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Randomized controlled trial of morphine in elderly patients with acute abdominal pain

Akut karın ağrısı olan yaşlı hastalarda morfinin randomize kontrollü bir çalışması

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BACKGROUND

The objective of this study was to determine the clinically important change in diagnostic accuracy and physical examination in the morphine *vs.* placebo group.

METHODS

Subjects were randomized in a 1:1 ratio to receive a single dose intravenous morphine or placebo in a blinded fashion. Primary outcome measure was to determine if there was a clinically important change in diagnostic accuracy and physical examination in the morphine *vs.* placebo group.

RESULTS

80 subjects (39 were assigned to morphine and 41 to placebo) were included in the final analysis. Clinically important diagnostic accuracy rate was found to be 80% in the morphine group (31/39) and 78% in the placebo group (32/41), with a difference rate of 2% (95% CI -7% to 13%, p=0.9802. There was a statistically significant change in abdominal rigidity finding (15%) in morphine group in all of the abdominal physical examinations findings; however there was no change in placebo group (0%). The difference between two groups was also statistically significant (95% CI 2.3% to 30.5%, p= 0.031).

CONCLUSION

Administration of opioid analgesia is safe and does not seem to impair clinical diagnostic accuracy in elderly patients with acute undifferentiated abdominal pain. Nevermore, opioids may change the physical examination findings such as abdominal rigidity.

Key Words: Analgesia/pain control; clinical assessment; emergency departments.

AMAÇ

Bu çalışmanın amacı, morfin ve plasebo gruplarındaki klinik olarak önemli tanısal doğruluk ve fizik muayenedeki değişiklikleri belirlemektir.

GEREÇ VE YÖNTEM

Hastalar 1:1 oranında kör olarak morfin veya plasebo almak için randomize edildi. Çalışmanın birincil takip verisi, morfin ve plasebo gruplarındaki tanısal doğruluk ve fiziksel incelemede klinik olarak önemli değişiklikler olup olmadığını belirlemektir.

BULGULAR

Seksen hasta (39 morfin ve 41 plasebo) çalışmaya dahil edildi. Klinik olarak önemli tanısal doğruluk oranı morfin grubunda %80 (31/39), plasebo grubunda %78 (32/41) ve %2'lik bir fark oranı saptandı (güven aralığı [GA] %95, -7% ile 13%, p=0,9802). Morfin grubundaki hastaların tüm fiziksel inceleme bulguları içinde sadece abdominal rijidite bulgusunda (%15) istatistiksel olarak anlamlı değişiklik saptandı, ancak plasebo grubunda herhangi bir değişiklik (%0) yoktu. İki grup arasındaki fark anlamlı idi (GA %95, %2.3 ile %30.5, p=0.031).

SONUÇ

Bu çalışma ile acil serviste opioid analjezi uygulanmasının güvenli olduğu ve akut nonspesifik karın ağrısı olan yaşlı hastalarda klinik olarak önemli tanısal değişikliğe neden olmadığı, fakat hastalarda abdominal rijidite gibi önemli fiziksel inceleme bulgularını değiştirebileceği sonucuna varılmıştır.

Anahtar Sözcükler: Analjezi/ağrı kontrolü; klinik değerlendirme; acil servis.

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Analgesia before surgical consultation has traditionally been an area of controversy and was withheld until a definitive diagnosis was established for fear of masking the symptoms, changing physical findings or ultimately delaying diagnosis and treatment of a surgical condition.[1]

Recent studies and systematic reviews have shown that administration of opioid analgesics in adult patients with undifferentiated acute abdominal pain, prior to making a decision and while the diagnostic process was underway, did not increase the risk of inadequate treatment decisions and may have significantly improved patient comfort when compared with a placebo.[2,3]

Elderly patients who have undifferentiated acute abdominal pain require careful, timely evaluations and aggressive management because of the high risk and subtle presentations of serious pathologic conditions.[4,5] The evidence supporting the use of analgesia in the elderly with undifferentiated acute abdominal pain is limited and based on clinical experience.

The objective of this study was to determine if there is a clinically important change in the diagnostic accuracy and physical examination in the morphine vs. placebo group.

MATERIALS AND METHODS

Study Design

In this single-center, prospective, randomized, double-blind, placebo-controlled clinical trial, elderly patients with undifferentiated acute abdominal pain were divided into two groups, receiving either intravenous morphine or placebo.

