Oral clonidine reduces bleeding in pelvic and acetabular fractures surgery: A randomized controlled trial

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INTRODUCTION: High blood loss results in major complications in pelvic and acetabular surgeries. Pelvic and acetabular fractures can lead to substantial hemorrhage not just originating from the site of the fracture but also from significant blood vessels or nearby organs in proximity to the affected area. Blood loss during surgery increases the need for a blood transfusion, which causes different adverse reactions, such as transfusion-related infection, hemolysis, and allergic reactions. Decrement of blood loss during and after surgery reduces morbidity and mortality of the patients. It is well known that deliberate hypotension during surgery can decrease blood loss, decrease intraoperative bleeding, shorten surgery time, and improve the visual field intraoperatively. Clonidine is an antihypertensive alpha-2 agonist that has been shown to reduce blood pressure and heart rate by dilating the arteries and reducing blood loss in different surgeries. However, its potential effects on reducing blood loss and pain management remained unclear in pelvic and acetabulum fracture surgeries. This study aims to evaluate the effects of preoperative oral administration of clonidine in patients who underwent surgery for pelvic and acetabulum fractures.

METHODS: A randomized, triple-blinded clinical trial was conducted on patients referred to a tertiary hospital from March 2022 to December 2023. Patients were diagnosed with a pelvic or acetabular fracture using plain radiographs and were randomly divided into two groups. The patient, surgeon, nurses, care providers, and analyzer were blinded throughout the study, and an investigational nurse randomly allocated patients. The intervention group received 200 mcg of oral clonidine 75 to 90 minutes before anesthesia. Control groups received a placebo with a similar color and shape to clonidine. The following data were also recorded: age, gender, BMI, type of surgery, duration of surgery, preoperative coagulation tests, hemoglobin, and hematocrit levels before and (one and three days) after the surgery. We compared two groups regarding the blood loss volume, postoperative pain, quality of the surgical visual field, and day one and three postoperative hemoglobin levels. Data were analyzed using SPSS version 29 (IBM Corp., Armonk, NY). Parametric data were expressed as mean ± standard deviation (SD) and analyzed by independent *t*-test, paired t-test, one-way ANOVA, and repeated measurement analysis of variance. Nonparametric data were analyzed using the Mann-Whitney *U,* Wilcoxon Signed Rank, and Kruskal–Wallis tests. Chi-square tests were used to analyze categorical data. The correlation between variables was evaluated using Pearson and Spearman correlation. A P-value<0.05 was considered statistically significant.

RESULTS:

Of 145 patients, 89 had the criteria to be enrolled in the study. One patient was lost to follow-up due to not having third-day lab tests. 88 patients (79 men and 9 women) scheduled for pelvic or acetabular fracture surgery. The final number of patients in the study included 44 patients in the control group and 44 patients in the treatment group. Demographics and Preoperative coagulant tests were similar between the two groups (P valu>0.05)(Table 1). Of the patients, 36 (40.9%) had pelvic fractures, and 52 (59.1%) had acetabular fractures. The most common types of fractures were both column fractures in 30 (34.1%) and lateral compression type 2 fractures in 25 (28.5%) patients (Table 2).

Postoperation hemoglobin level was significantly dropped in both groups (P<0.05). Post-surgery, the hemoglobin level difference between the groups increased and became significant by day three (9.8 ± 1.2 Vs. 8.4 ± 1.2, P=0.02) (Table 3). The number of patients who required postoperative blood transfusion in the intervention group was less than in the control group (3 vs. 10, P=0.03). Preoperative clonidine significantly reduced postoperation pain and improved the quality of the surgeon's visual field (P<0.001) (Table 4).

DISCUSSION AND CONCLUSION:

Preoperative oral clonidine administration reduces blood loss and the number of postoperative transfusion units in pelvic and acetabular fracture surgeries. In addition, it improved the surgeon's visual field quality and reduced postoperative pain. Therefore, clonidine could be considered a drug of choice to reduce bleeding during and after orthopedic surgeries.

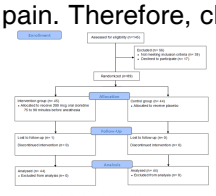

Figure 1. Flow diagram of participants in this randomized clinical trial.

Table 1. Demographic variables of patients

	Intervention	Control	Total	P Value
Patients number	44	44	88	n.s.
Gender	Male: 39 (88.7%)	Male: 40 (9.1%)	Male: 79 (89.8%)	n.s.
	Female: 5 (11.3%)	Female: 4 (9%)	Female: 9 (10.2%)	
Age, y	38.44 ± 18.12	36.30 ± 9.15	38.22 ± 49.11	n.s.
BMI, kg/m2	26.18 ± 3.64	26.75 ± 3.48	26.42 ± 3.42	n.s.

BMI, Body mass index; n.s., Not Statistically Significant (P>0.05)

Table 2. Comparisons of fracture types between two groups.

Type of fracture	Total N (%)	Intervention N (%)	Control N (%)	P-value
LC2	25 (28.5%)	11 (25.0%)	14 (32.0%)	0.98
LC3	5 (5.4%)	2 (4.5%)	1 (2.3%)	
APC2	4 (4.5%)	2 (4.5%)	2 (4.5%)	
APC3	4 (4.5%)	2 (4.5%)	2 (4.5%)	
Anterior column	8 (9.1%)	4 (9.1%)	4 (9.1%)	
Posterior column	12 (13.6%)	5 (11.3%)	7 (15.9%)	
Both column	30 (34.1%)	17 (38.6%)	13 (29.6%)	
Transverse	2 (2.3%)	1 (2.3%)	1 (2.3%)	

LC2: Lateral compression type 2, LC3: Lateral compression type 3, APC2/3: Anterior Posterior Compression type 2/3

Table 3. Comparison of hemoglobin levels preoperatively and 1st and 3rd day postoperatively. (mean ± SD)

Group	Hemoglobin (Preoperative)	Hemoglobin (1st day)	Hemoglobin (3rd day)	P value (Group vs. 3rd day)	P value (1st day vs 3rd day)
Intervention	11.9 ± 1.2	10.0 ± 1.3	9.8 ± 1.2	**0.012**	0.08
Control	12.0 ± 1.0	9.9 ± 1.1	8.4 ± 1.2	**0.001**	**0.03**

Table 4. Pain index, Bleeding volume, rate of transfusion, and surgical field quality. (mean ± SD)

Variable	Intervention	Control	P value
Visl index for pain	4.9 ± 1.0	8.2 ± 1.4	**<0.001**
Intraoperative bleeding volume (cc)	1088.7 ± 207.9	1420.9 ± 344.0	**<0.001**
Postoperative bleeding volume (cc)	25 ± 9.2	24 ± 10.3	0.30
Patients required blood transfusion (n)	3 (6.8%)	10 (22.7%)	**0.03**
Mean surgical field quality score	5.7 ± 1.1	5.1 ± 1.5	**<0.001**
Duration of operation, min	58.6 ± 20.2	62.0± 21.3	0.45

VAS: Visual Analogue Scale