Pentazocine Pain Relief in Adult Patients With Acute Abdominal Pain: A Prospective Randomized Clinical Trial.

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Background: Reported studies in the African population, on early pain relief in patients with acute abdominal pain are few. The objective of the study was to evaluate the effect of pentazocine (PZ) on pain relief, diagnostic accuracy and treatment decisions in patients with acute abdominal pain. Methods: This was a prospective randomized clinical trial undertaken at the emergency department, Federal Medical Centre, Abeokuta. Seventy adult patients with acute abdominal pain were randomized to receive equal volumes intravenously, normal saline, (control group) or pentazocine 30mg (PZ group). Pain was measured with a standard 0 – 100mm Visual analogue scale (VAS). Pain score, diagnosis and treatment decision were recorded before and 60minutes after the injection. A VAS score change > 12mm was considered as clinically significant. Outcome measures were the differences in these parameters between the two study arms. Results: Twenty patients in the PZ group and 9 patients in the control group had a VAS score drop >12mm. This difference is statistically significant. (X^2= 6.56: p <0.02). In two patients pentazocine interfered with correct diagnosis and treatment. The initial decision to operate was deferred. Conclusion: Pentazocine provided analgesia in patients with acute abdominal pain. Its administration caused delay in correct diagnosis and treatment in some patients.

Introduction

Reports of studies conducted in the Caucasian population and a critical appraisal of the aggregate weight of information contained in clinical trials published in the English literature suggest that early administration of analgesia to patients with acute abdominal pain is safe [1,2, 3,4,5,6.] One study reported some adverse outcomes in some patients[7].However, in spite of these publications, evaluation of attitudes and practices of general surgeons in the United Kingdom and the United States of America in 1999 revealed that 38- 67% believed that analgesia risks masking diagnostic findings [8].

In the African population there are additional challenges faced by patients and doctors. These challenges include difficult access to, or non-availability of, narcotic analgesics in most of these countries, a scarcity of modern diagnostic tools and qualified medical specialists. Studies on this subject of early pain relief in adult patients with acute abdominal pain in the African population are few. We therefore decided to investigate the safety of early administration of pentazocine in adult patients with acute abdominal pain.

Patients and Methods

In this study, a clinical trial was designed to determine whether pentazocine administration achieved significant pain relief compared to a placebo, and whether pentazocine administration to patients with acute abdominal pain resulted in changes in physical findings, diagnostic accuracy and treatment decisions. Pentazocine was chosen because morphine is not readily available in most hospitals in the country. Pentazocine is an opioid analgesic, less potent than morphine. It acts by binding to opiate receptors in the central nervous system causing inhibition of ascending pain pathways thereby altering the perception of, and response to pain. Following intravenous injection, onset of action is 2-3 minutes and duration of action is 2-3 hours. Pentazocine is approved for use as an analgesic throughout the world. Its side effects include hypotension, dizziness, nausea and vomiting. It may be used as a premedication prior to anaesthesia.

This was a prospective randomized double blind placebo controlled trial that compared the effect of administration of 30mg of intravenous pentazocine against placebo (equal volume of 0.9%saline) on Emergency Department(ED) patients with acute abdominal pain (AAP). Endpoint measures were, pain relief, and changes in physical examination findings, diagnostic accuracy, and treatment decisions. The study was conducted in the emergency department of the Federal Medical Centre Abeokuta. This department treats over 10,000 adults annually. The study was approved by ethical review committee of the hospital. All patients provided informed consent.

***Sample size*:** It was estimated that 70% of patients in the PZ group, and 30% of patients in the control group, would experience clinically significant drop in VAS score. These values were based on the earlier studies with morphine as the study drug[6]. With level of power at 80% and a 5% significance level, a sample size of 21 patients in each study arm, was obtained.

***Selection of participants*:** The study population was enrolled in a consecutive fashion during the study period. Patients were eligible if they were 18yrs or older, had non-traumatic abdominal pain of less than 72 hours` duration and were judged by the attending physician to require surgical consultation.

Excluded were patients who were pregnant, had systolic blood pressure of 90mm Hg and below, were not fully conscious, declined participation or were allergic to pentazocine. Hypotensive patients were excluded because the study drug may lower the blood pressure further. Patients who are not fully conscious may have a drop in the level of consciousness because the study drug acts by causing inhibition of some pathways in the central nervous system.

***Intervention and randomization*:** Seventy patients were randomized to receive 30mg pentazocine intravenously or an equal volume of normal saline solution administered as a single bolus. In view of the fact that identical vials were not available for the pentazocine and the placebo, randomization was done as follows: The E.D physician determined the eligibility of the patient. He enrolled him/her and obtained consent. He picked from a box, an opaque numbered sealed envelope, out of the 10 envelopes designed to enroll equal number to pentazocine and placebo. There were seven batches of such envelopes.

