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**Original Research Article**

# Analgesic, anti-inflammatory and immuno-modulatory effects of dezocine-propofol anesthesia combination following colonoscopy

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## Abstract

***Purpose:*** *To study and compare the analgesic, anti-inflammatory and immuno-modulatory effects of dezocine-propofol, and fentanyl-propofol combinations in colonoscopy.*
***Methods:*** *One hundred and thirty-four patients who received painless colonoscopy in Eastern Medical District of Linyi People's Hospital, Linyi City, Shandong Province, China, from June 2013 to December 2016 were randomly divided into two groups. Patients in the observation group (aged 42 - 65 years) received dezocine-propofol combination as anesthesia, while those in the control group (aged 41 - 67 years) were anesthetized with fentanyl-propofol. Serum levels of pain and inflammatory mediators, as well as contents of immune response molecules were determined prior to, during and after colonoscopy using either enzyme-linked immunosorbent assay (ELISA) or electro-chemiluminescence kits.*
***Results:*** *There were no statistically significant differences in the serum levels of 5-hydroxytryptophan (5-HTP), 5-hydroxy indole acetic acid (5-HIAA), substance P (SP), prostaglandin E2 (PGE2), C-reactive protein (CRP), heat shock protein 70 (HSP70), Interleukin-1 β(IL-1β), adrenocorticotropic hormone (ACTH), Cortisol (Cor), Inositol (Ins), c-peptide (C-P), immunoglobulin G (IgG) and immunoglobulin A (IgA), complement 3 (C3) and complement 4 (C4) before and during colonoscopy between the two groups of patients. However, after the examination, serum levels of 5-HTP, 5-HIAA, SP, PGE2, CRP, HSP70, IL-1 beta, ACTH, Cor, Ins and C-P in the observation group were significantly lower than those in control group ($p < 0.05$), while IgG, IgA, C3 and C4 contents were significantly higher than those of the control group ($p < 0.05$).*
***Conclusion:*** *These results suggest that the analgesic effect of dezocine-propofol combination after colonoscopy examination is superior to that of fentanyl-propofol combination, due to its effectiveness in inhibiting inflammatory reactions and improving immune response.*

***Keywords:*** *Colonoscopy, Dezocine, Propofol Fentanyl, Pain mediators, Analgesic, Inflammatory reaction, Immune response*

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## INTRODUCTION

Fiber colonoscopy is an important auxiliary examination procedure for diagnosing colorectal diseases in clinics. However, during inspection, the patient may feel pain and discomfort when colonoscopy goes across the hepatic and splenic flexure. These feelings are experienced in severe situations, leading to various degrees of abdominal discomfort and pain after the inspection. Painless colonoscopy is a newly developed technique that relieves the pain and discomfort associated with colonoscopy

examination through the use of a combination of a sedative and an analgesic [1,2]. Dezocine-propofol and fentanyl-propofol are two kinds of frequently used anesthetic combinations for achieving painless colonoscopy. Dezocine and fentanyl exert analgesic effects, the former through activation of κ receptor in the cerebral cortex, and the latter through excitation of μ and δ receptors in the central nervous system (CNS) [3-5]. The present study was carried out to compare the anti-inflammatory and immuno-modulatory effects of these two types of unaesthetic combination at various stages of colonoscopy.

## METHODS

### Subjects

One hundred and thirty-four patients who received painless colonoscopy in our hospital (Eastern Medical District of Linyi People's Hospital, Linyi City, Shandong Province, China) from June 2013 to December 2016 participated in this study. This research was approved by Ethical Committee of The People's Hospital of Pingyi County (approval no. LY2013053) and was carried out according to the guidelines of Declaration of Helsinki promulgated in 1964, as amended in 1996 [6]. All the patients presented with colonoscopy indications, voluntarily accepted receiving painless colonoscopy, and signed informed consent. They were randomly divided into observation and control groups, each having 67 patients. Patients in the observation group (42 males and 25 females, aged 42 - 65 years) received dezocine-propofol combination anesthesia, while those in the control group (40 males and 27 females, aged 44- 63 years) were anesthetized with a combination of fentanyl and propofol. There were no significant differences in general characteristics between patients in the two groups ($p > 0.05$).

