The Effect Of Analgesic Drugs (Voltaren,Profen and Panadol) In Some Physiological Characteristics In Patients

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Abstract

Overuse of analgesics, particularly readily available over-the-counter (OTC) medications like acetaminophen, aspirin, and other NSAIDs, contributes to a worldwide problem of analgesic misuse in both developed and developing nations.NSAIDs are a necessary choice for managing pain because they target the COX pathway, which is central to both inflammation and pain signaling. Cyclooxygenase enzymes, COX-1 and COX-2, play a key role in the production of prostaglandins (PGs). By inhibiting these enzymes, the production of prostaglandins is reduced. This study aimed to investigate the effect of analgesic medications, including Voltaren (diclofenac), Profen (ibuprofen), and Panadol (paracetamol/acetaminophen),on hormones(ANP,ADH and Aldosterone) ,after two month and four month of having these drugs. This study included sixty participants and they were divided into four groups of 15 individuals each: 15 individuals taking Voltaren 25 mg, 15 individuals taking Profen 1000 mg, 15 individuals taking Panadol 1000 mg, daily and 15 individuals not using any analgesic medications, who served as the control group. After two months and four month of having the drugs that mention above there was a significant decrease in concentration of each of ANP and aldosterone, and increase in concentration of ADH hormone compared with control group.

Key words: Analgesic, Diclofenac, Non-steroid anti-inflammatory drugs, ADH,ANP.

Introduction

In 2020, IASP gave a scientific definition of pain which described it as a complicated and discomforting experience involving the interplay of sensory and emotional components ,this experience was related to, or mimicking, the sensation of tissue damage whether real or analogous to that damage[1].The fundamental function of pain within the human body is to provide a crucial warning signal of potentially harmful stimuli or established tissue damage ,this sensory experience also facilitates the initiation of appropriate behavioral responses designed to minimize exposure to such stimuli[2].Pain perception results from a complex interplay of sensory neuron activation, electrochemical signal transmission along neural pathways, and central processing in higher brain regions ,this experience is subject to modulation by stimulus characteristics (intensity, duration), emotional state, and contextual factors[3].Analgesics, commonly referred to as painkillers, are pharmaceuticals employed

to alleviate pain, these agents are broadly classified into two categories: opioid (narcotic) and non-opioid (non-narcotic),opioid analgesics, derived from opium alkaloids, are indicated for the management of pain ranging from mild to severe, non-opioid analgesics encompass acetaminophen (paracetamol) and non-steroidal anti-inflammatory drugs (NSAIDs), these agents are readily available as over-the-counter (OTC) medications, their mechanism of action involves modulation of both peripheral nerve receptors and the central nervous system[4].Non-steroidal anti-inflammatory drugs (NSAIDs) constitute a pharmacotherapeutic class approved by the U.S. Food and Drug Administration (FDA) for their antipyretic, anti-inflammatory, and analgesic properties [5]. The mechanism of action of NSAIDs, as determined by John Vane in 1960 through in vitro experimentation, is the inhibition of the cyclooxygenase (COX) enzyme, which plays a pivotal role in prostaglandin biosynthesis [6] . Hypertension prevalence is expected to rise due to aging populations and increasing obesity, a frequently overlooked cause of secondary hypertension is drug-induced hypertension, this can be caused by over-the-counter, illicit, or prescription drugs, including Acetamenophin and NSAIDs[7].The perturbation of blood pressure regulation and cardiovascular outcomes associated with nonsteroidal anti-inflammatory drug (NSAID) administration is significantly correlated with the attenuation of renal vasodilatory prostanoid synthesis, specifically prostaglandin E2 (PGE2) and prostacyclin (PGI2), where cyclooxygenase-2 (COX-2) plays a crucial role in catalyzing this process under circumstances of compromised renal perfusion[8].The Nurses' Health Study II demonstrated a dose-dependent relationship between acetaminophen use and the risk of hypertension, Regular use of acetaminophen was associated with a relative risk (RR) of 2.00 for developing hypertension, compared to an RR of 1.86 for nonsteroidal anti-inflammatory drugs (NSAIDs),stratified analysis by daily dose revealed a progressive increase in risk, with RRs of 1.38 and 2.38 observed in participants consuming 100 to 500 mg and >500 mg, respectively[9].Atrial natriuretic peptide (ANP) is a 28 amino-acid is peptide synthesized in the heart atria and brain[10]. (ANP) exerts a range of physiological actions, encompassing natriuresis, diuresis, vasodilation, and smooth muscle relaxation, in addition to inhibiting renin-angiotensin-aldosterone system (RAAS) secretion, while it is expressed in both atrial and ventricular cardiomyocytes, atrial expression levels are substantially greater, ranging from 250 to 1000 times higher than those observed in the ventricles[11]. Plays a crucial role in blood pressure regulation through its actions on the kidneys [12]. Stimuli such as volume expansion, increased sodium intake, and rapid blood pressure increases trigger ANP release from the atria, resulting in decreased blood pressure and preserved cardiac function[13].Aldosterone, mineralocorticoid, is produced by the zona glomerulosa cells of the adrenal cortex[14].Exerts its effect on blood pressure by acting on the nephron to regulate sodium reabsorption, this

