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ORIGINAL RESEARCH

COMPARISON BETWEEN DEXMEDETOMIDINE AND PROPOFOL ON INTERLEUKIN-6 LEVELS IN PATIENTS WITH CHRONIC RHINOSINUSITIS UNDERGOING FUNCTIONAL ENDOSCOPIC SINUS SURGERY

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ABSTRACT

Background: Dexmedetomidine and propofol are expected to serve as intravenous anesthetic agents that reduce inflammatory factors in patients with chronic rhinosinusitis (CRS), particularly those undergoing functional endoscopic sinus surgery (FESS).

Aim: This study aims to compares dexmedetomidine and propofol before and after FESS.

Materials and Method: A quasi-experimental, cross-sectional, and analytical study was conducted involving patients with chronic rhinosinusitis (CRS) who underwent elective functional endoscopic sinus surgery (FESS) at Dr. Soetomo General Hospital, Surabaya, Indonesia. CRS patients scheduled for FESS were recruited for this study. Interleukin-6 (IL-6) levels were measured using ELISA 5 minutes after induction and 5 minutes before extubation. The Wilcoxon signed-rank test and Mann-Whitney test were used to determine changes in IL-6 levels before and after the procedure. A total of 24 CRS patients undergoing FESS were included in this study.

Results: The median IL-6 levels in the dexmedetomidine group before and after surgery were 20.24 ng/mL and 34.09 ng/mL, respectively, indicating a significant increase in IL-6 levels (p0.05).

Conclusion: There was a significant change in IL-6 levels in both the dexmedetomidine and propofol groups before and after surgery. However, there was no significant difference between dexmedetomidine and propofol in terms of changes in IL-6 levels among CRS patients undergoing FESS. Further studies are needed to evaluate the economic impact of using dexmedetomidine and propofol as controlled hypotensive agents in FESS procedures.

Keywords**:** CRS, FESS, Dexmedetomidine, Propofol, Interleukin-6.

INTRODUCTION

Chronic Rhinosinusitis (CRS) represents a commonly encountered health disorder affecting communities and represents a major health concern that affects 5% to 12% of the population at large. The European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) delineates the classification of rhinosinusitis based on clinical symptoms accompanied by signs of nasal mucosal inflammation based on endoscopic or radiological examination.[1] Health statistics reports in the United States in 2019 mentioned that all age groups can be affected with an incidence reaching 12.3% of the population. The impact of CRS affects the

community's economy with estimated costs of 10-13 billion dollars annually, so CRS places considerable health and financial responsibilities upon those affected encompassing the individual, family, community, and societal dimensions.[2]

Research conducted in the period 2016-2018 in the Rhinology Division, Department of ENT-HNS, Dr. Mohammad Hoesin Hospital Palembang found a proportion of CRS in adults of 33.3%. The average number of adult CRS patients in rhinology clinics over 3 years was 83.8% at Dr. M. Djamil Hospital Padang, 83.5% at Dr. Kariadi Hospital Semarang, 85.9% at Dr. Saiful Anwar Hospital Malang, 65.5% at Dr. Soetomo Hospital Surabaya, and 28.9% at Sanglah Hospital Bali. Another study conducted at Sanglah Hospital Bali in 2016 identified the largest group of CRS patients in the 46–60 year age range (37.7%).[3]

This chronic sinus disease causes inflammatory processes and is followed by increased inflammatory factors. An investigation by Marlina et al. found increased IL-6 levels in tissues of CRS patients without nasal polyps and also in CRS patients with nasal polyps.[4] The increase in IL-6 indicates that IL-6 plays a pathogenic role in CRS. Initial extrinsic aggression factors in CRS such as fungi, bacteria, and lipopolysaccharide (main outer membrane component of Gram-negative bacteria) cause increased IL-6 expression.[5]

Management of CRS cases includes medical treatment and surgical procedures. Variations range from simple procedures with simple equipment to surgery using sophisticated endoscopic equipment. Functional Endoscopic Sinus Surgery (FESS) is a sinus surgical procedure using endoscopic instruments. A staged approach in FESS provides good results, especially in CRS cases, and provides wide and safe access when handling structures outside the sinuses.[6]

FESS surgical procedures often require controlled hypotension techniques. Propofol and dexmedetomidine as anesthetic agents play important roles in achieving controlled hypotension techniques.[6] The use of dexmedetomidine in controlled hypotension techniques is increasingly becoming a choice. Dexmedetomidine itself, besides having the ability to provide hypotension, also has the capacity to inhibit excessive production of various inflammatory markers including TNF-α, IL-1β, and IL-6 in several studies on humans and animals. Dexmedetomidine provides anti-inflammatory effects in many neurological conditions by reducing neural inflammation.[7,8]

