

# Effect Of Ketamine On Inflammatory Markers And Postoperative Analgesia In Patients Undergoing General Anaesthesia

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## Abstract

**Background:** Ketamine's anti-inflammatory effects appear to be mediated through an antagonism of nuclear factor-kappa B (NFkB). **Aims:** To know the anti-inflammatory role of ketamine for prevention of systemic inflammatory response and to study the effect of ketamine on postoperative analgesic requirements in patients undergoing surgery under general anaesthesia. **Settings and design:** The study was conducted on 60 patients of either sex, aged between 15 to 65 years belonging to ASA I and II undergoing abdominal surgery of <24 hours duration under general anaesthesia. **Methods:** Patients were randomized in two groups of 30 each by using computer generated random number table one group receiving low dose ketamine (0.25mg/kg) along with fentanyl prior to induction, and other receiving only fentanyl prior to induction, blood sample for inflammatory markers were collected before premedication and at the end of surgery, VAS score calculated at the end of surgery and amount of analgesic required within 24 hours was calculated. **Statistical Analysis:** Data were summarized as Mean  $\pm$  SE, The dependent (pre and post) observations (IL-6, IL-10 and CRP) of each group were compared separately by non parametric Wilcoxon matched pair (Z) test. The change (post-pre) in inflammatory markers, VAS scores and drug requirements of two independent groups were compared by non parametric Mann-Whitney U test. A two-sided ( $\alpha=2$ )  $p<0.05$  was considered statistically significant. **Results:** In both groups, the levels of IL-6 increases after the treatments but the increase was evident lower in Test group (8.2%) than Control group (23%). the levels of IL-10 increases after the treatments and the increase was evident higher in Test group (3.3%) than Control group (2.7%), the levels of CRP increases after the treatments and the increase was evident lower in Test group (4.7%) than Control group (12.4%). On comparing the VAS, U test revealed significantly different and lower (26.3%) pain in Test group as compared to Control group ( $5.97 \pm 0.21$  vs.  $4.40 \pm 0.20$ ,  $U=156.50$ ;  $p<0.0001$ ). On comparing the drug requirement, U test revealed significantly different and lower (37.1%) analgesic requirement in Test group as compared to Control group ( $206.67 \pm 10.65$  vs.  $130.00 \pm 9.77$ ,  $U=169.00$ ;  $p<0.0001$ ). **Conclusions:** Ketamine pretreatment may reduce inflammatory response to surgical trauma and may prevent auto-destruction of the host through secondary damage to tissues/organs not originally affected by the surgery; by reducing inflammation it also reduces postoperative pain and analgesics required and may help in postoperative pain management.

## INTRODUCTION

The systemic inflammatory response refers to an inflammatory process that can arise from or in the absence of infection. The systemic elaboration of inflammatory mediators may be beneficial by heightening the host

## METHODS

The study design was prospective, randomized control study. The present study was conducted on 60 patients of either sex, aged between 15 to 65 years belonging to ASA I and II undergoing abdominal surgery of < 2 hours duration

under general anaesthesia. Exclusion criteria was refusal for consent, contraindication for ketamine, patients on long term steroid therapy and patients with immune related disorder. All patients were properly assessed for medical illness and were premedicated with midazolam.

Patients were randomized in two groups of 30 each by using computer generated random number table with group I patient receiving low dose ketamine (0.25mg/kg) along with fentanyl prior to induction and group II patient receiving only fentanyl prior to induction and all were induced with propofol, succinylcholine and maintained on nitrous oxide, atracurium and halothane.

Two blood samples of 5ml each was taken before

premedication and at the end of surgery and degree of pain was calculated using visual analogue scale at the end of surgery. Post operatively injection tramadol IV 100mg was given as required and amount of analgesic required within 24 hours was calculated.

## RESULTS

### Inflammatory markers

1. IL-6- The effect of treatments on inflammatory marker IL-6 were shown graphically in Fig. 1. The levels of IL-6 increases after the treatments but the increase was evident lower in Test group (8.2%) than Control group (23%). On comparing the level of IL-6 at post from pre, Wilcoxon matched pairs (Z) test revealed that the levels of IL-6 in both Control group (164.43

## DISCUSSION

On statistical analysis patients randomized to a single small prophylactic dose of ketamine (0.25 mg/kg) exhibited statistically significantly lower serum IL-6 , CRP levels at the end of surgery. IL-10 levels were more elevated at the end of surgery in ketamine pretreatment group but the difference in elevation in both the groups were not statistically significant.

This finding is consistent with the study done by Roytblat et al. (2002) [1] in a study designed to assess the impact of low dose ketamine on serum IL-6 levels. In this study, patients randomized to a single small prophylactic dose of ketamine (0.25 mg/kg) exhibited statistically significantly lower serum IL-6 levels at the end of surgery and postoperatively. In a study done by Lange M et al. (2006) [2] on Role of ketamine in sepsis and systemic inflammatory response syndrome have shown that ketamine exerts anti inflammatory properties by inhibiting the release of pro inflammatory cytokines, such as tumor necrosis factor-alpha and interleukin-6. In addition, there is increasing evidence that early ketamine administration reduces mortality in experimental sepsis models. This is also consistent with our findings.

Yang Z et al (2006) [3] Studied Effects of subanesthetic dose of ketamine on perioperative serum cytokines in orthotopic liver transplantation and concluded that Ischemia and reperfusion injury of the liver and surgical stress induce pro- and anti-inflammatory cytokine responses during liver transplantation, in which event IL-6 and IL-10 are more sensitive than TNF-alpha. Ketamine can inhibit the production of TNF-alpha and IL-6 but not IL-10.

Taniquchi T et al (2003) [4] Studied Effects of ketamine and propofol on the ratio of interleukin-6 to interleukin-10 during endotoxemia and found that ketamine and propofol administration attenuated the increase in TNF-alpha, IL-6, and IL-10, and ketamine attenuated the increase in the ratio of IL-6 to IL-10. While the mechanisms responsible for the inhibitory effects require further investigation, results suggest that proper use of ketamine as an anesthetic agent may offer certain advantages in the management of patients with endotoxemia.

K.S. Helmer et al. (2003) [5] Study on Ketamine attenuates endotoxin-induced pro-inflammatory cytokine expression indicate that ketamine is capable of inhibiting LPS-induced expression of several pro-inflammatory cytokines without effecting LPS-induced expression of the anti-inflammatory cytokine IL-10. This suggests that ketamine may specifically down regulate the pro-inflammatory cascade while preserving up regulation of anti-inflammatory cytokines during endotoxemia. Moreover, ketamine may be beneficial to patients with impending bacteremia or in critically ill patients with endotoxin-induced inflammation.

Dale O et al (2012) [6] in there study

## CONCLUSION

Low dose ketamine (0.25mg/kg) pretreatment for patients undergoing general anaesthesia attenuates the rise in pro-inflammatory markers IL-6 and C Reactive Protein but maintains anti-inflammatory marker IL-10 to pretreatment levels and thus potentially has a role in reducing inflammation caused by surgical trauma. Postoperative pain and analgesics required postoperatively are also reduced, possibly due to reduced inflammatory response to surgical trauma.

Hence ketamine pretreatment may reduce inflammatory response to surgical trauma and may prevent autodestruction of the host through secondary damage to tissues/organs not originally affected by the surgery; by reducing inflammation it also reduces postoperative pain and analgesics required and may help in postoperative pain management.

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