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COMPARING THE IMPACT OF DICLOFENAC SODIUM, HYDROCORTISONE AND A COMBINATION OF BOTH ON PAIN MANAGEMENT AFTER ELECTIVE CAESAREAN SECTION UNDER SPINAL ANESTHESIA

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ABSTRACT

Background and aim:Principles of a multimodal strategy include control of postoperative pain to allow early mobilization, early enteral nutrition and attenuation of the perioperative stress response through the use of regional anesthetic techniques and a combination of analgesic agents. This study aimed to evaluate the impact of diclofenac, hydrocortisone and a combination of both on prevalence and postoperative pain on women underwent elective cesarean section.

Materials and Methods: This double-blind clinical trial was performed on 150 pregnant females who were candidates for cesarean section surgery. The patients were randomly divided into three groups of 50 subjects. Group I received 100 mg sodium diclofenac suppository and 2cc intravenous normal saline, Group II received 100 mg intravenous hydrocortisone and a placebo suppository and Group III received a combination of hydrocortisone and diclofenac suppository. Mean arterial blood pressure and heart rate in each group were monitored and compared 10 minutes before the spinal anesthesia (prior to catheterization of the bladder) at the end of surgery and one hour after recovery. Postoperative pain was assessed with numerical pain scale for up to 24 hours after surgery in all three groups and tranquilizer was administered if needed as well as the first time to request analgesics and total analgesic dosage levels in each of the groups were recorded and compared. If pain severity has reached an elevated level (Severity Level 4), the dose of diclofenac suppository administrated is recorded in the file. If the pain becomes worse and more constant, Pethidine Ampoule (25 mg) is administered intravenous (suppository is repeated in less than 8 hours if necessary). Data analysis was performed using SPSS software.

Findings: There was no significant difference between the three groups in terms of age and gestational age. Changes in mean arterial pressure in the in the third group (combination) were less than the other two groups. Patients in the hydrocortisone group received a higher dose of analgesics and a combination therapy group received a lower dose of HER ($P < 0.05$).

Conclusion:According to the results, administration of diclofenac suppository with intravenous hydrocortisone in reducing pain after cesarean section is more effective than any of the medications alone.

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Introduction

Principles of a multimodal strategy include control of postoperative pain to allow early mobilization, early enteral nutrition and attenuation of the perioperative stress response through the use of regional anesthetic techniques and a combination of analgesic agents [1].

Transmission of nociceptive stimuli to the CNS from the periphery result in the neuroendocrine stress response, a combination of local inflammatory substances (e.g., cytokines, prostaglandins, Leukotrienes, TNFα) and systemic mediators of neuroendocrine response [1].

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Suprasegmental reflex responses to pain result in increased sympathetic tone, increased catecholamine and catabolic hormone secretion (e.g., cortisol, adrenocorticotropic hormone, antidiuretic hormone, glucagon, aldosterone, renin, angiotensin II), and decreased secretion of anabolic hormones.

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The effects include sodium and water retention and increasedlevels of blood glucose, free fatty acids, ketone bodies, and lactate. A hypermetabolic, catabolic state occurs as metabolism and oxygen consumption are increased and metabolic substrates are mobilized from storage depots.

The extent of the stress response is influenced by many factors, including the type of anesthesia and intensity of the surgical injury, with the extent of the stress response being proportional to the degree of surgical trauma [1].

Uncontrolled postoperative pain may activate the sympathetic nervous system and thereby contribute to morbidity or mortality. Sympathetic activation may increase myocardial oxygen consumption, which may be important in the development of myocardial ischemia and infarction, and may decrease myocardial oxygen supply through coronary vasoconstriction and attenuation of local metabolic coronary vasodilation [2].

Standardized administration of NSAIDs may prevent post-operative analgesia and minimize analgesic-related complications. NSAIDs are effective in mild to moderate pain and are often used in combination with opioids in treating mild or severe pain. These drugs are administered orally or prenatal, especially as part of the multimodal analgesic regimen, because they decrease pain via different mechanism other than opioids and topical anesthetics.

It is unlikely that patients with normal urine output and renal function will develop kidney dysfunction with these drugs.