Propofol is an anesthetic agent most commonly used as general anesthesia. It can rapidly lowering BP and MAP.[9] Not only capable of rapidly lowering blood pressure, but propofol itself has the ability to inhibit the release of inflammatory factors. Findings reported by Jia et al. reveals that propofol can prevent inflammatory responses by reducing the release of cytokines and inflammatory mediators by inhibiting IL-6, IL-8, and TNF-α in RAW 264.7 cells stimulated by lipopolysaccharide.[10] The ability of dexmedetomidine and propofol to inhibit inflammatory factors aligns with therapeutic goals in patients with CRS. The use of dexmedetomidine in FESS surgery is expected to be very effective in achieving success in controlled hypotension while reducing inflammation in CRS. Therefore, this research becomes relevant to conduct so it can serve as a reference in providing appropriate anesthetic drug choices for surgical procedures and patient clinical conditions.

METHODS

Research Design

This research is a quasi-experimental study with cross-sectional data collection and analytical study approach. CRS patients undergoing FESS were grouped into two treatment conditions: dexmedetomidine group and propofol group.

Time and Location of Research

The research was conducted at the Integrated Central Surgery Building (GBPT) of Dr. Soetomo Hospital Surabaya. The research implementation time began in October 2024 and will continue until the planned sample size is met.

Research Population

The research population consists of patients with CRS undergoing FESS surgery at the Integrated Central Surgery Building (GBPT) of Dr. Soetomo Hospital Surabaya.

Research Sample

The research sample consists of patients with CRS undergoing FESS surgery at the Integrated Central Surgery Building (GBPT) of Dr. Soetomo Hospital Surabaya who meet the research criteria. Sampling was obtained from patients who met inclusion criteria and were selected consecutively according to the research implementation time.

Sample size determination used the formula.[11] Sampling technique used random allocation from previous research examining the use of propofol in reducing IL-6 levels[12], resulting in a minimum total sample of 11 people in each group. Considering the possibility of dropouts, each group was increased by 10%, resulting in a sample of 24 people with 12 people in each group.

Inclusion and Exclusion Criteria

1) Inclusion Criteria:
   a. Patient age between 18-65 years
   b. Patient physical status according to American Society of Anesthesiologists (ASA) class I or II
   c. Patients with written consent
2) Exclusion Criteria:
   a. Patients with a history of allergy to dexmedetomidine and propofol
   b. Obese patients with BMI more than 30
   c. Patients with uncontrolled hypertension, history of heart disease, and stroke
   d. Pregnant or nursing women
3) Drop-out Criteria:
   a. Patients who experience intolerance to dexmedetomidine and propofol drugs used during surgery
   b. Patients with blood pressure drop to shock requiring vasopressors until end of surgery.
   c. Patients who choose to withdraw from the research or cannot continue their participation

Research Variables

The research variables consisted of the independent variable, namely the anesthetic agent, and the dependent variable, namely interleukin-6.

Research Data Collection Method

Patients with CRS planned for elective FESS surgery at GBPT Dr. Soetomo Hospital Surabaya under general anesthesia who meet inclusion and exclusion criteria were taken as samples. IL-6 examination in blood was performed 5 minutes after induction and 5 minutes before extubation.

Data Processing and Analysis Techniques

Collected data was recorded and tabulated. Data processing in this research used applications. All demographic characteristic data (age, gender, etc.) were summarized using descriptive statistics. All measurement data were expressed as mean ± standard deviation. Statistical tests used in this research were:

a. Paired difference test: To differentiate changes in IL-6 levels before induction and after extubation in the dexmedetomidine group and propofol group. If data was normally distributed, tested with Paired T Test; when normality is not met, with Wilcoxon Signed Rank Test.
b. Group mean difference test: To compare mean changes in IL-6 levels between dexmedetomidine and propofol groups. When normality was satisfied, independent t-test applied; when normality is not met, Mann Whitney test hence adopted.

Ethical Considerations

All data in this research are confidential and will be used solely for scientific purposes. Patients and their families were provided with explanations regarding the objectives of the study, and those willing to participate were asked to sign a written informed consent form. Ethical clearance for this research will be obtained from the Ethics Committee of the Faculty of Medicine, Airlangga University/ Dr. Soetomo General Hospital.