### Fiber colonoscopy

The upper extremity venous access was conventionally employed with ECG monitor and nasal catheter for oxygen inhalation. Anesthesia was induced and maintained in patients in the observation group by intravenous injection of 5mg dezocine, 1 – 2 mg/kg propofol, as well as intra-operative micro-pump injection of 2 – 4 mg/kg/h propofol. On the other hand, patients in the control group were anesthetized by intravenous injection of 0.05 mg fentanyl, 1 – 2 mg/kg propofol and intra-operative micro-pump injection of 2 – 4 mg/kg/h propofol. At the onset of anesthesia, the same group of doctors conducted colonoscopy on both groups of patients, sent the patients to the recovery room after the examination, and stayed there with them until they regained consciousness and stable vital signs were stable.

### Determination of biochemical indices

Peripheral blood samples (3 - ml) were collected from the two groups of patients before, during and after colonoscopy, and allowed to clot. Serum samples were obtained by centrifugation and used for assay of 5-HTP and5-HIAA (by RIA kits); SP, PGE2, CRP, HSP70, ACTH, Cor, IL-1 beta, C-P, IgG IgA, C3 and C4 (by ELISA kits), and Ins (by electro-chemiluminescence kits) [6].

### Statistics

SPSS 20.0 software was used to analyze the data from serum assays. The data are expressed as mean ± standard deviation (mean ± SD); data from the two groups were analyzed by t–test. $P < 0.05$ was considered as indicative of statistical significance.

## RESULTS

### Serum levels of pain indicators

No statistically significant differences were observed in serum levels of 5-HTP, 5-HIAA, SP and PGE2 between the two groups prior to, and during colonoscopy ($p > 0.05$). However, after colonoscopy, serum levels of 5-HTP, 5-HIAA, SP and PGE2 in the observation group were significantly lower than corresponding values in the control group ($p < 0.05$). These results are shown in Table 1.

**Table 1:** Serum levels of pain indicators before and after colonoscopy examination (mean ± SD)

| Group | Time point | 5-HTP (μmol/L) | 5-HIAA (μmol/L) | SP (mg/L) | PGE2 (ng/L) |
|---|---|---|---|---|---|
| Observation | Before | 42.51 ± 6.62 | 57.29 ± 8.21 | 2.15 ± 0.35 | 68.49 ± 9.31 |
| | During | 53.59 ± 7.81 | 63.24 ± 9.18 | 2.95 ± 0.42 | 74.28 ± 8.93 |
| | After | 62.19 ± 8.72* | 74.18 ± 9.63* | 3.47 ± 0.61* | 89.21 ± 9.74* |
| Control | Before | 43.03 ± 6.92 | 58.02 ± 7.98 | 2.23 ± 0.38 | 69.11 ± 9.83 |
| | During | 53.21 ± 7.25 | 64.18 ± 8.69 | 3.01 ± 0.49 | 74.19 ± 9.58 |
| | After | 79.35 ± 9.68* | 93.82 ± 11.02* | 6.58 ± 0.93* | 141.58 ± 18.76* |

**P < 0.05 when compared to the control group at the same time point*

**Serum levels of inflammatory cytokines**

The results obtained showed that there were no statistically significant differences in serum levels of CRP, HSP70 andIL-1β between the two groups of patients before and during colonoscopy. Interestingly, after colonoscopy, serum levels of CRP, HSP70 and IL-1β in the observation group were significantly lower than those in the control group (Table 2, $p < 0.05$).

**Serum contents of inflammation-related endocrine hormones**

Prior to, and during colonoscopy, there no significant differences in serum ACTH, Cor, Ins and C-P levels between patients in the observation group and patients in the control group ($p > 0.05$). However, after colonoscopy, serum levels of these parameters were significantly lower in the observation group than those in the control group ($p < 0.05$). These results are presented in Table 3.