Study Setting

Study participants were recruited from the emergency department (ED) of a tertiary-care university hospital with an annual census of approximately 80,000 adult visits. Both local and central government ethics committees approved the study protocol and all subjects provided written informed consent. Subjects presenting to the ED between April 1, 2009 and December 31, 2009 on weekdays between 08:00 a.m. and 24:00 p.m., the interval covering the shifts of two attending emergency physicians in the ED, were enrolled into the study.

Selection of Participants

Elderly (65 years or older) patients with non-traumatic undifferentiated acute abdominal pain of less than 48 hours' duration were included in the study. Participants were required to have an undifferentiated acute abdominal pain and report either "mild" or greater pain intensity on a four-point verbal rating scale (VRS) or at least 20 mm on a 100 mm visual analogue scale (VAS). Exclusion criteria included known allergy or contraindication to morphine or any opioid analgesic, hemodynamic instability (systolic blood pressure <100 mmHg), and use of any analgesic within six hours before ED presentation; patients who refused to participate in the study, who were uncooperative with respect to the VAS, who had isolated flank pain or previous study enrollment, and those with known renal, pulmonary, cardiac or hepatic failure were also excluded.

Interventions

Subjects were randomized in a 1:1 ratio to receive a single dose intravenous morphine (0.1 mg/kg in 100 ml normal saline) or placebo (100 ml normal saline) in a blinded fashion. The randomization schedule, constructed with a random numbers table, was prepared before the beginning of the study by an assistant blinded to the study. Treatment allocation assignments were contained in sealed and labeled envelopes and placed into a box. When the treating physician decided to include a patient into the study, the study nurse drew an envelope from the box randomly and premixed the study drug. A second nurse blinded to the study administered the prepared drug to the patient and recorded the previously labeled drug number on the study form.

Methods of Measurements

After enrollment, emergency residents gathered basic demographic information of participants using a standardized data collection form. Subjects reported pain intensity on both a 100 mm VAS (bounded by "no pain" and "worst pain") and a four-point VRS (no, mild, moderate, or severe pain) immediately prior to receiving the study drug, and at 30 minutes after drug administration. Subjects were blinded to their prior reports. Before receiving the study drug, the first attending ED physician evaluated the patient's history, signs of acute abdomen (abdominal tenderness, abdominal rigidity and rebound tenderness) and determined the three most likely diagnoses for that patient. At that time, study drugs were given as bolus infusion in five minutes. Thirty minutes after drug administration, a second attending ED physician on the same work shift who was blinded to the patient and to the first attending physician's possible diagnosis, evaluated the patient's history, signs of acute abdomen (abdominal tenderness, abdominal rigidity and rebound tenderness) and determined the three most likely diagnoses for that patient. The quantification of abdominal signs was stated as present, absent or debatable. The preliminary diagnosis provided by the second physician was made without access to any laboratory or radiographic information in order to minimize diagnostic suspicion bias. After receiving the preliminary diagnosis, if the patients were judged to have inadequate pain relief at 30