RESULTS

Patient Characteristics

Patient characteristics are displayed according to the type of data available. For categorical (nominal) and ordinal data, they are presented as frequency and percentage. While numerical data on ratio and interval scales are displayed as mean ± standard deviation if normality test results show normal results, and if not normal, in median (range) form. Range is the display of minimal – maximal data.

Table 1. Patient Characteristics

Characteristic	Number (n) People	Percent (%) Mean ± SD (Kg/m²)
Gender		
Male	6	25
Female	18	75
Age (years)		
18-25	8	33,3
26-33	7	29,2
34-41	2	8,3
42-49	2	8,3
50-57	1	4,1
58-65	1	4,1
PS ASA		
PS ASA 1	2	8,3
PS ASA 2	22	91,7
BMI	24	23,46 ± 4,72

Research results show gender proportion dominated by females with a total of 18 (75%), with the majority ASA PS being ASA PS 2, namely 22 patients (91%). Patient demographic description based on age obtained 4 people or 16.7% of patients aged <20 years, 7 people or 29.2% of patients aged 21-30 years, 7 people or 29.2% of patients aged 31-40 years, 4 people or 16.7% of patients aged 41-50 years, and 2 people or 8.3% of patients aged >50 years.

Interleukin 6 Level Measurement Results

The first step in analyzing IL-6 level results was assessing sample distribution using normality test techniques. Normality test is testing to determine research data distribution, whether normally distributed or not. Testing was performed using the Shapiro-Wilk test with the following results.

Table 2. Interleukin-6 Normality Test Results

Group	p	Note
Pre dexmedetomidine	0.005	Not normally distributed
Post dexmedetomidine	0.000	Not normally distributed
Pre propofol	0.068	Normally distributed
Post propofol	0.054	Normally distributed

Note: Significance p< 0.05

Normality test results for IL-6 levels in the dexmedetomidine group in pre-test and post-test testing obtained significance values less than 0.05 (p < 0.05), so IL-6 level data in the dexmedetomidine group was not normally distributed. Additionally, normality test results for IL-6 levels in the propofol group in pre-test and post-test testing obtained significance values greater than 0.05 (p > 0.05), so IL-6 level data in the propofol group was normally distributed.

Table 3. IL-6 Level Description Results for Dexmedetomidine Group

Group	n	Median (ng/L)	Minimum-Maximum (ng/L)
Pre dexmedetomidine	12	20.24	3.75-109.16
Post dexmedetomidine	12	34.09	16.93 – 164.27

Note: n: number of samples

IL-6 level measurement results in the dexmedetomidine group before treatment (pre dexmedetomidine) obtained a median value of 20.24 ng/L, then after treatment (post dexmedetomidine) obtained a median value of 34.09 ng/L (45.584% increase). These results show that after dexmedetomidine administration, patients' IL-6 levels increased.

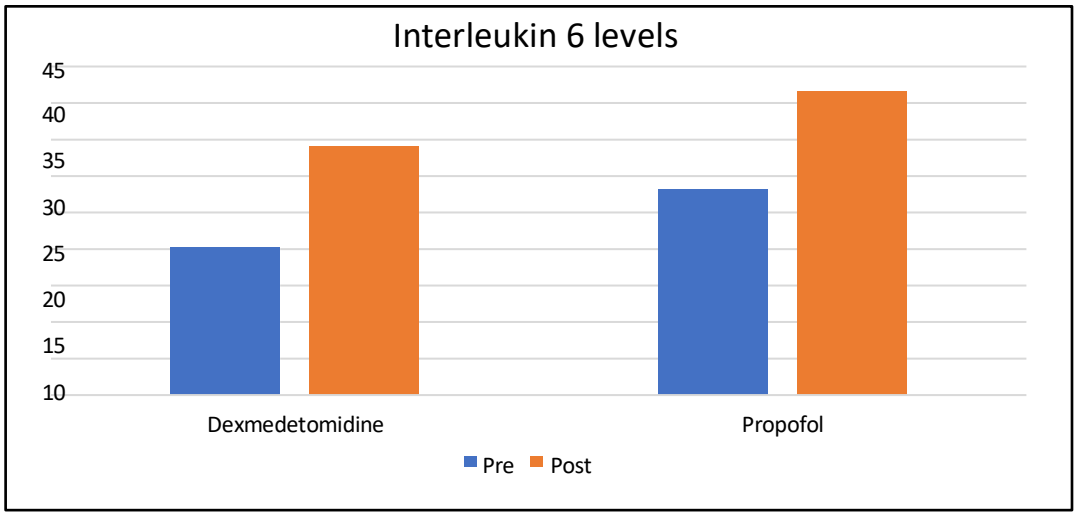

Figure 1. Mean IL-6 Levels of Patients Pre-Operation and Post-Operation

Table 4. IL-6 Level Description Results for Propofol Group

Test	n	Mean (ng/L)	SD (ng/L)
Pre propofol	12	28.157	18.318
Post propofol	12	41.646	25.779