regulation, in turn, influences water reabsorption, ultimately affecting extracellular fluid (ECF) volume and thus blood pressure[15]. Antidiuretic hormone (ADH) is a small neuropeptide produced in the hypothalamus. It plays a crucial role in maintaining the body's osmotic balance, regulating blood pressure, managing sodium levels, and ensuring proper kidney function[16].

Material and Methods

Study Area

This research was carried out in the Department of Biology/ Faculty of Science /University of Mosul, Iraq.

Experimental Design

This study investigated 60 male subjects aged 30 to 60 years, with body weights ranging from 65 to 85 kg. The subjects were stratified into four cohorts of 15 individuals each, as follows:

1. Group 1 served as the control group and received no analgesic treatment.

2. Group 2 included patients who received daily Voltaren 25 mg.

3. Group 3 included patients who received daily Profen 1000 mg dose.

4. Group 4 included patients who received daily Panadol 1000 mg.

Biological samples were collected from the patients and their clinical status was monitored over a period of four months. Patients with chronic diseases such as hypertension, diabetes, and cardiovascular diseases were excluded from the study.

Sample Collection

Blood samples were collected to evaluate the effects of analgesics on several renal function parameters in the serum of patients. Approximately 3 ml of blood was drawn from each participant and collected in serum separator tubes (gel tubes). The tubes were allowed to clot at room temperature for 20 minutes. The samples were then centrifuged at 3000 rpm for 15 minutes to obtain serum, which was then used for the required analysis

Statistical Analysis

To analyze the results of the tests and determine the mean and standard deviation, a One-way analysis of variance (ANOVA) was performed to determine the mean and standard deviation in a completely randomized design (CRD).The study aimed to identify differences among the groups of analgesic users receiving treatment at different intervals, compared to the control group. To determine these intergroup differences, Duncan's Multiple Range Test was used for all studied variables. Differences were considered statistically significant at a probability level of $P < 0.05$. Statistical analysis was performed using the Statistical Analysis System software to calculate the mean and standard deviation [17].

Result

Figure (1). show a significant decrease in atrial natriuretic peptide (ANP) levels in the patient group receiving Voltaren at a dose of 25 mg/kg body weight ($p \leq 0.05$). The mean

ANP concentration in this group was 50.28 ± 0.08 ng/L. In comparison, the group treated with Profen at 1000 mg/kg body weight had an average ANP concentration of 56.14 ± 1.55 ng/L, while those receiving Panadol at the same dose of 1000 mg/kg had a mean of 60.43 ± 0.09 ng/L. The control group displayed the highest ANP concentration, with a mean of 72.12 ± 0.17 ng/L.