**Serum levels of humoral immune response molecules**

There were no statistically significant differences in serum levels of the humoral immune response molecules IgG, IgA, C3 and C4 between the two groups of patients before and during colonoscopy ($p > 0.05$). However, after colonoscopy, results revealed that serum levels of IgG, IgA, C3 andC4 in the observation group were significantly higher than those in the control group ($p < 0.05$).

## DISCUSSION

Dezocine-propofol, and fentanyl-propofol are two anesthetic combinations frequently used in painless colonoscopy. Propofol has a sedative effect, while both dezocine and fentanyl exert analgesic effects. Dezocine activates κ receptor in cerebral cortex, leading to slow onset and long duration of analgesia [3,7,8],

**Table 2:** Comparison of serum levels of inflammatory cytokines in the two groups of patients before and after colonoscopy examination (mean ± SD)

| Group | Time point | CRP (mg/L) | HSP70 (ng/mL) | IL-1β (ng/L) |
|---|---|---|---|---|
| Observation | Before | 2.95 ± 0.52 | 0.56 ± 0.08 | 5.68 ± 0.93 |
| | During | 3.41 ± 0.59 | 0.70 ± 0.09 | 6.61 ± 0.84 |
| | After | 4.29 ± 0.61* | 0.81 ± 0.11* | 7.93 ± 0.97* |
| Control | Before | 3.02 ± 0.47 | 0.52 ± 0.06 | 5.73 ± 0.88 |
| | During | 3.29 ± 0.61 | 0.72 ± 0.10 | 6.82 ± 0.92 |
| | After | 6.58 ± 0.94* | 1.21 ± 0.18* | 11.29 ± 1.86* |

*P < 0.05 when compared to the control group at the same time point*

**Table 3:** Serum levels of inflammation-related endocrine hormones before and after colonoscopy examination (mean ± SD)

| Group | Time point | ACTH (pmol/L) | Cor (nmol/L) | Ins (mIU/L) | C-P (ng/mL) |
|---|---|---|---|---|---|
| Observation | Before | 15.22 ± 2.35 | 265.21 ± 36.75 | 6.97 ± 0.95 | 0.52 ± 0.08 |
| | During | 18.95 ± 2.95 | 294.35 ± 42.19 | 7.71 ± 1.02 | 0.70 ± 0.11 |
| | After | 22.14 ± 4.82* | 362.52 ± 46.79* | 9.32 ± 1.16* | 0.83 ± 0.12* |
| Control | Before | 15.51 ± 1.95 | 266.31 ± 32.52 | 7.04 ± 0.85 | 0.55 ± 0.05 |
| | During | 19.25 ± 2.86 | 298.42 ± 42.86 | 7.93 ± 1.08 | 0.78 ± 0.10 |
| | After | 34.25 ± 6.85* | 478.49 ± 65.28* | 14.28 ± 1.86* | 1.21 ± 0.18* |

**P < 0.05 when compared to the control group at the same time point*

**Table 4:** Serum levels of humoral immune response molecules before and after colonoscopy examination (mean ± SD)

| Group | Time point | IgG (mg/L) | IgA (mg/L) | C3 (g/L) | C4 (g/L) |
|---|---|---|---|---|---|
| Observation | Before | 12.83 ± 1.62 | 26.48 ± 3.52 | 0.95 ± 0.12 | 0.64 ± 0.09 |
| | During | 12.17 ± 1.56 | 25.03 ± 3.26 | 0.91 ± 0.13 | 0.61 ± 0.10 |
| | After | 11.32 ± 1.95* | 23.47 ± 3.15* | 0.85 ± 0.09* | 0.55 ± 0.08* |
| Control | Before | 12.91 ± 1.88 | 26.91 ± 3.66 | 0.97 ± 0.14 | 0.65 ± 0.11 |
| | During | 12.08 ± 1.86 | 24.58 ± 3.16 | 0.90 ± 0.11 | 0.62 ± 0.08 |
| | After | 9.49 ± 1.28* | 20.12 ± 3.09* | 0.72 ± 0.09* | 0.42 ± 0.07* |

**P < 0.05 when compared to the control group at the same time point*

while fentanyl brings about fast onset but short-lived analgesia through activation of the μ and δ receptors in the central nervous system (CNS). Thus the use of fentanyl after colonoscopy examination is not ideal. Pain relief after inspection is an outstanding feature of painless colonoscopy [9].