Note: n: number of samples; SD: standard deviation

IL-6 level measurement results in the propofol group before treatment (pre propofol) obtained an average of 28.157 ng/L with a standard deviation of 18.318, then after treatment (post propofol) obtained an average of 41.646 ng/L with a standard deviation of 25.779. These results show that after propofol administration, patients' IL-6 levels increased.

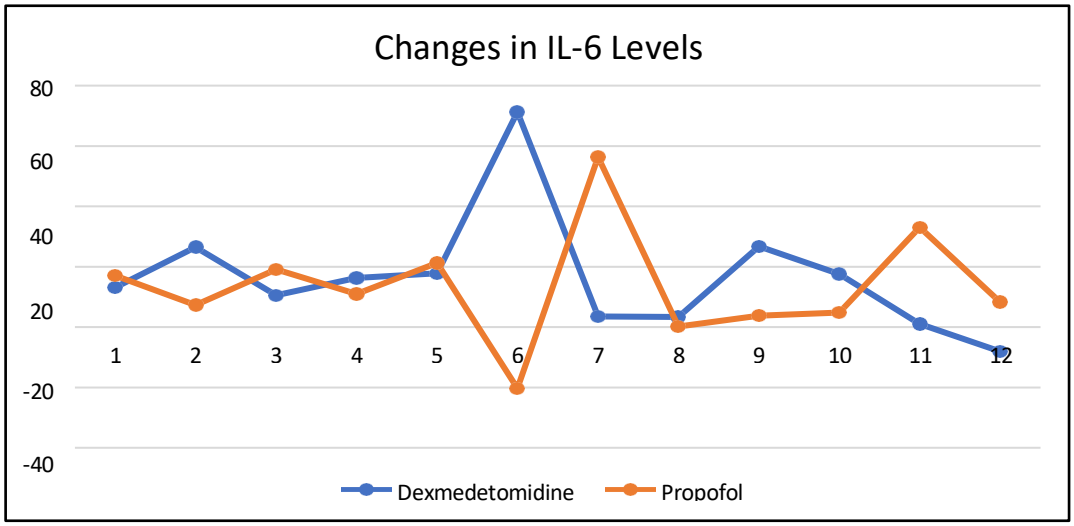

Figure 2. Changes in IL-6 levels after dexmedetomidine and propofol administration

Measurement results in each group showed changes in IL-6 levels after drug administration (can be seen in Figure 2). There was an increase in IL-6 levels in both treatment groups. However, in the dexmedetomidine group, only 1 sample experienced a decrease in IL-6 levels, while in the propofol group, 1 sample also experienced a decrease in IL-6 levels.

Effects of Dexmedetomidine and Propofol Administration on IL-6 Levels

To determine the effect of drug administration on IL-6 levels, paired comparison tests and inter-group comparison tests were needed. Paired comparison test is testing to compare data before treatment (pre) and after treatment (post). Test results are presented as follows.

Table 5. Paired Comparison Test Results

Dexmedetomidine Group			Propofol Group		
n	Median (ng/L) (Minimum- Maximum)	p	n	Mean ± SD (ng/L)	p
12	13,85 (1,033-71,259)	0,006	12	13.4 ± 5,4	0,030

Note: n: number of samples; SD: Standard deviation; Significance p<0.05

IL-6 level comparison results before treatment (pre) and after treatment (post) in the dexmedetomidine group using the Wilcoxon test obtained a significance value (p) of 0.006. These results show a significance value less than 0.05 ($p < 0.05$), so it was stated that there was an increase in IL-6 levels after dexmedetomidine administration. Moreover, IL-6 level comparison results before treatment (pre) and after treatment (post) in the propofol group using paired sample t-test obtained a significance value (p) of 0.030. These results show a significance value less than 0.05 ($p < 0.05$), so it was stated that there was an increase in IL-6 levels after propofol administration.

Inter-group comparison test is testing to compare data between the dexmedetomidine group and the propofol group. Test results are presented as follows.