He gave the envelope to a nurse who administered the study medication. The envelope number was recorded on the patient's case note. A register matching the envelope number with drug assignment was kept in a location unknown to the investigators. The opened envelope with its content was dropped into another locked box kept in the E.D for that purpose.

***Methods of Measurements*:** The measurements were taken by medical officers working in the surgery department. One medical officer takes the measurements before and 60minutes after administration of the trial drug, unaware of whether it was pentazocine or placebo. The medical officer asked patient to rate his/her pain intensity on a standard horizontal 100mm VAS ranging from, O for no pain, to 100 for worst possible pain. The VAS has been shown to be a valid and reliable instrument for measurement of acute abdominal pain in E.D patients[10]. After this, the medical officer performed a clinical examination and recorded the following:

a. provisional diagnosis and differential diagnosis (2 items only),
b. area of tenderness if any, using the nine quadrants of the abdomen as reference,
c. provisional disposition of the patient, that is whether patient, definitely requires surgery, or definitely does not require surgery or is borderline.

He then left the patient while the drug was administered and returned 60minutes later to repeat and record the VAS score and clinical findings on a fresh sheet of paper. The patient was then off the study and was treated as was the practice in the hospital. However all the patients are admitted for observation for a minimum of 24 hours. Final diagnosis and final disposition were obtained from the patient's hospital records usually within 14days. Non specific abdominal pain was entered for patients, who after

laboratory or/and radiological investigation had no apparent cause for the pain. A VAS score change of at least 13mm was considered as clinically significant[11]. Pearson's chi square tests were done. A p-value < 0.05 was considered significant.

Results

Out of the 70 patients randomized, 5 patients allocated to the placebo group and 3 patients allocated to the PZ group were disqualified for incomplete records. Thirty-two patients received PZ while 30 patients received normal saline. Sixty-two patients were available for analysis. The characteristics of the study population are shown in Table 1.Twenty patients (62.5%) in the PZ group had a VAS score drop >12mm compared to nine patients (30%) in the control group. This was statistically significant (p <0.02). Two patients in the control group had an increase in the VAS score of 4mm and 3mm post injection.

Table 1. Characteristics of the study population

Parameters	***PZ***	***NS (control)***
Mean age in years (range)	35 (21-52)	37 (19 -56)
Proportion of female (no)	56.3% (18)	60% (18)
Initial VAS score Mean +/- SD (mm)	81 +/- 12	78 +/- 11
Post injection VAS score (Mean mm)	53	69
Mean VAS score change (mm)	28	9
No of patients with VAS score drop > 12mm	20 (62.5%)	9 (30%)

Table 2. Final diagnoses for Control and PZ Groups:

Diagnosis	***PZ (n=32)***		***Control (n= 30)***	
	No	(%)	No	(%)
Appendicitis	9	(28.1)	6	(20)
Peptic ulcer disease	3	(9.3)	6	(20)
Primary peritonitis	2	(6.3)	2	(6.7)
Pelvic inflammatory disease	4	(12.5)	5	(16.7)
Hepatoma	0	(0)	2	(6.7)
Colon obstruction	1	(3.15)	1	(3.3)
Food poisoning/enteritis	3	(9.3)	1	(3.3)
Degenerating fibroid	0	(0)	1	(3.3)
Omental cyst	1	(3.15)	0	(0)
Abdominal wall hernia	5	(15.6)	2	(6.7)
Non specific abdominal pain	1	(3.15)	3	(10)
Intestinal obstruction	1	(3.15)	1	(3.3)
Ovarian cyst	2	(6.3)	0	(0)
Total	32	(100)	30	(100)

Table 3. Clinically Important Differences Between Pre Injection, Post Injection and Final Diagnoses

Pre injection diagnosis	***Post injection diagnosis***	***Final diagnosis***	***Allocation***
Gastritis	Peptic ulcer disease	Gastritis	pentazocine
Gaseous distension	Paralytic ileus	Ileus (dm*)	control
Appendicitis	Ovarian cyst	Appendicitis	Pentazocine
Enteritis	Appendicitis	Enteritis	Control
Ovulation related pain	Appendicitis	Ovulation related pain	Control
Bowel obstruction	Gastritis	Bowel obstruction (cb**)	Pentazocine
Peritonitis	Ruptured appendicitis	1^0 peritonitis (dm*)	Control

Key: dm= diabetes mellitus, cb = congenital band. 1^0 = Primary

Table 4. Provisional and final disposition by allocation group

	Pentazocine (no=32)		*Control (no= 30)*	
	Provisional	Final	Provisional	Final
For surgery	15	17	12	13
Not for surgery	7	15	7	17
Uncertain	10		11	

***Changes in physical findings*:** In between the two examinations, there was a slight change in severity of tenderness in 11 out of 32 patients (34.4%) in the PZ group, and 12 out of 30 (40%) of the control. The pre and post injection diagnoses were the same in these cases. There was complete disappearance of tenderness in 2 patients in the PZ group and in 1 patient in the control group. The pre injection diagnoses of mesenteric adenitis and appendicitis in the PZ group were changed to post injection diagnoses of nonspecific abdominal pain. One patient in the control group had a diagnosis of acute appendicitis changed to gastroenteritis. Over the subsequent 24hrs, while these patients were under observation, the tenderness did not return.