Cortisol (hydrocortisone*)* is a corticosteroid with both glucocorticoid and mineralocorticoid activity and effects. It is injected intramuscularly (into *a* muscle*) or* intravenously (into a vein) and it starts to work immediately following the injection, but the drug effect at peak is not unknown. The drug and its inactive conjugated metabolites are more readily excreted by the kidney [3].

The aim of this study was to investigate the impact of diclofenac, hydrocortisone and a combination of both on prevalence and postoperative pain on women undergoing elective cesarean section so that they can be widely used in postoperative pain management if its effect on pain relief has demonstrated.

Materials and Methods:

This double-blind clinical trial was performed on 150 pregnant women referred to Qazvin Kosar Hospital for elective cesarean section and underwent spinal anesthesia. After obtaining informed consent from the patient and approval of the Vice-Chancellor's Ethics Committee in number ** as well as after obtaining registration code number ****** from clinical l patients regarding diclofenac suppositories and hydrocortisone ampoules and their beneficial effects and unwanted side trials in Iran, the study began. Subjects were selected using random sampling and adequate explanations were provided for affects.

Exclusion criteria were history of corticosteroid use or allergy (reaction) to NSAIDs, patients with infectious febrile, peptic ulcer, uncontrolled diabetes, and thyroid and asthma diseases. Group I received 100 mg sodium diclofenac suppository and 2cc intravenous normal saline, Group II received 100 mg intravenous hydrocortisone and a placebo suppository and Group III received a combination of hydrocortisone and diclofenac suppository. Mean arterial blood pressure and heart rate in each group were monitored and compared 10 minutes before the spinal anesthesia (prior to catheterization of the bladder) at the end of surgery and one hour after recovery. Postoperative pain was assessed with numerical pain scale for up to 24 hours after surgery in all three groups and categorized into mild pain (0-3), moderate pain *(*4-*7),* and *(*8-10*).* Tranquilizer was administered if needed and the first time to request analgesics and total analgesic dosage levels in each of the groups were compared in 24 hours. If pain severity has reached an elevated level (Severity Level 4), the dose of diclofenac suppository administrated was recorded in the file. If the pain becomes worse and more constant, Pethidine Ampoule (25 mg) was administered intravenous (suppository is repeated in less than 8 hours if necessary).

A self-made questionnaire including information about date of surgery, age and patient’s weight, surgical duration, gestational age, receiving or non-receiving of diclofenac suppository, receiving or non-receiving of hydrocortisone ingestion and diclofenac suppository, blood pressure before anesthesia induction at the end of surgery and every half an hour to one hour after admitting to the recovery room, blood pulses rate before induction of anesthesia at the end

of the surgery, and every half an hour to one hour after admitting to the recovery room, the presence or absence of pain for up to 24 hours after surgery, pain severity, dose of painkiller up to 24 hours after surgery, was employed for data collection.

These data were collected based on the checklist and entered in the SPSS software. Quantitative data were analyzed using ANOVA and T-test and qualitative data with Chi-square test.

Findings:

This study was conducted on 150 pregnant women in three groups of 50 subjects who received diclofenac suppositories, hydrocortisone ampoules and a combination of both. The mean age among the three groups was 27.6 ± 7.4, 27.5 ± 6 and 28.1 ± 6.4 and gestational age was 38 ± 0/6, 37.9 ± 0.6 and 1/1 ± 37.6, respectively and no significant difference was observed among the groups.

No significant difference was found between the two groups in terms of heart rate and mean arterial pressure (Fig. 1 and 2). ANOVA analysis did not show a significant difference between the mean time of first request for painkiller in the three groups (p = 0.00). Analysis of the difference between two groups using Tukey test revealed a significant difference between hydrocortisone group with diclofenac suppository and hydrocortisone combination (p = 0.00). A significant difference was also found between diclofenac suppository group and hydrocortisone (P = 0.00). Patients in the hydrocortisone needed to immediately take painkiller.

In addition, Chi-square test showed a significant difference between the received doses of painkiller up to 24 hours after administration in different drugs, and the hydrocortisone group took painkiller more than others.