Table 6. Inter-Group Comparison Test Results

Group	n	Mean ± SD (ng/L)	p	Note
Pre (dexmedetomidine + propofol)	24 (12+12)	12.58	0.954	Not significant
Post (dexmedetomidine + propofol)	24 (12+12)	12.42	0.954	Not significant

Note: n: number of samples; SD: standard deviation; Significance p <0.05

IL-6 level comparison results between the dexmedetomidine group and propofol group before treatment (pre) using the Mann-Whitney test obtained a significance value (p) of 0.954. A significance value above 0.05 confirmed the absence of meaningful differences within the dexmedetomidine and propofol groups at the pre-treatment stage. Additionally, IL-6 level comparison results between the dexmedetomidine group and propofol group after treatment (post) using the Mann-Whitney test obtained a significance value (p) of 0.954. Likewise, a significance value exceeds 0.05 confirmed the absence of significant differences between the dexmedetomidine and propofol groups at the post-treatment stage.

DISCUSSION

CRS Demographics

CRS is a clinical condition of persistent inflammation of the nasal mucosa and paranasal sinuses, lasting 12 weeks or more.[13] Data collected by EPOS in 2020 found a fairly high prevalence of CRS annually with 13-16% incidence each year[1], while at Dr. Soetomo Hospital, control patients at the polyclinic with CRS each year were 65.5% of all patient visits at the ENT-HNS polyclinic.[14]

Young adult age (21-40 years) was the most common age suffering from CRS undergoing FESS surgery in this study, namely 14 patients (58.3%). Different from international epidemiological studies showing a clear correlation between age and chronic rhinosinusitis prevalence. Research shows that chronic rhinosinusitis with nasal polyps is rarely diagnosed at a young age, and CRS prevalence increases sharply after age 50. A very significant finding is that patients aged 60 years and above have twice the risk of experiencing CRS compared to the 19-39 year age group.[15] Meanwhile, studies conducted at various hospitals in Indonesia show different age distribution patterns from global findings, although they still show a relationship between age and chronic rhinosinusitis incidence. Research at Royal Prima Hospital Medan shows that the largest age group affected by CRS is 20–29 years (28.4%). Meanwhile, studies at Zainoel Abidin Hospital Banda Aceh found the highest distribution in the 36–45 year age group (22.69%).[16] Investigations carried out at Dr. Mohammad Hoesin Hospital Palembang shows the highest prevalence in the 46–53 year age group (21.2%), while another study at the same hospital in a different period found the highest distribution in the 37–47 and 48–58 year age groups (21.6% each).[17] Studies at Dr. Soetomo Hospital Surabaya found the highest distribution in the age 18-55 year age group (93.48%).[18]

Women were found to be higher than men in this study with a ratio of 1:3 (75% women and 25% men). A number of prior studies have likewise found higher CRS prevalence in women. For example, research at Dr. M. Djamil Hospital Padang showed 56% female patients and 44% male patients.[19] Studies at RSPAL Dr. Ramelan Surabaya also reported a majority of female patients (76.66%) compared to male patients (23.33%).[20] Research in Medan and Banda Aceh also showed higher female proportions, namely 56.3% and 56.12% compared to males 43.8% and 43.88%.[21] Hormonal changes in women can affect the body's response to inflammation and infection, including more active immune responses compared to men, which can cause chronic inflammatory reactions to occur more frequently in the upper respiratory tract, so hormones become one of the factors causing higher CRS incidence rates in women compared to men.[22]

Changes in Interleukin 6 Levels with Dexmedetomidine Administration

Changes in IL-6 levels were found in 24 research samples. There was a statistically significant increase in IL-6 levels in the dexmedetomidine group (Wilcoxon test, p = 0.006) after intervention.

Currently, there are no studies specifically examining the effect of dexmedetomidine on IL-6 levels in patients undergoing FESS. There is a relationship between IL-6 and dexmedetomidine use in other types of surgery, as shown in the work of Munawar et al.[23] about the difference between dexmedetomidine and the combination of fentanyl and midazolam in craniotomy patients, showing that both can reduce IL-6 levels at 6 to 12 hours post-surgery which found decreased IL-6 levels. Nevertheless, both groups showed increased IL-6 levels immediately after surgery completion. The study by Munawar et al.[23] aligns closely with the present research, namely the combination of dexmedetomidine and fentanyl. However, it differs in the type of surgery. Dexmedetomidine has neuroprotective effects[24], so its use in craniotomy

surgery in his research becomes relevant.[23]