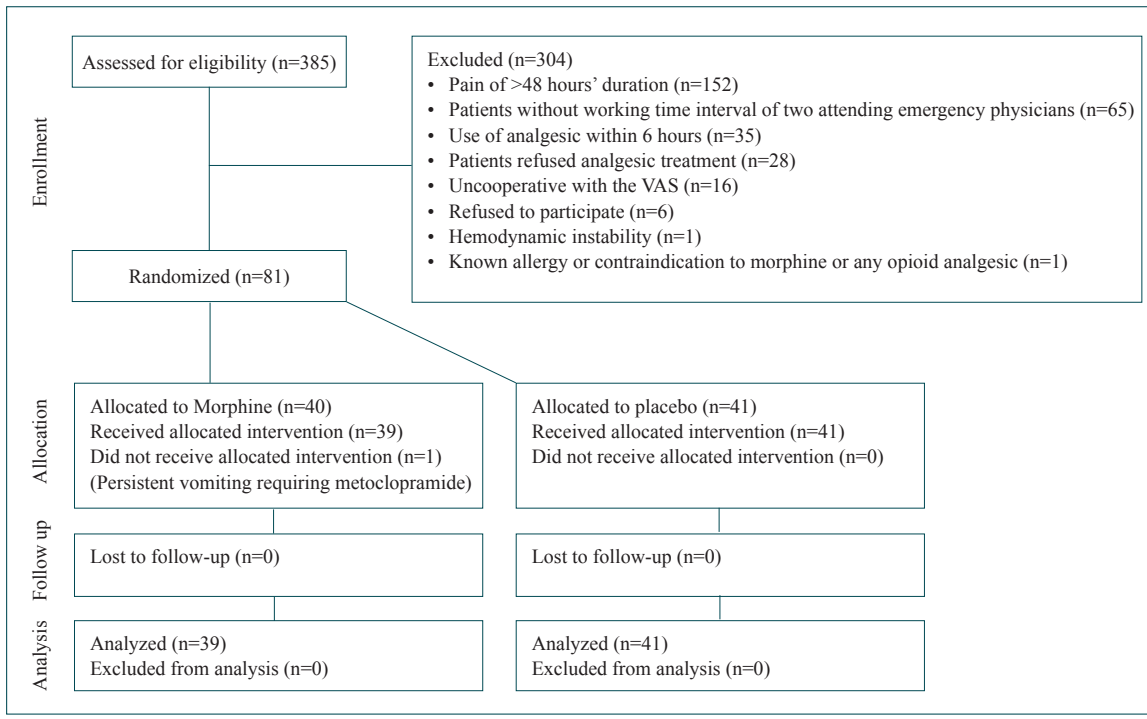

Fig. 1. CONSORT diagram, patient flow chart.

minutes, they received rescue drugs such as additional analgesia, proton pump inhibitors, or any other agents deemed appropriate by the first physician treating the patient. The first attending ED physician had no role in determining the diagnostic accuracy. Reports of adverse events were collected spontaneously and categorized as nausea/vomiting, altered mental status, dizziness, hypotension, headache, allergy/pruritus, urinary retention, ventilation failure, and dry mouth. Any additional adverse events were noted as "other" and described on the case report form.

A research assistant performed a retrospective medical chart review, recording results of all diagnostic tests, and contacted all subjects by telephone to determine if anyone had a surgical intervention or hospital readmission, had undergone a diagnostic or therapeutic medical procedure, or was consulted to another physician. Final diagnosis was obtained through follow-up at least four weeks after their index ED visit and determined by a convincing radiological or pathological diagnosis, response to medical or surgical intervention, or spontaneous resolution according to the patient's physician, medical records, or patient self-report.

Outcome Measures

Our primary outcome measure was to determine if there was a clinically important change in diagnostic accuracy or physical examination in the morphine vs. placebo group. Our secondary outcome measures were to evaluate the analgesic effectiveness and safety of intravenous morphine vs. placebo, the need for rescue drugs at 30 minutes, the presence of at least one adverse event, demographic features, and final diagnosis of the patients.

After follow-up information was obtained and patient data were recorded on the Statistical Package for the Social Sciences (SPSS) data chart, two coauthors (a general surgeon and an emergency physician) blinded to the study collaboratively determined the clinically important diagnostic accuracy and change in physical examination. Any disagreement between the preliminary and final diagnosis that might be expected to have an adverse effect on the patient's general status was defined as a clinically important diagnostic error. If coauthors decided an instance of diagnostic error as clinically important, this was coded "diagnostic discordance" for statistical analysis. When the preliminary diagnosis was determined as accurate or not different from the final diagnosis, this was coded as "diagnostic accuracy" for statistical analysis. Diagnostic accuracy was determined between the second attending physician's preliminary diagnosis and final diagnosis of the patients.

Data Analysis

All statistical analyses were performed using SPSS version 15.0 for Windows and MedCalc for Windows, version 9.3.0.0 (MedCalc Software, Mariakerke, Belgium). Continuous variables were expressed as mean±standard deviation and categorical variables as percentage. Frequent variables were expressed as rates. Comparison of two independent groups was performed by Student t-test while the related com-

parison of two groups was performed by paired t-test for continuous variables. Related comparison of two groups was performed by McNemar test for categorical variables. Kolmogorov Smirnov test was used in order to analyze the distribution of the data as normal or abnormal. To detect a difference of 20 mm with an 80% power and a two-sided level of significance, 37 patients were needed for each group. All the hypotheses were constructed as two-tailed and the critical alpha value was accepted as 0.05.

RESULTS

Three hundred and eighty-eight consecutive patients were assessed for eligibility, and 304 patients met one of the exclusion criteria and one patient was not included into the analysis because of protocol violation (Fig. 1). Ultimately, 80 subjects were included into the final analysis: 39 assigned to morphine and 41 to placebo.