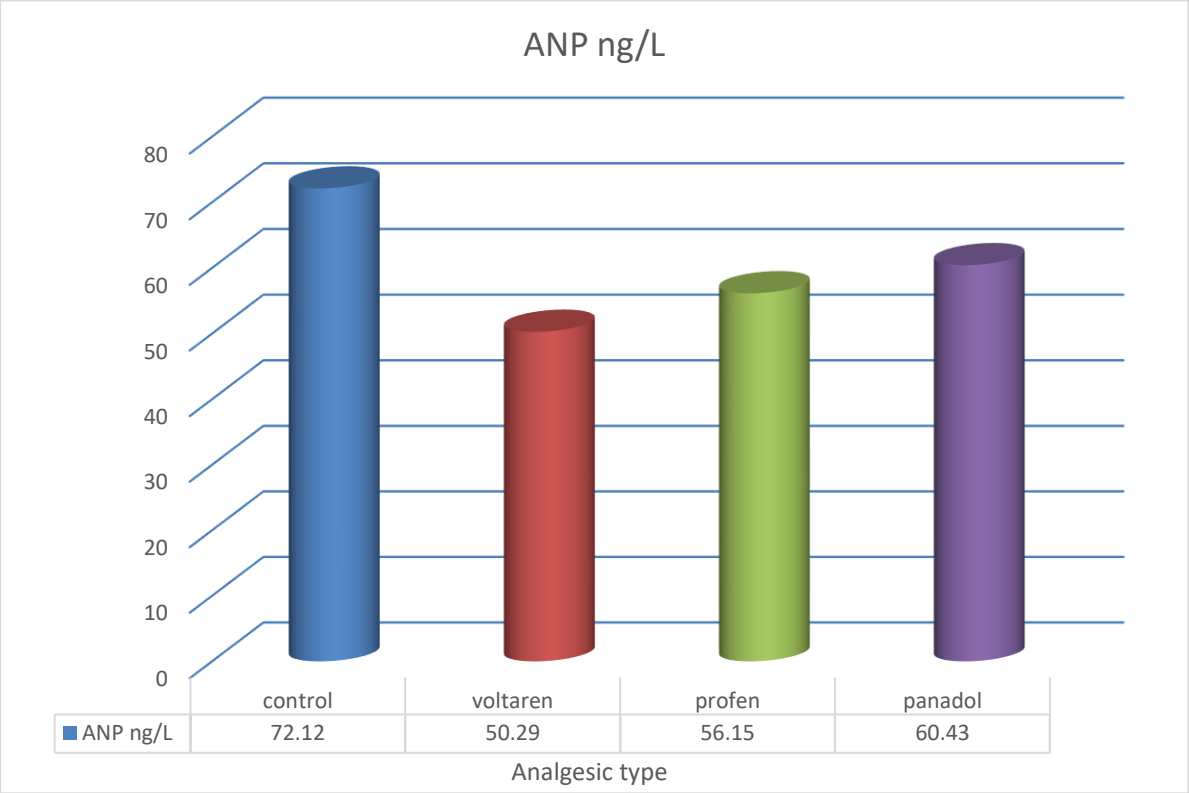
Figure (2) shows a significant increase in aldosterone concentration in the group of patients taking Voltaren 25 mg/kg body weight at a probability level (P≤0.05). With an arithmetic mean of (0.16 ± 160.69) picograms/ml, the arithmetic mean for the group of patients taking Brufen at a dose of 1000 mg/kg body weight was (0.05 ± 158.19) picograms/ml, while the arithmetic mean for the group of patients taking Panadol at a dose of 1000 mg/kg body weight was (0.08 ± 150.24) picograms/ml, and finally the arithmetic mean for the control group was (0.22 ± 142.31) picograms/ml.