A meta-analysis by Lei et al.[25] on 1,400 patients showed that dexmedetomidine reduced IL-6 levels on the first post-surgical day, which correlated with reduced risk of cognitive dysfunction through neuroinflammation inhibition. A further study by Youssef et al.[26] evaluated the effects of intravenous dexmedetomidine infusion on 50 patients aged 18–70 years undergoing open heart surgery with cardiopulmonary bypass (CPB). Research results showed that the dexmedetomidine group experienced significant suppression of intraoperative and post-surgical IL-6 level increases (13.69 ± 1.03 pg/mL vs. 32.11 ± 0.98 pg/mL in the placebo group; P<0.0001). However, another research found increases occurred. M. Liu et al.[27] through their research comparing dexmedetomidine with midazolam in laparotomy patients, found that serum IL-6 levels 24 hours post-surgery were significantly higher in the dexmedetomidine group (45.2 pg/mL) compared to midazolam (32.1 pg/mL; $p < 0.05$). The proposed mechanism relates to α_2-adrenergic receptor activation that modulates stress responses through NF-κB and MAPK pathways differently, increasing pro-inflammatory cytokine production.

Interleukin-6 reaches peak concentrations 6–12 hours post-surgical trauma and remains elevated up to 48–72 hours, depending on the extent of tissue damage and procedure complexity.[25] Dexmedetomidine, an α2-adrenergic agonist with an elimination half-life of 2–3 hours, shows pharmacokinetic limitations in suppressing IL-6 production during the prolonged post-surgical phase.[26] Studies in craniotomy patients revealed that significant IL-6 level reduction by dexmedetomidine was only observed at 12–24 hours post-surgery ($p < 0.05$), while measurements within the first 6 hours still showed significant elevation (145.2 ± 32.1 pg/mL vs. 89.5 ± 28.7 pg/mL). This phenomenon is caused by dexmedetomidine's shorter duration of action compared to IL-6's biological half-life, so its anti-inflammatory effects do not cover the entire period of post-surgical trauma cytokine production.[23]

In other major surgical procedures such as esophagectomy, IL-6 levels in thoracic drainage fluid were reported to reach 100 times higher than peripheral serum levels, caused by IL-6 release from tissues experiencing ischemia-reperfusion and endothelial cell damage. Although clinical doses of dexmedetomidine (0.2–0.7 μg/kg/hour) show anti-inflammatory effects, their short pharmacokinetics (2–3 hour half-life) and limitations in suppressing massive IL-6 production after severe surgical trauma can reduce their efficacy in balancing cytokine outcomes.[28]

Another factor that can influence IL-6 level increases is hyperglycemia conditions. In vitro studies show that dexmedetomidine significantly inhibits interleukin-1β (IL-1β)-induced IL-6 synthesis in C6 glial cells, but is ineffective against TNF-α-mediated IL-6 production.[29] In diabetic patients, hyperglycemia increases NADPH oxidase 2 (Nox2) expression and oxidative stress, which then stimulates IL-6 production independently from α2-adrenergic pathways, so dexmedetomidine's anti-inflammatory effects become limited under severe oxidative stress conditions.[30]

IL-6 inhibition by dexmedetomidine triggers compensatory increases in IL-8 and TNF-α, which activate NF-κB to re-stimulate IL-6 production. A study combining dexmedetomidine with TLR4 antagonist (resatorvid) in cerebral ischemia models showed more effective IL-6 suppression (42.3 ± 5.1 pg/mL vs. 68.7 ± 6.9 pg/mL; $p < 0.05$) compared to monotherapy.[31] This shows alternative inflammatory pathways (TLR4/MyD88) resistant to α2-adrenergic agonists.[29]

Short duration of dexmedetomidine administration, only during surgery (1-2 hours), can be one cause of failure to reduce post-surgical IL-6 levels. Low-dose dexmedetomidine infusion (0.2–0.4 μg/kg/hour) for 24–48 hours post-surgery is recommended to maintain optimal IL-6 suppression. A study in major abdominal surgery patients showed that this regimen reduced IL-6 levels from 89.7 ± 15.2 pg/mL to 54.6 ± 12.3 pg/mL ($p < 0.001$) within 48 hours, with bradycardia risk (heart rate <50 bpm) only 4.8% compared to 18.3% at doses >0.7 μg/kg/hour.[32] Linear dexmedetomidine pharmacokinetics allows gradual accumulation to maintain stable plasma concentrations (8–12 ng/mL), needed to continuously inhibit NF-κB pathways. Infusion duration >24 hours also increases α2-adrenergic receptor availability in monocyte cell membranes, prolonging anti-inflammatory effects without increasing hypotension risk (OR = 0.7; 95% CI: 0.5–0.9).[5]