Characteristics of Study Subjects

The mean age of the study subjects was 73±7 and 46% (n=37) of them were male. The subject groups appeared to be well-matched for baseline characteristics and diagnostic study results. Demographic features of the study groups are shown in Table 1.

Main Results

The baseline pain intensity was similar in the morphine (75.3±22 mm) and placebo (68.6±28.5 mm) groups. The mean reduction in pain intensity at 30 minutes was statistically significant in both groups: 31.6±29.7 mm in morphine group (p<0.0001; 95% confidence interval [CI] 41.2 to 22.0), and 18.8±28.6 mm in placebo group (p=0.0001; 95%CI -27.8 to -9.7), but the difference between the two groups had a borderline statistical significance (12.8 mm, 95%CI -25.8 to 0.1; p: 0.0529) (Table 2, Fig. 2a, b).

The accuracy of the final diagnosis by the second physicians was similar in both groups (80% *vs.* 78%; 2%, 95%CI: -7% to 13%; p=0.9802, respectively).

The abdominal tenderness in the physical examination did not decrease significantly in either group (8%, 95%CI: -3.2% to 7.7% *vs.* 8%, 95%CI: -5.3 to 12, respectively).

Although the reduction in abdominal rigidity was 15% (95%CI: -5.8 to 29.9; p=0.17) in the morphine group, abdominal rigidity increased 5% (95%CI: -13 to 20.4; p=0.77) after the placebo infusion. The difference in reduction rates between the two groups was statistically significant (d: 15%, 95%CI: 2.3% to 30.5%; p= 0.031).

Rebound tenderness also decreased in the morphine group (13%, 95%CI -7.62 to 27.3, p=0.266); however, as in abdominal rigidity, the rebound tenderness rate was higher after placebo infusion (10%, 95%CI: -7.5 to 21; p=0.34), and the difference between the two groups was 13% (95%CI: 0.7% to 27.4%; p=0.05) with a borderline statistical significance (Table 3).

Forty-three patients (53.7%) were discharged from the ED, and 37 patients (46.3%) were hospitalized. Of

Table 1. Demographic features of the study groups

	Morphine (n=39)	Placebo (n=41)	*p*
Age (mean±SD)	73.3±7.2	73.1±7.9	0.90
Gender			
Female	21 (53.8%)	22 (53.6%)	0.99
Male	18 (46.2%)	19 (46.4%)	
Hypertension	21 (53%)	21 (51.2%)	0.87
Diabetes mellitus	10 (25.6%)	11 (26.8%)	0.95
History of an operation	11 (28.2%)	18 (43.9%)	0.64
History of CAD	8 (20.5%)	2 (4.9%)	0.048
Vital Signs			
Systolic blood pressure	144±24	135±25	0.07
Diastolic blood pressure	79±13	74±12	0.07
Pulse/min	83±13	84±16	0.83
Fever ◦C	36.6±0.6	36.3±0.4	0.001
Respiratory rate/min	18±2	17±2	0.52
Pulse oximetry	98±2	98±2	0.47
Diagnosis			
Abdominal US	19 (48%)	17 (41%)	
Abdominal CT	12 (31%)	8 (20%)	
Surgical intervention	2 (5%)	0	
Plain radiography	3(8%)	1 (2%)	
Follow-up	10 (26%)	7 (17%)	
Endoscopy	0	1 (2%)	