"Figure (3) demonstrate a significant increase in ADH concentration in the patient group receiving Voltaren at a dose of 25 mg/kg body weight ($p \leq 0.05$). The mean ± standard deviation (SD) of ADH concentration in this group was (9.57 ± 0.21) pg/mL. In contrast, the mean ± SD of ADH concentration was (7.39 ± 0.09)pg/mL in the group receiving Profen at a dose of 1000 mg/kg body weight, (6.77 ± 0.15) pg/mL in the group receiving Panadol at a dose of 1000 mg/kg body weight, and (5.16 ± 0.05) pg/mL in the control group.

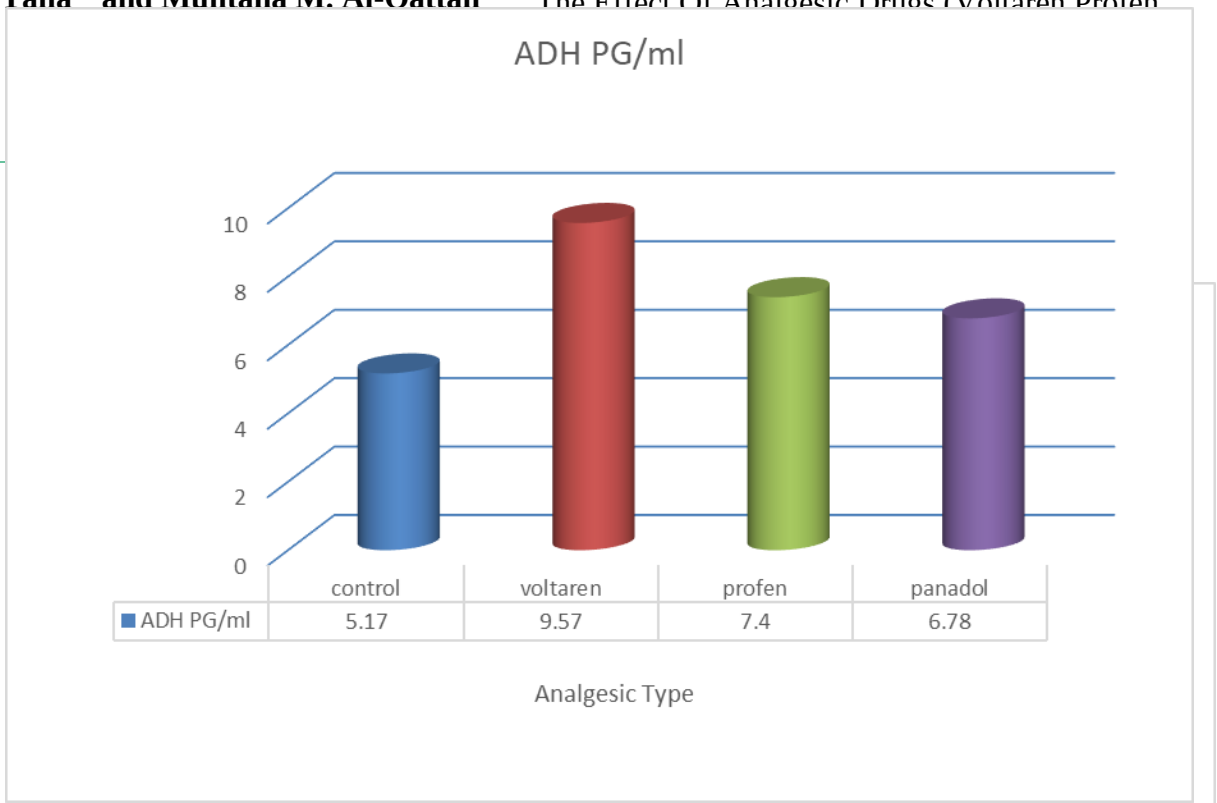
Figure (4) demonstrate a significant decrease in ANP (atrial natriuretic peptide) concentration in the patient group receiving Voltaren at a dose of 25 mg/kg body weight ($p \leq 0.05$). The mean ± standard deviation (SD) of ANP concentration in this group was (45.86 ± 0.09) ng/L. In contrast, the mean ± SD of ANP concentration was (45.91 ± 0.39) ng/L in the group receiving Profenat a dose of 1000 mg/kg body weight, (48.33 ± 0.36) ng/L in the group receiving Panadol at a dose of 1000 mg/kg body weight, and (72.40 ± 0.05) ng/L in the control group.