Figure 1. Changes in heart rate among the three groups of patients receiving diclofenac suppository, intravenous hydrocortisone and a combination of both drugs for pain management after cesarean section under spinal anesthesia

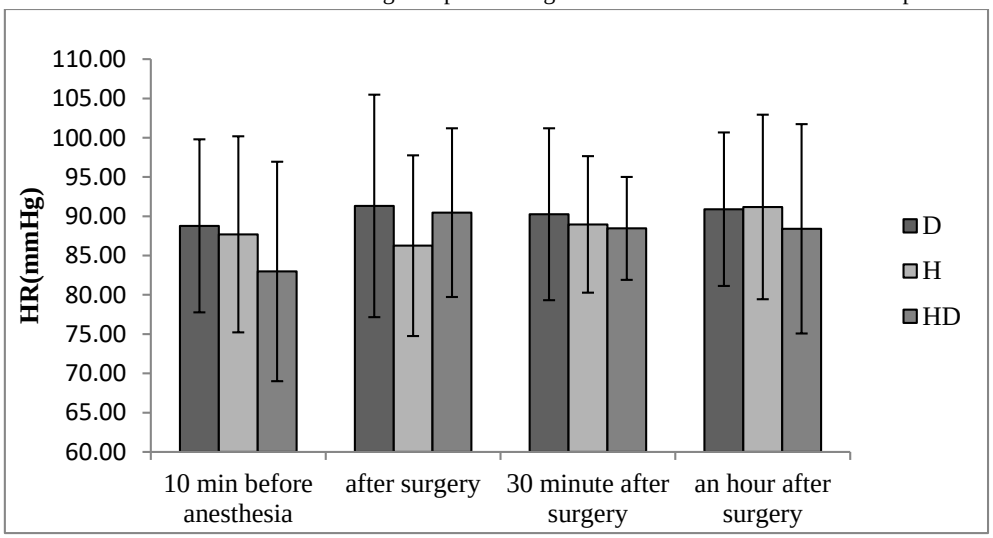

Figure 2. Changes in mean arterial blood pressure in the three groups of patients receiving diclofenac suppository, intravenous hydrocortisone and a combination of both drugs for pain management after cesarean section under spinal anesthesia

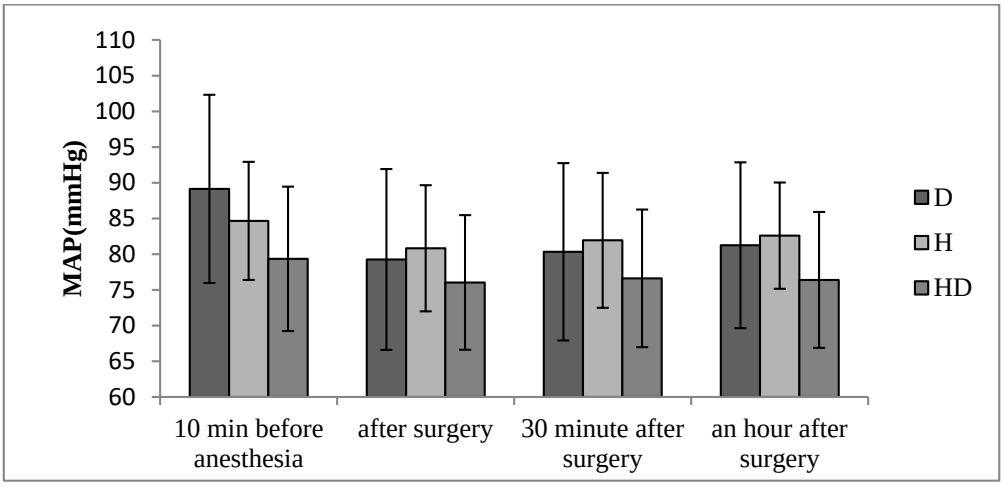

Table 1. Relative frequency distribution of administration doses of painkiller in subjects up to 24 hours post operation in three groups of patients receiving diclofenac suppository, intravenous hydrocortisone and a combination of both drugs for pain management after cesarean section under spinal anesthesia

Group receive painkiller dose	Diclofenac suppository		Intravenous hydrocortisone		Diclofenac suppository and intravenous hydrocortisone	
	Number	Percent	Number	Percent	Number	Percent
1	13	26	1	2	11	22
2	25	50	11	22	34	68
3	12	24	38	76	5	10
P-value	0.00					