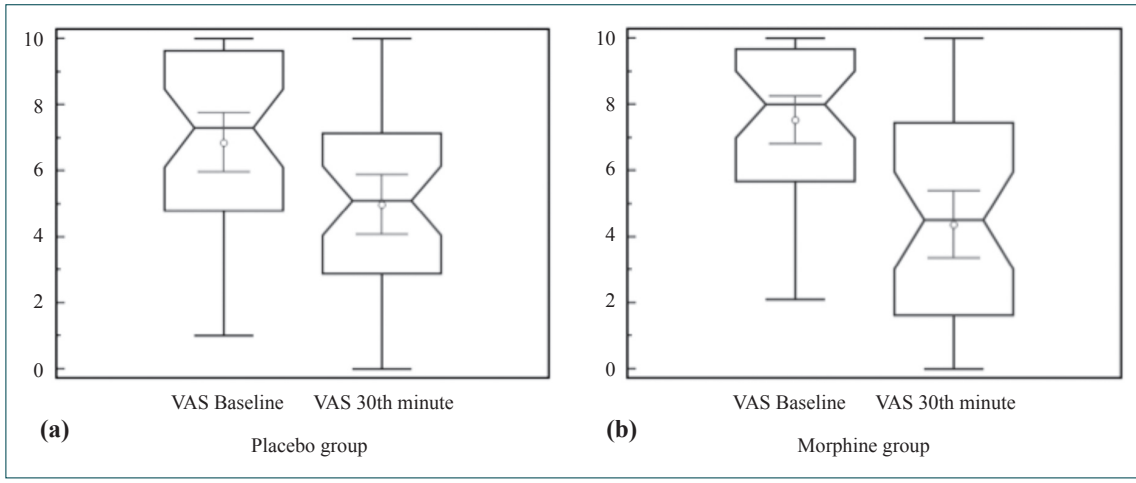

Fig. 2. **(a, b)** Box and whisker plot of the mean reductions in pain scores at the 30th minute after the treatment. The midlines of the boxes represent the medians and the outline of the boxes represents interquartile ratios. The thin lines inside the boxes are for the 95%CI of the means. The lines above and below the boxes show the minimum and maximum values of each group.

the 37 patients, 15 (20%) were operated and 3 died. The most common diagnosis was biliary tract disease followed by dyspepsia and small bowel obstruction (Table 4). Five (12.8%) patients in the morphine group and 4 (9.7%) in the placebo group were hospitalized within the 15-day follow-up after ED discharge (d: 3%, 95%CI: -12 to 18; p: 0.68).

Although none of the study patients complained of serious side effects, the incidence of side effects was higher in the morphine group, with lack of statistical significance (28% vs. 12%, d: 16%, 95%CI: -4 to 36, respectively; p=0.10) (Table 5).

The need for rescue drug did not differ significantly between groups (46% *vs.* 54%; d: 8%, 95% CI: -15 to 30; p=0.62). The satisfaction was better in the morphine group (70.3±28 mm *vs.* 44.7±31.3; d: 25.5,

Table 2. The mean reductions in pain intensity in the two groups

VAS Scores	Morphine	Placebo
Initial VAS Score±SD	75.3±22.1	68.6±28.5
30th minute VAS Score±SD	43.6±31.4	49.8±28.6
Mean Reduction in VAS Score±SD	-31.6±29.7	-18.8±28.6
95% CI	-41.2 to -22.0	-27.8 to -9.7
p value	<0.0001	<0.0001

SD: Standard deviation; VAS: Visual analogue scale; CI: Confidence interval.

Table 3. Changes in physical examination and diagnostic accuracy after the study drug administration

Physical examination findings before and after study drug administration	Morphine group difference within group (95% CI)	Placebo group difference (95% CI)	Difference between two groups (95% CI)
Abdominal tenderness	100% *vs.* 92% d: 8% (-3.2 to 7.7) p=0.25	98% *vs.* 90% d: 8% (-5.3 to 12) p=0.375	0% (-15 to 14) p=0.68
Abdominal rigidity	51% *vs.* 36% d: 15% (-6 to 30) p=0.17	34% *vs.* 39% d: 5% (-13 to 20.4) p=0.77	15% (2.3 to 30) p=0.03
Rebound tenderness	38% *vs.* 25% d: 13% (-7.6 to 27.3) p=0.26	19% *vs.* 29% d: 10% (-7.5 to 21) p=0.34	13% (0.8 to 28) p=0.05
Diagnostic accuracy	80%	78%	2% (7% to 13%) p=0.9802

Table 4. Final diagnosis, surgical interventions and rehospitalization of the study patients

Final diagnosis	Morphine	Placebo
Biliary tract disease	9	7
Small bowel obstruction	3	9
Acid-peptic disease	5	7
Nonspecific abdominal pain	4	6
Renal colic	2	4
Diverticulitis	2	1
Gastroenteritis	3	2
Acute coronary syndrome	3	0
Appendicitis	1	1
Incarcerated inguinal hernia	2	0
Splenic infarction	1	0
Ovarian disease	1	0
Psoas hematoma	0	1
Hepatic cyst hydatid	0	1
Malignancies	0	1
Pancreatitis	0	1
Right heart failure (hepatic congestion)	1	0
Urinary tract infection	2	0
Surgical intervention	8 (20.5%)	7 (17%)
Rehospitalization	5 (12.8%)	4 (9.7%)
	d: 3%, 95%CI: -12 to 18 p=0.68	

95CI%: 12.3 to 38.8; p=0.0003).