Figure (5) demonstrate a significant decrease in aldosterone concentration in the patient group receiving Voltaren at a dose of 25 mg/kg body weight ($p \leq 0.05$). The mean ± standard deviation (SD) of aldosterone concentration in this group was (175.19 ± 0.21) pg/mL. In contrast, the mean ± SD of aldosterone concentration was 160.34 ± 0.04 pg/mL in the group receiving Profenat a dose of 1000 mg/kg body weight, (157.46 ± 0.36) pg/mL in the group receiving Panadol at a dose of 1000 mg/kg body weight, and (142.21 ± 0.08) pg/mL in the control group.

Figure (6) demonstrate a significant increase in ADH (antidiuretic hormone) concentration in the patient group receiving Voltaren at a dose of 25 mg/kg body weight ($p \leq 0.05$). The mean ± standard deviation (SD) of ADH concentration in this group was (12.17 ± 0.04) pg/mL. In contrast, the mean ± SD of ADH concentration was (10.35 ± 0.04) pg/mL in the group receiving Profen at a dose of 1000 mg/kg body weight, (9.64 ± 0.09) pg/mL in the group receiving Panadol at a dose of 1000 mg/kg



body weight, and (5.13 ± 0.04) pg/mL in the control group.



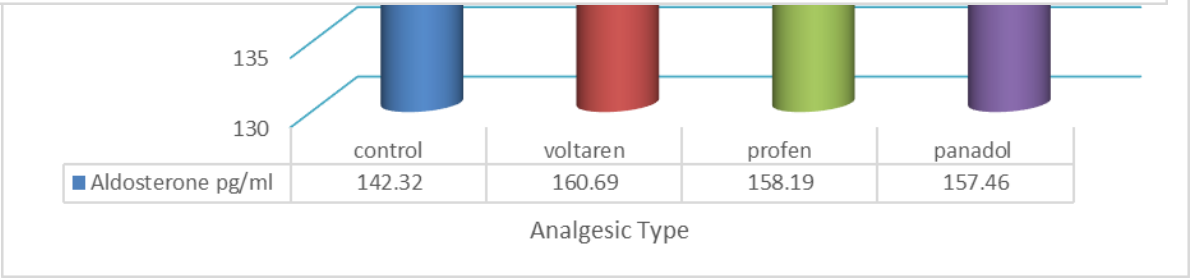


Fig 1. The Effect of Analgesic on ANP Hormone Level After Two Month

Fig 2. The Effect of Analgesic on Aldosterone Hormone Level After Two Month

Fig 3. The Effect of Analgesic on ADH hormone level after two month

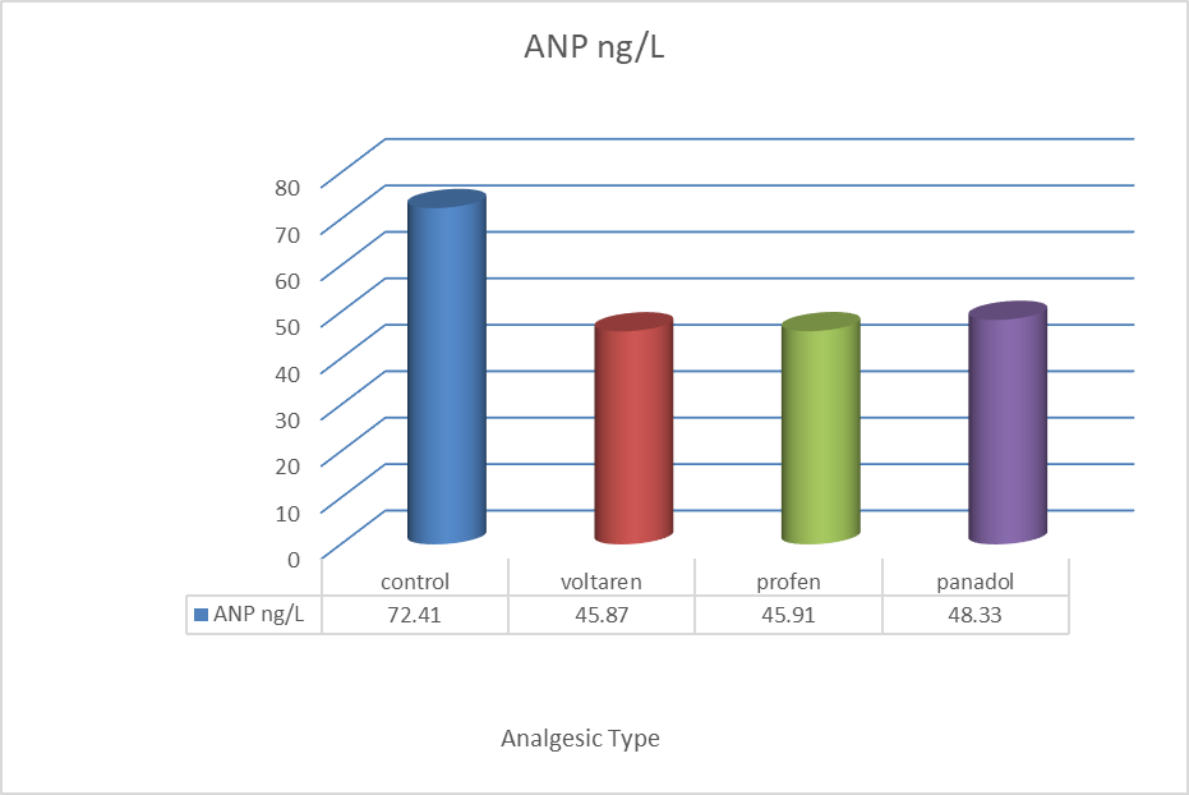
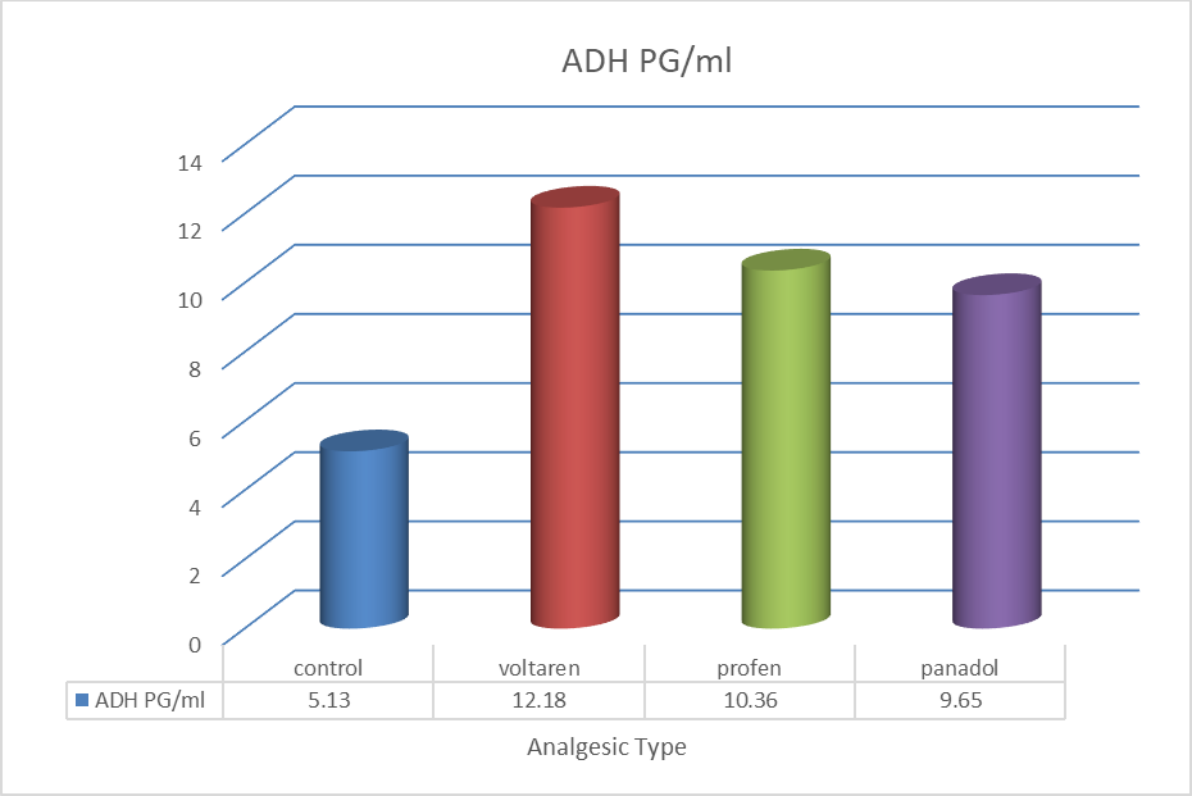
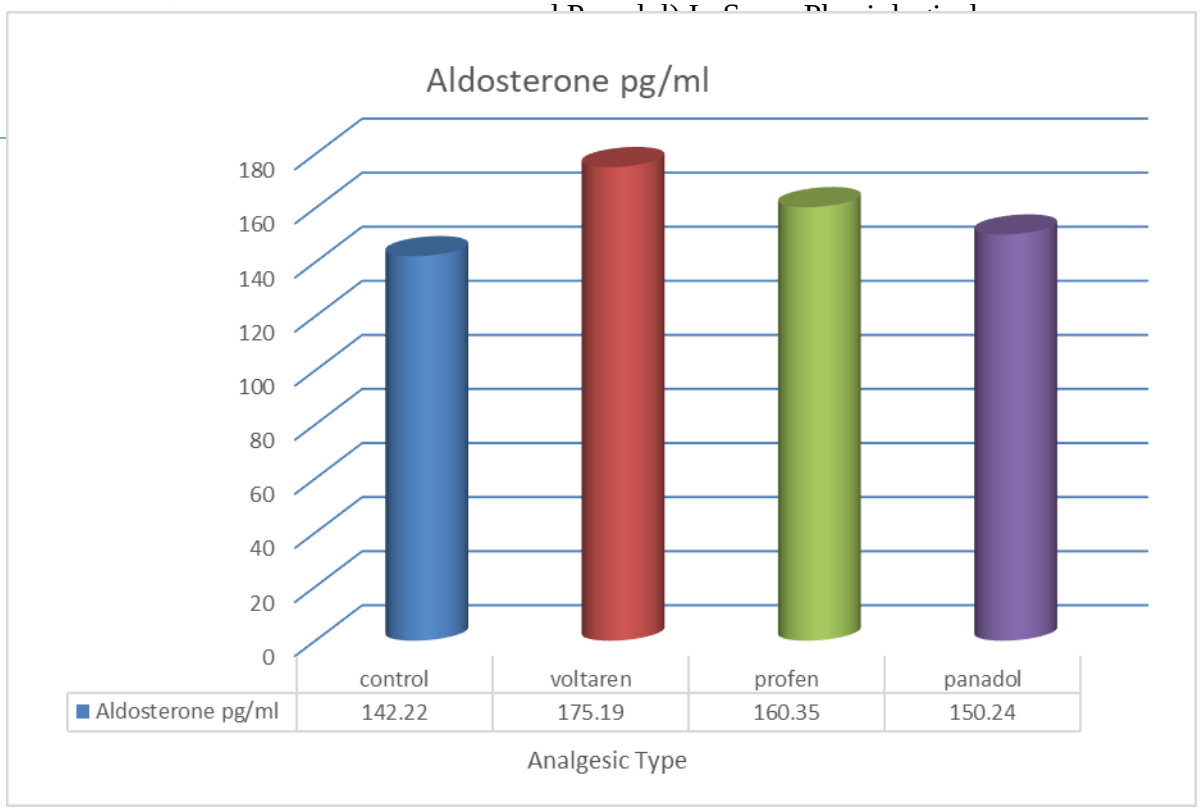