Table 2. Comparison of the mean time of first request for painkiller in the three groups of patients receiving diclofenac suppository, intravenous hydrocortisone and a combination of both drugs for pain management after cesarean section under spinal anesthesia

Drug	Mean (hour)	SD	P value
Diclofenac suppository	3.3	1.5	0.00
Intravenous hydrocortisone	2.2	0.7	
Diclofenac suppository and intravenous hydrocortisone	3.5	1.1	

Discussion and Conclusion:

According to the results of this study, pain management in the combination treatment group with hydrocortisone and diclofenac was According to the results of this study, pain management in the combination treatment group with hydrocortisone and diclofenac was improved compared to the other two groups and the request for painkiller found a significant decrease in this group as well.

A lot of studies have been done on the impact of a number of drugs on postoperative pain in spinal anesthesia and there are different types of point of view and discussion, but no agreement has yet been reached in this regard. For example, it was found in a study that Ketorolac administration reduced the pain in the first two hours after cesarean section in patients with its anti-inflammatory effect [4-5], but according to findings from another study, Pareaxib was able to further reduce postoperative pain in the first 24 hours compared to the ketorolac [6].

In addition, the results of studies by Singh Pawar in 2011 [7] and E lmawgood in 2012 [8] showed a significant difference between heart rate changes in the experimental and control groups, which was consistent with our study results.

NSAIDs inhibit prostaglandin synthesis and may decrease pain through inhibition of phosphodiesterase enzymes, increased cAMP, and prostaglandin secretion, leukotriene, bradykinin, serotonin and histamine [4].

Postoperative pain was assessed with numerical pain scale for up to 24 hours after surgery in all three groups and tranquilizer was administered if needed as well as the first time to request analgesics and total analgesic dosage levels in each of the groups were compared. Others studied used non-opioid drugs for pain treatment and management.

The impact of Ketorolac as an injectable nonnarcotic analgesic has been examined in some studies, and is comparable with as a component of NSAIDs [4 , 5]. In a study by Horn EP et al (1999) on patients undergoing knee surgery, one group of patients received intra-articular lidocaine resulting in significant pain decrease after surgery. Patients in the experimental group experienced less shivering than control group and it was concluded that proper management can reduce postoperative shivering [9].

Moreover, the results of a study in 2007 indicated that addition of dexamethasone to a non-steroidal anti-inflammatory drug (rofecoxib) can increase the duration of postoperative analgesia from 24 to 72 hours [10].

In our study, the first time of request for painkiller was on average 3.8 hours in the diclofenac group, 2.4 hours in the hydrocortisone group and 3.5 hours in the combination treatment group.

After comparing these groups, it was clear that patients in the hydrocortisone group received a higher dose of the painkiller and the combination group received fewer doses. There was a statistically significant difference between different groups in terms of taking painkiller. Overall, according to the results of this study, pain management in the combination treatment group with hydrocortisone and diclofenac was improved compared to the other two groups and the request for painkiller found a significant decrease in this group as well.

It was also shown that the first time of request for painkiller after surgery in the diclofenac group was on average 3.33 hours, 2.4 hours in the hydrocortisone group and 3.5 hours in the combination treatment group. Therefore, the hydrocortisone group had a significantly urgent need for painkiller while combination treatment group requested it later.

Patients in the hydrocortisone group received the highest dose of painkiller and the lowest in the combination treatment group and the difference in receiving painkiller in different groups was statistically significant.

According to our pre-study assumptions, changes in systolic and diastolic blood pressure were lower in the combination treatment group. However, our study showed the lowest systolic changes was observed in the group receiving hydrocortisone.

The lowest change in diastolic blood pressure was related to the group receiving combination treatment group, which was consistent with previous assumptions.

Changes in systolic and diastolic blood pressure were also correlated with other factors, including the patient's pre-existing condition, the history of drug use, and the conditions for use of spinal anesthesia, intravenous drugs, and the like. It seems therefore that shivering as an independent variable cannot be considered as a change agent only.

Additionally, changes in heart rate in each group were evaluated and the mean of changes in each group was measured and compared. There was no significant difference between heart rate changes in different groups.

Therefore, our study results support the initial assumptions for better management of pain with combination treatment group using hydrocortisone and diclofenac.

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