Pain leads to secretion and release of some pain-associated neurotransmitters. Indole neurotransmitters such as 5-HTP and 5-HIAA are involved in amplification of pain sensation and pain signal transduction [10]. Substance P (SP) is a nerve fiber neuropeptide involved in the transmission of pain signals from the peripheral to the CNS [11]. PGE2, an inflammatory pain transmitter which functions at nerve endings, increases the sensitivity of nerve endings to pain stimulation, and also decreases pain threshold [12]. In order to compare the analgesic effects of the two anesthesia combinations, the present study analyzed the serum levels of pain mediators associated with their use before, during and after colonoscopy. The results showed that before and during colonoscopy, there were no statistically significant differences in 5-HTP, 5-HIAA, SP andPGE2between patients in the observation group and those in the control group. However, after colonoscopy inspection, serum contents of these pain mediators were significantly lower in the observation group when compared to the control group. This implies that the analgesic effect of dezocine-propofol combination after colonoscopy was superior to that of fentanyl-propofol combination.

Pain is associated with the activation of inflammatory reactions which are mediated by cytokines. Activation of inflammatory response results in release CRP, HSP70, IL-1β and other cytokines into the blood circulation. CRP is a liver-synthesized reactive protein released in the acute phase of inflammation. A variety of pro-inflammatory factors stimulate the synthesis and secretion of CRP. The extent of release of the latter is directly proportional to the degree of inflammation [13].

HSP70 is a member of the heat shock protein family which regulates the stability of intracellular peptides [14]. Its secretion is increased in response to inflammatory reactions [14]; IL-1β is an important pro-inflammatory mediator derived from mononuclear macrophages and lymphocytes. It mediates the amplification cascade of inflammatory reactions [15,16]. The results obtained in this study indicate that before and during colonoscopy inspection, there were no significant differences in the serum contents of CRP, HSP70 and IL-1βbetween the two groups. Interestingly, after colonoscopy, serum CRP, HSP70 and IL-1β levels in the observation group were significantly lower than corresponding values in the control group. This means that the extent of inflammation-associated cytokine release into the blood after colonoscopy was lower in the observation group than in the control group. This finding lends further credence to the superiority of the analgesic effect of dezocine-propofol combination over that of fentanyl-propofol combination.

The release of inflammatory cytokines is a direct manifestation of activation of inflammation reaction. Inflammatory reactions provoke abnormal hormone secretion and inhibition of immune response [17]. The HPA axis is an axis through which the endocrine glands respond to stress response. Studies have shown that stressors activate the HPA axis and increase the secretion of ACTH which acts on adrenal cortex and increases the secretion of Cor [18,19]. It has been reported that Cor can suppress the immune response to a certain extent, and it also influences the synthesis and secretion of IgG, IgA and C3 [20,21].

In the present study, there were no significant differences in serum levels of ACTH, Cor, Ins and C-P between patients in the observation group and those in the control group, before and during colonoscopy. However, after colonoscopy examination, results showed that these parameters were significantly lower in the serum samples from the observation group when compared to the control group. This indicates that, following colonoscopy, the dezocine-propofol combination elicited release of less inflammation-associated hormones than the fentanyl-propofol combination, which implies less inhibition of humoral immunity after colonoscopy. This view is supported by the higher levels of IgG, IgA, C3 and C4 levels in the observation group after the procedure. It also provides additional evidence for the superior analgesic effect of dezocine-propofol formulation over that of fentanyl-propofol combination.

## CONCLUSION

The results of serological analysis obtained in the present investigation suggest that after colonoscopy examination, the analgesic and anti-inflammatory effects of dezocine-propofol formula were superior to those of fentanyl-propofol combination. Thus, dezocine-propofol combination suppresses the secretion of pain mediators, relieve pain and improve immune response more effectively than fentanyl-propofol combination.

## DECLARATIONS

### *Acknowledgement*

None declared.

### *Conflict of Interest*

No conflict of interest associated with this work.

### *Contribution of Authors*

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.



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