Changes in Interleukin 6 Levels with Propofol Administration

Changes in IL-6 levels were found in 24 research samples. Evidence pointed to a statistically meaningful increase in IL-6 levels in the propofol group (paired t-test, $p = 0.030$) after intervention. Until now, there is still no research specifically examining the effect of propofol on Interleukin-6 (IL-6) levels in patients undergoing FESS surgery. However, there is research examining propofol's effects on IL-6 level changes in patients undergoing craniotomy. The findings reported by Priambodo et al.[33] explored the comparative influence of propofol and sevoflurane on IL-6 levels and neutrophil counts

in patients undergoing craniotomy procedures. This study was experimental research with a randomized controlled approach on two patient groups receiving anesthesia with propofol or sevoflurane respectively. The outcomes suggested that IL-6 levels increased in both groups post-surgery, but this increase was more significant in the propofol group compared to the sevoflurane group. The evidence lends support to the notion that propofol can trigger higher systemic inflammatory responses compared to sevoflurane in neurosurgery contexts.[33] This is similar to our research findings that the propofol group experienced increased IL-6 levels after FESS surgery.

Propofol's effects on post-surgical IL-6 levels vary depending on the type of surgical procedure, surgery duration, and patient immune response.[34] The largest meta-analysis (n=1,611 patients) showed that propofol significantly reduced systemic IL-6 levels in breast cancer surgery (SMD = -3.09; 95% CI: -5.70 to -0.48; p = 0.021) compared to inhalation anesthesia.[35]

Another inquiries uncover that propofol inhibited IL-6 expression up to 3.09 pg/mL (p = 0.021) in HER2-positive breast cancer cells by suppressing NF-κB pathways and increasing miR-149-5p expression, which targets the IL-6 gene epigenetically.[36] This mechanism reduced cancer cell proliferation by 40% (p < 0.001) and inhibited mammosphere formation, a metastasis potential indicator. In a retrospective clinical with n = 2,645, breast cancer patients receiving Total Intravenous Anesthesia (TIVA) with propofol had 10% higher 2-year recurrence-free survival (RR = 1.10; 95% CI: 1.00–1.20) compared to inhalation anesthesia.[37] Propofol also reduced vascular endothelial growth factor (VEGF) levels up to 30% (p < 0.05) by inhibiting cyclooxygenase-2 (COX-2) activity, thus reducing angiogenesis and tumor cell invasion. These antitumor effects were consistently observed in colorectal and hepatocellular cancer surgeries, where propofol reduced systemic IL-6 by 58% (p = 0.003) and reduced post-surgical metastasis incidence by 22% (OR = 0.78; 95% CI: 0.65–0.94). This recommendation is supported by a meta-analysis conducted by Lee with n = 1,611 concluding that propofol increases overall survival in cancer patients (HR = 0.82; 95% CI: 0.75–0.90) compared to volatile anesthesia.[34] All these findings support propofol's role in suppressing IL-6 inflammatory factors.[34]

Fekkes et al. conducted prospective observational studies on 28 patients undergoing abdominal hysterectomy (n=14) or vulvectomy (n=14) to evaluate the relationship between intravenous propofol administration and perioperative interleukin-6 (IL-6) levels.[38] Research results showed significant differences in post-surgical IL-6 concentrations between both groups: IL-6 levels at surgery completion were statistically higher in the hysterectomy group. In their research, they concluded that inflammatory responses measured through IL-6 were more influenced by procedure invasiveness (shown by significant differences between hysterectomy and vulvectomy) and surgery duration, not by propofol anesthetic regimens.[38] This shows significant positive correlation between surgery duration and post-surgical interleukin-6 (IL-6) level increases, with correlation coefficients r = 0.554–0.773 (p < 0.01). Propofol's anti-inflammatory effects become more significant in surgical procedures >2 hours through mechanisms inhibiting IL-6 mRNA expression and Nrf2 pathway activation, which requires longer exposure time to achieve optimal therapeutic effects.[38]