Limitations

This study had several limitations that should be mentioned. We chose to remove patients from analysis if they required rescue analgesics within the first 30 minutes of the study and if their final diagnosis was unclear. In retrospect, we should have planned an intent-to-treat analysis; however, one patient was excluded from the analysis because of protocol violation.

Some adverse effects such as nausea and vomiting may be related to the abdominal pathology rather than the study drug. Although we collected adverse effect data, we did not assess the likelihood that the adverse effect could be attributed to the study drug at the time of data collection. In addition, we did not weigh our subjects and relied on self-report of weight to calculate morphine doses. It is possible that the doses used were based on poor weight estimates; however, we suspect such errors were small and randomization should minimize any impact on study outcomes.

Another limitation was the lack of interobserver consistency at the beginning of the study. Although this can be thought to cause differences between the physicians evaluating the study patients, the parameters of the physical examinations detected in the study were routine and classical findings that all physicians learn similarly in their clinical practice; thus, we did not feel that interobserver consistency was necessary for this study. Nevertheless, future researchers can consider this fact before beginning their studies.

The time interval between the first and second examinations was also a limitation. We determined an interval of 30 minutes, which may not have been adequate to demonstrate physical examination differences for some patients. New studies with different time intervals or with multiple examination repeats in different time frames can give more information on this point.

The final limitation was the lack of a standardized algorithm for evaluating the patients in the study. In fact, there is no universal algorithm for acute abdominal pain as found for acute coronary syndromes.

All of the attempts applied to the patients were convenient, scientific and academic interventions necessary for their final diagnosis.

We designed a placebo-controlled trial to assess the clinically important change in diagnostic accuracy and physical examination in the morphine *vs.* placebo group. We preferred to use normal saline solution as placebo, as it was colorless and easy to find and prepare. Furthermore, it is essential to use a placebo for designing this kind of study. The use of placebo was not an unethical method because administering placebo could improve subjective and objective outcomes in up to 30-40% of patients with a wide range of clinical conditions beyond the pain.[6] Thus, it is the patient's perceptions of effective treatment that reduce pain or pain behavior. As a result, pain scores may decrease in the placebo group as well as the intervention group. In our study design, study medication or placebo was administered and then patients were given 30 minutes to achieve pain relief. This methodology was similar

Table 5. Comparison of side effects between the two groups

Side effects	Morphine (n, %)	Placebo (n, %)	Difference % (95% CI)	*p*
Nausea and vomiting	5 (12.8%)	2 (4.9%)	8 (-5 to 21)	0.23
Hypotension	1 (2.6%)	0 (0%)	2.6 (-2 to 7)	0.30
Headache	1 (2.6%)	1 (2.4%)	0.1 (-7 to 7)	0.97
Fatigue	4 (10%)	2 (5%)	5 (-6 to 17)	0.40
Total	11 (28)	5 (12)	16 (-4 to 36)	0.10

to that of most previous studies, which have allowed for reassessment of parameters in as early as 15 to 30 minutes. If the patients were judged to have inadequate pain relief at 30 minutes, they then received rescue drugs such as additional analgesia, proton pump inhibitors, or any other agents deemed appropriate by the first physician treating the patient. Intervention time was finished at 30 minutes after the study drug administration. The Institutional Human Studies Committee believed strongly that a study period should not exceed one hour because of the potential dangers of opioid administration and also the need for patients to be able to be "off protocol" relatively quickly so they could receive analgesia as clinically indicated.

DISCUSSION

The use of analgesia for acute abdominal pain in emergency departments has been debated for many years. Because of the concerns about masking important physical examination findings or ultimately delaying diagnosis and treatment of a surgical condition, analgesics were withheld in undifferentiated abdominal pain patients. This concept used to be useful and valid in the past when the medical science and diagnostic modalities were limited and mostly invasive. However, in today's advanced era, with different and noninvasive diagnostic modalities, alleviating the pain with opioid analgesics instead of leaving patients in distress for long periods is more humanitarian and rational.

According to our study results, morphine administration to relieve acute abdominal pain in patients over 65 years of age may change physical examination findings such as abdominal rigidity and rebound tenderness, but only the change in abdominal rigidity was statistically significant. Despite the change in the physical examination findings, the final diagnosis of the patients was not changed significantly. In light of the above, morphine administration for pain relief to patients over 65 years of age with acute abdominal pain can be applicable. However, the fact that physical examination findings can change with analgesia should not be forgotten, and further diagnostic tests with high sensitivity and specificity should be ordered for precluding diagnostic errors in patient management.

