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The Administration of Ketorolac in Reducing the Degree of Peritoneal Adhesion among Post Laparotomic Patients

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Abstract

The formation of permanent adhesion depends on the balance between pro-inflammatory and anti-inflammatory processes in which can be regulated through the admission of ketorolac. This study was conducted to obtain knowledge about the relationship between the administration of ketorolac and the degree of peritoneal adhesion in patients underwent laparotomy surgery. Comparative experimental case study by treating two groups that had been randomly selected by using randomized controlled trial method. Patients treated with ketorolac have a significant reduction in peritoneal adhesion occurrence with the mean value of adhesion score of 3.0333 as compared to the control group.

Keywords: Keterolac; analgesic; peritoneal adhesion, score

La Administración De Ketorolac Para Reducir El Grado De Adhesión Peritoneal Entre Pacientes Laparotómicos Posteriores

Resumen

La formación de adhesión permanente depende del equilibrio entre los procesos proinflamatorios y antiinflamatorios en los que se puede regular mediante la admisión de ketorolaco. Este estudio se realizó para obtener conocimiento sobre la relación entre la administración de ketorolaco y el grado de adhesión peritoneal en pacientes sometidos a cirugía de laparotomía. Estudio de caso experimental comparativo mediante el tratamiento de dos grupos que se seleccionaron al azar mediante el método de ensayo controlado aleatorio. Los pacientes tratados con ketorolaco tienen una reducción significativa en la aparición de adherencias peritoneales con el valor medio del puntaje de adhesión de 3.0333 en comparación con el grupo control.

Palabras clave: Keterolac; analgésico; adhesión peritoneal, puntaje

1. INTRODUCTION

Intraperitoneal adhesions are fibrous adhesions (connective tissue) that is abnormally formed between the adjacent peritoneum surfaces, either between the visceral peritoneum or between the visceral and parietal peritoneum (Thors and Drukker, 1997). In laparotomy surgical procedure, the risk for adhesion complications to

occur post-surgery can be up to 90% which causing emotional as well as financial burden for the patients (Barmparas et al., 2010).

In Western countries, peritoneal adhesion is the most prevalent cause of small bowel obstruction, which found in 64% to 79% of cases (Liakakos et al., 2010). The resulted morbidity and mortality due to the complications is high and consequently causes a number of severe effects. In term of management cost, United States spent as much as 1.18 million dollars in bearing the costs for adhesiolysis annually (Ray et al., 1998). Therefore, various efforts had been devoted for the past years in an effort to overcome this problem. A number of researches had been carried out in the last two decades to gain insight on the aetiopathogenesis and pathophysiology of peritoneal adhesion at both cellular and molecular level. Various studies have also been carried out to develop different types of drugs that can act as adjuvant therapy to prevent adhesion formation.

Histopathological studies show a clear sequence of events beginning from peritoneal injury to adhesion formation. Peritoneal inflammation leads to the formation of inflammatory exudates containing fibrin strands. The organisation of fibrin exudation and fibroblasts invasion are followed by collagen deposits and permanent formation of fibrous connective tissue. However, this process is not inevitable due to fibrinolytic activity of mesothelial tissue just like peritoneum which, if does not experience failure, will lyse fibrin in the inflammatory exudate organisation. The balance in these biological processes are important to determine when the permanent adhesion occurs after the peritoneal healing period has

ended (Ryan, Grobéty & Majno, 1971; Bellingan et al., 2002; Sulaiman et al., 2002).

Ketorolac tromethamine is one of the anti-inflammatory non-steroidal drugs which has analgesic effects and strong anti-inflammation properties (Rooks 2nd et al., 1985). It has been used since 1993 as postoperative analgesic effect equivalent of opium. Because of its anti-inflammatory effects, some researchers have studied the effects of the drug to prevent peritoneal adhesion in experimental animals. The porcine model study found differences in the mean adhesion between flatus intestinal loops and intrapelvic cavities after radical pelvic surgery when compared with the control groups (Montz, 1993). Nevertheless, the potential for ketorolac to prevent postoperative adhesion in humans with clinical trials has never been conducted before.

2. METHODOLOGY

The study population is the people living in South Sumatra and seek treatment at Digestive Surgery Department, Dr. Moh Hoesin General Hospital, and Palembang Indonesia. 62 patients were taken by consecutive sampling technique and were divided equally into the treatment and control group (Govindasamy et al, 2018). The treatment group was administered ketorolac post laparotomy surgery and the control group was given a pure analgesic drug without any anti-inflammatory properties, tramadol. The data collected were analyzed

using the SPSS 16.0 software to assess the significant association between ketorolac treatment and the occurrence of peritoneal adhesion. The occurrence of peritoneal adhesion was assessed according to Zuhlke-Lorenz gradation system where a score of 0-12 was used.

3. RESULTS and DISCUSSION

The patients were observed for a week post-surgery and the mean score for peritoneal adhesion were tabulated in Table 1 below:

Table 1: The differences in adhesion score between treatment and control groups

Group	Mean score	Std. Deviation	Std. Error	P value
Treatment	3.033	1.564	0.286	0.002
Control	6.375	2.882	0.5905	

The results show that the peritoneal adhesion mean score in the ketorolac-treated group is significantly lower ($p=0.002$, 95% significant at $p<0.5$) than in the control group. Thus, the results indicated that patients that were treated with anti-inflammatory analgesic drug have lower probability of contracting peritoneal adhesion as compared to patients without anti-inflammatory treatment.

The results of this study show that ketorolac treatment can also be used as clinical treatment in humans and thus supporting the

pioneer study conducted in animal model (Montz, 1993). Research by Carvalho et al., (2013) suggested that the reduction of adhesion score is mainly attributed to the changes in the level of interleukin-10, an anti-inflammatory cytokine. *Ketorolac tromethamine* is thought to increase the release of IL-10 and thus concomitantly preventing the occurrence of peritoneal adhesion. The mechanism for preventing ketorolac adhesion by ketorolac is related to its inhibitory effects on prostaglandin and bradykinin synthesis, which, in turn, results in reduced vascular permeability, PMN activation, neovascularization, fibroblast migration and proliferation as well as collagen production. Thus, the perioperative administration of ketorolac will act as double-sword treatment, one as the analgesic to reduce the pain as well as causing adhesions reduction past laparotomy surgery.

4. CONCLUSION

Ketorolac can act as an efficient pre-operative treatment drug for laparotomy surgery for its analgesic properties as well as its role in reducing the degree of peritoneal adhesion.

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