Fig 4. The Effect of Analgesic on ANP hormone level after four month

Fig 5. The Effect of Analgesic on Aldosterone hormone level after four month

Fig 6. The Effect of Analgesic on ADH hormone level after four month




Aldosterone pg/ml
180
160
140
120
100
80
60
40
20
0
control
voltaren
profen
panadol
Aldosterone pg/ml
142.22
175.19
160.35
150.24
Analgesic Type

Discussion

The observed reduction in ANP concentration in patient groups receiving analgesic agents (Voltaren, Brufen, and Panadol), with Voltaren exhibiting the most pronounced effect, may be attributed to the mechanism of action of these compounds. These agents function by inhibiting cyclooxygenase-2 (COX-2), leading to a diminished synthesis of prostacyclin (PGI2) by vascular endothelial cells. PGI2, a potent inhibitor of platelet aggregation and a vasodilator, plays a crucial role in maintaining vascular homeostasis. The resultant disruption in the delicate equilibrium between prothrombotic factors and antithrombotic mediators (specifically PGI2) engenders an augmented propensity for thrombus formation. This prothrombotic state, in turn, may contribute to an increased risk of hypertension, potentially mediated by the suppression of ANP secretion from atrial cardiomyocytes[18].

The patient groups receiving analgesic medications showed higher aldosterone levels compared to the control group, with the most noticeable increase in the group treated with voltaren at a dose of 25 mg/kg body weight, is likely due to the influence of these medications on renal function and the renin-angiotensin-aldosterone system (RAAS),the kidney secretes renin in response to decreased blood pressure or low sodium levels, which stimulates aldosterone production,this hormone aids in elevating blood pressure and maintaining normal sodium and potassium levels, which are essential for proper nerve and muscle function, therefore, an elevated or decreased aldosterone level indicates a potential underlying issue[19].

These analgesics may exert their effects by inhibiting the cyclooxygenase (COX) enzyme. This enzyme catalyzes the synthesis of prostaglandins, which influence glomerular filtration, tubular transport, and renin secretion, ultimately affecting aldosterone release from the adrenal gland. Elevated blood potassium levels also stimulate the adrenal cortex to release more aldosterone, promoting potassium excretion in the urine to lower blood potassium levels ,this contributes to explaining the elevated blood pressure observed in patients using analgesics[20].

The patient groups receiving analgesic medications had higher antidiuretic hormone (ADH) levels, with the most significant increase observed in the group receiving Voltaren at a dose of 25 mg/kg body weight, may be attributed to the impact of these medications on renal function. Prolonged use of these analgesics for four months may induce renal dysfunction, as these agents inhibit cyclooxygenase (COX) enzyme activity, specifically both COX-1 and COX-2.

COX-2 is an inducible enzyme which is overexpressed during tissue damage. Since analgesics inhibit COX-2, this inhibition primarily occurs at the target tissue site, which in this case is the kidney, the primary target organ for ADH released from the posterior pituitary gland[16]. Rendering the kidneys less responsive to this hormone. In other words, these analgesics affect the kidneys' ability to reabsorb water and may

also disrupt the regulation of ADH secretion or its downstream signaling pathways[21].

Conclusion

We conclude that taking analgesic had decrease the level of ANP and aldosterone, and raise the level of ADH hormone after two months and four month , and the effect of voltaren was the strongest, followed by ibuprofen, and finally, Panadol.

Conflicts of interest

The authors declare that they have no financial or personal relationships that could be perceived as creating a conflict of interest related to the research and information presented in this paper.

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