip arthroplasty, mostly by blocking voltage-dependent sodium

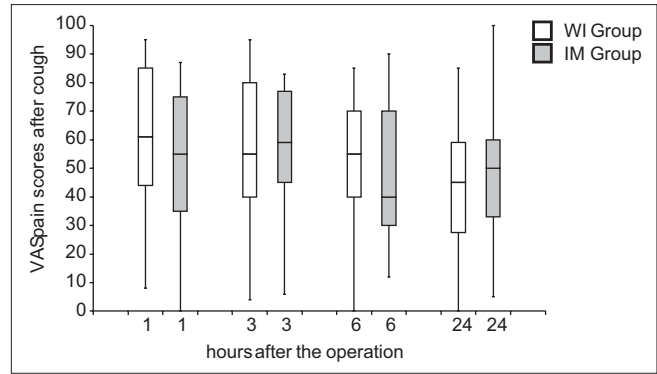


Figure 2: Box plots with visual analog scale pain scores after cough over the 24 h postoperative period after arrival in the gynecology ward. Data are presented as median visual analog scale with 25th to 75th percentiles (box) and range (whiskers)

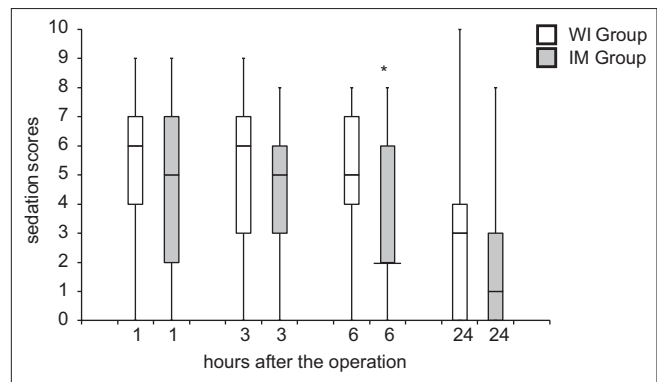


Figure 4: Box plots with sedation scores (scale 0–10) over the 24 h postoperative period after arrival in the gynaecology ward. Data are presented as median sedation scores with 25th to 75th percentiles (box) and range (whiskers). **P* < 0.05

channels on the nerve endings and also by interacting with μ - and δ -opioid receptors.^[23] Furthermore, Oztürk *et al.* showed that perineural administration of pethidine blocked both sensory and motor conduction in a dose-dependent way, thus when pethidine concentration was reduced from 2% to 1%, the degree of regional block achieved was reduced considerably.^[10]

Of note, there is one study describing the failure of pethidine in WI to reduce postoperative pain after laparoscopic tubal ligation.^[33] The result was attributed probably to the dose of pethidine administered, and to the fact that the visceral pain described from the patients was more dominant, compared with the pain related to the wound in the trocar insertion, where the infiltration was performed. Toward that direction, Klein *et al.* along with Cobby and Reid found that WI with a local anesthetic had no opioid-sparing effect after abdominal hysterectomy, with morphine consumption being identical between the two groups for the first 24 h period.^[21,34]

This study has several limitations. First, we did not consider the extent of surgical incision as an important factor affecting postoperative pain intensity or even duration. However, all surgeries were performed by the same surgical team,

so we hypothesized that it was unlikely that the WI group had received different surgical infiltration approaches since the analgesic solution was injected in the peritoneal layers following the same pattern.

There might be also concerns regarding the “optimal” dose of pethidine that we decided to deliver to each group. Previous studies examining the efficacy of pethidine as a local anesthetic solution infiltrated postoperatively into the surgical wound, commonly use a solution of 1%, even in surgeries where the incision is much smaller and more superficial than those concerning the abdominal cavity. For example, WI with 1% pethidine after uncemented total hip arthroplasty revealed an opioid-sparing effect for the first 24 postoperative h, whereas other studies showed that when the concentration of pethidine is reduced from 2% to 1%, the efficacy of the block declines.^[23]

As far as sedation score is concerned, we decided not to evaluate the sedation effect of opioids according to the validated Ramsay Sedation Scale, although it is a more established method. This had to do with the fact that it was more convenient for our patients, in the postoperative period with residual anesthesia, to respond to this 0–10 numeric scale.

Finally, our observations were limited to the first 24 h of the postoperative period. Thus, we did not examine the implications of our analgesic interventions on our patients as far as early ambulation and discharge from the hospital are concerned or even the development of chronic neuropathic pain.

CONCLUSIONS

Our study with the intrafascial WI of 0.5 mg/kg pethidine, as a part of a multimodal analgesia regimen in patients undergoing TAH under general anesthesia, showed that morphine consumption was consistently, but not significantly, lower in the IM group as compared to the WI group, at all examined time points. In a matter of clinical importance, the results of our study were not in accordance with previous studies. Further investigation may be required to examine whether a higher dose of pethidine must be employed to exert its local anesthetic properties.

Acknowledgments

The authors gratefully acknowledge the assistance of nursing staff during the various phases of this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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