A prospective double-blind study by Roh et al. on 50 patients undergoing robot-assisted laparoscopic radical prostatectomy (RALRP) found that the propofol group (n=25) showed significantly lower IL-6 level increases during and after pneumoperitoneum compared to the desflurane group (n=25).[39] Serum IL-6 measurements were performed at 10 minutes after anesthesia induction (T1), 100 minutes after CO2 insufflation (T2), and 10 minutes after CO2 deflation (T3). Results showed IL-6 increases of 38.6 pg/mL in the desflurane group versus 14.56 pg/mL in the propofol group (p<0.05) at T3, with significantly higher intraoperative urine output ratios in the propofol group (0.9±0.3 vs 0.6±0.2 mL/kg/hour; p<0.01). This study concluded that IL-6 will still increase with propofol use, but propofol selectively suppresses inflammatory responses through mechanisms inhibiting IL-6 production by macrophages and regulating intracellular calcium signaling pathways, without affecting other inflammatory parameters such as TNF-α or CRP.[39]

A prospective randomized double-blind study by Lleshi et al. on 40 breast surgery patients showed that the Target Control Infusion-Total Intravenous Anesthesia (TCI-TIVA) group experienced significantly lower interleukin-6 (IL-6) level increases 24 hours post-surgery (14.56 pg/mL) compared to the Sevoflurane Inhalation Anesthesia (SIA) group (36.34 pg/mL; p < 0.05).[40] IL-6 measurements were performed at four times: before induction (T0), during surgery (T1-T2), and 24 hours post-surgery (T3), with statistical analysis using paired t-tests and repeated ANOVA. Researchers associated this difference with propofol's anti-inflammatory effects in TCI-TIVA that inhibit cortisol release and pro-inflammatory cytokine production through pre-translational suppression

mechanisms, while sevoflurane inhalation anesthesia potentially triggers stress responses and systemic inflammation through NF-κB pathway activation.[40]

Different from several other studies, high post-surgical IL-6 levels were found to correlate with factors such as surgical procedure length and intraoperative bleeding volume. A study by Rettig et al. evaluated changes in IL-6 levels in patients undergoing major gastrointestinal surgery.[32] This research showed that IL-6 levels increased significantly within the first six hours after surgery and peaked within 24 hours. This study concluded that IL-6 can be used as a sensitive biomarker to assess surgical stress levels and post-surgical inflammatory responses, and potentially predict complication risks.[32]

Based on this analysis, dexmedetomidine has the potential to reduce inflammation levels 24 hours post-surgery. However, IL-6 levels will still increase in the first 6 hours. Dexmedetomidine's effects on IL-6 levels are influenced by dexmedetomidine's shorter duration of action compared to IL-6's biological half-life and the time of peak IL-6 release into systemic circulation. Additionally, surgery duration also determines IL-6 level changes. Short duration of dexmedetomidine exposure causes failure in reducing post-surgical IL-6 levels. Similarly, with propofol, this drug has the potential to reduce post-surgical IL-6 levels in several types of surgical procedures, although its effects are not consistent in all clinical conditions. Propofol's effects on IL-6 levels can be influenced by various factors such as surgery type, surgical duration, administration timing, dose, and individual patient factors. Long surgical duration will cause exposure to surgical stress and extensive trauma areas that can affect IL-6 level changes. Similarly with long propofol exposure duration, in relatively short surgery duration, patient exposure to propofol is also lower, which can cause IL-6 level increases.

Comparison of Dexmedetomidine with Propofol on Interleukin 6 Level Changes

In this research, no meaningful variation was detected in IL-6 level changes between the dexmedetomidine and propofol groups. When inter-group comparisons were performed, both groups showed IL-6 level changes before and after intervention that were not statistically different. This is similar to research conducted by Munawar et al. comparing the effects of dexmedetomidine with propofol on interleukin-6 (IL-6) levels in critical patients, the findings did not differ significantly in IL-6 level reduction after 24 hours of both drug administration.[23] Nevertheless, dexmedetomidine tended to provide additional benefits in the form of reduced mechanical ventilation duration and ICU stay length.[23] The limitations of this research include the absence of a control group, as the study only examined treatment drug groups. As such, it is not possible to determine whether one drug or both are effective in reducing or suppressing the production of interleukin-6 levels. In addition, the sampling was limited to only two time points, which prevents a comprehensive description of the interleukin-6 level reduction process under single-drug treatment.

CONCLUSION

Changes in IL-6 levels were observed in chronic rhinosinusitis (CRS) patients before and after functional endoscopic sinus surgery (FESS) with the use of either dexmedetomidine or propofol. However, no notable difference in IL-6 levels was found among the two anesthetic agents in CRS patients undergoing FESS. Both dexmedetomidine and propofol may be considered suitable agents for controlled hypotension in FESS procedures. Further research is recommended to examine the economic impact of using these agents in such surgical settings.

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Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable.

Competing interests

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