There have been various previous reports in the literature about administrating opioid analgesia for abdominal pain. The outcome measures for these studies vary; however, many of them analyzed diagnostic accuracy, management decisions, pain measurements, adverse events, and changes in physical examination findings. In 1992, Attard et al.[7] conducted a study with papaveretum and measured pain scores, patient comfort and diagnostic accuracy. Since the study subjects were patients with significant abdominal pain who were admitted to the hospital, the results cannot be adapted to ED patients entirely. Nevertheless, as the action of papaveretum is similar with opioids, the study is worthy for showing no significant negative effects of opioids on diagnostic accuracy. In 1999, Vermeulen et al.[8] considered morphine versus placebo in the ED patients who were suspected of acute appendicitis, and the diagnostic accuracy was found to be 89% in the morphine group and 91% in the placebo group. Although the selected patient population of the study impeded the generalization of the results, which the authors of the study determined was a limitation, the strong pain relief and both the patient and physician comfort and satisfaction with morphine streamlined the study results. Similar to these results, Gallagher et al.[3] found high patient comfort in their study, and concluded that morphine administration relieved pain and raised patient comfort without clinically significant diagnostic changes. In correlation with the results stated above, we found high patient satisfaction and pain relief without diagnostic errors in the present study.

Despite the belief regarding changes in the physical examination, this variable was reported in only four studies.[9-12] Pace and Burke[9] conducted the first randomized double-blind controlled trial with adequate allocation concealment in ED patients with acute abdominal pain in 1996 and concluded that morphine did not lead to any diagnostic error or physical examination alteration. Contrary to these results, physical examination findings changed in the present study, but did not lead to any diagnostic error. In 1997, Lo Vecchio et al.[10] randomized 48 patients admitted to the ED with acute abdominal pain and measured changes in the physical examination and adverse events. A statistically significant change in the physical examination was noted in both groups receiving analgesics; however, the diagnostic accuracy between the preliminary and final diagnosis was not different, and the authors concluded that no adverse events or delays in diagnosis could be attributed to the administration of analgesics. Although the heterogeneity of the study population and the disparity in groups decreased the power of the statistical analysis, as the authors concluded was a limitation, the concordance in diagnostic accuracy rates between the groups was expressive and similar to those of the present study. Furthermore, the changes in physical examination findings were similar to those determined in the present study. In another study, the changes in physical examination signs were not statistically significant and diagnostic accuracy was unchanged.[11] These results were similar with the present study. Mahadevan et al.[12] randomized 66 ED patients suspected of acute appendicitis with right lower quadrant (RLQ) pain equally to tramadol or

placebo in their double-blind controlled trial in 2000 and measured the presence and absence of seven abdominal signs (tenderness on light and deep palpation, tenderness in RLQ and elsewhere, rebound, cough, and percussion tenderness) before analgesic and 30 minutes after analgesic. The difference between the groups was not statistically significant (RR: 1.27 (95%CI: 0.68 to 2.38).

As was to be expected and compatible with the literature mentioned above, abdominal rigidity and rebound tenderness findings differed and decreased in the morphine group in the present study. Furthermore, both abdominal rigidity and rebound tenderness findings increased in the placebo group. Rational explanations for the increase would be the progression of the clinical signs by the time of the second examination or failure to meet the patient's expectations regarding the alleviation of pain in the waiting period. The statistically significant decrease in abdominal rigidity finding should withhold administering morphine analgesics. On the other hand, the decline in abdominal rigidity in the morphine group could minimize the voluntary rigidity, thus improving the diagnostic process and facilitating the physician's decisions. The unchanged diagnostic accuracy between the morphine and placebo groups can be considered supporting evidence for the latter opinion. Nevertheless, it is clearly known that whether opioid analgesics are used or not, the diagnostic process in elderly patients with abdominal pain is problematic and complicated and needs the greatest attention.

In conclusion, the findings of the present study about diagnostic accuracy are parallel with the literature in adult and pediatric patients. Nonetheless, opioid administration to the elderly with acute abdominal pain has not been studied before. Early administration of opioid analgesia is safe and does not seem to impair clinical diagnostic accuracy in elderly patients with acute undifferentiated abdominal pain. Nevertheless, opioids can change physical examination findings such as abdominal rigidity.

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