Diagnostic accuracy: The diagnostic accuracy in the PZ group was 90.6%. Three patients had a post-injection diagnosis that was different from the final diagnosis Table 3. Two patients, one with appendicitis and the other with bowel obstruction due to bands, had post injection diagnoses of right ovarian cyst pain and gastritis respectively due to reduction in the severity of pain and abdominal tenderness.

While under observation the need for surgery was recognized and they were operated upon. They were provisionally allocated to the group not requiring surgery. Surgery was however delayed for 10hours and 12hours respectively. The diagnostic accuracy in the control group was 86.7%. Four patients in the placebo group had a more serious provisional diagnosis and were provisionally allocated to require surgery Table 3 When results of investigations became available final diagnoses were made and surgery was avoided. The patients received antibiotic combinations as part of the treatment of the initial diagnosis.

Final disposition: In all, 53.1% of the PZ group and 43.3% of the controls had surgery. These figures were comparable to 46 %(PZ) and 40 % (control) in the provisional disposition. The final diagnosis is shown in Table 2.

Complications: A drop in blood pressure to less than 90mm Hg occurred in 7 patients, 5 patients in the PZ group and 2 patients in the control group. They were treated with intravenous 0.9% saline solution. There was no mortality.

Discussion

In the last two decades several studies in the Caucasian population comparing morphine against placebo had been published, which support the early administration of analgesia to patients with acute abdominal pain[1,2,4,10.] However, in spite of these publications, evaluation of attitudes and practices of general surgeons in the United Kingdom and the United States of America in 1999 revealed that 38- 67% believed that analgesia risks masking diagnostic findings[8]. Studies on this subject in the African population are however few.

In this study pentazocine was used in place of morphine because morphine is available in only very few hospitals in Nigeria. Pentazocine is readily available but has weaker analgesic effect. The main findings of this study are that pentazocine administration significantly reduces discomfort. Diagnostic accuracy and treatment decisions were adversely affected in two (6.25%) patients that received pentazocine. The drop in VAS score of patients who received pentazocine was statistically significant when compared to the placebo. Twenty patients (62.5%) in the PZ group had a VAS score drop >12mm compared to nine

patients (30%) in the control group (P<0.02). This result is comparable to results from previous studies using morphine as the study drug[1,2]. However two patients in the PZ group, one with appendicitis and the other with bowel obstruction due to bands, had post injection diagnoses of right ovarian cyst and gastritis respectively due to reduction in the severity of pain and abdominal tenderness. While under observation the need for surgery was recognized and they were operated upon and recovered fully. They were provisionally allocated to the group not requiring surgery. Surgery was however delayed for 10 hours and 12 hours respectively. If the first surgical consultation was after the PZ injection such patient could be discharged from surgical service and might be treated as outpatient. The patient's clinical condition will deteriorate and he will be worse off at subsequent presentation later.

The situation is further compounded by lack of modern diagnostic tools such as CT scan and laparoscopic facilities which could aid diagnosis, in poor resource countries like Nigeria. In such countries every bit of physical finding counts. A second surgical consultation will also be required in a setting where the small number of experienced doctors is already overworked.

Limitation of study

Diagnostic suspicion bias. This form of detection bias could be introduced by the use of a physician who had already examined the patient before administration of the study drug. In such a before-after setting, the clinical information obtained from an initial examination before the administration of the study drug may be carried forward. This might bias findings acquired from a second examination by the same individual after administration of the study drug. However, the advantage of the two examinations being conducted by the same individual is the elimination of inter-observer variation. The single examiner is expected to pick out differences between the two examinations, thereby serving as his control.

Conclusion

- Result of this study shows that pentazocine provides analgesia when administered to patients with acute abdominal pain. However the drug masked important physical signs in a small number of patients. This resulted in delays in surgical intervention with attendant risk of increased complications. Repeated consultation was required to ensure such patients came to no harm. Patients with abdominal pain severe enough to require pentazocine should be admitted for a minimum of 24hrs, as was done in this study.
- The administration of this drug to patients prior to transfer to another hospital is not recommended. The temporary relief in discomfort may encourage the patient to go home rather than proceed to the next hospital.

Acknowledgement

This trial was funded with a grant from the Federal Medical Center Abeokuta for which we are very grateful. The contribution of the medical officers and staff of the emergency department, Federal Medical Center Abeokuta is hereby acknowledged.

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