Soluble IL-2R levels in patients receiving general anesthesia

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Interleukin-2 (IL-2) exerts its effect on cells of the immune system through a cell membrane receptor designated as Interleukin-2 receptor (IL-2R). Increase of the soluble form of this receptor (sIL-2R) may cause alterations in the immune system. General anesthesia has been shown to induce some changes in the immune system of the patient which may be detrimental. This study included 25 patients that underwent general anesthesia. sIL-2R levels were measured by ELISA before, during and after gent, -at anesthesia. This study demonstrated that sIL-2R levels decreased markedly after general anesthesia (p=0.001). This may be the major factor contributing to the changes in immune system during general anesthesia. [Turk J Med Res 1995, 13(3): 116-118]

Human interleukin-2 is a glycosylated protein mainly synthesized from active T cells and large granular lymphocytes and act on activated T cells, B cells, natural killer cells; causing these cells to differentiate and proliferate (1). It also has an important role in lymphokine activated tumor necrosis factor and interferon gamma. To exert its effect IL-2 must interact with specific cell membrane IL-2 receptor. Activated peripheral T cells, B cells and monocytes release a soluble form of IL-2R (1). Increased levels of this receptor may bind IL-2 and block the binding of IL-2 to membrane receptors of lymphocytes. The increased serum IL-2R levels may account for the immune dysfunction observed in such patients. Also increased levels of sIL-2R have been found in various malignant and non malignant disorders and may reflect disease activity (2). A decrease in the levels of SIL-2R can reflect a down regulation of the IL-2R on the effector cells of the immune system thus reflecting a state of hyporesponsiveness of the Immune system (1,3). General anesthesia and surgery may interact with Immune system and may be hazardous for both the patient and the anesthetist. Anesthesia and/or the stress of surgery has been shown to be associated with decreased lymphocyte recirculation, decreased lymphocyte responsiveness to mitogens and microbial agents, decreased delayed hypersensitivity, decreased natural killer activity, decreased mixed lymphocyte responses and enhanced antibody responses (4-10). These can cause a transient immunodepression that may contribute to the propagation of infection, impairment of wound healing and spread or growth of malignancies (5). Either the disturbance of neuroendocrine homeostasis or direct toxic effect of the anesthetic agents on the cells of the immune system may cause these disturbances (4-6). The alteration of the Immune defenses due to chronic exposure to anesthetics can explain the increased frequency of malignancies among operating room personnel (5,10).

In this study, we measured SIL-2R levels in patients receiving general anesthesia to see if sIL-2R can be the cause of most of the alterations in the immune system described above.

MATERIALS AND METHODS

Patients: The study included 25 patients who received general anesthesia. Informed consent was obtained from all patients. Care was taken not to include the patients with malignant, immune and infectious disorders. Characteristics of the patients are summarized in Table 1.

General anesthesia: 10 mg of Diazepam and 0.5 mg of atropine were administered intramuscularly for premedication, one hour before the operation. Following pre oxygenation, anesthesia was induced intra-

Table **1-** Patient characteristics
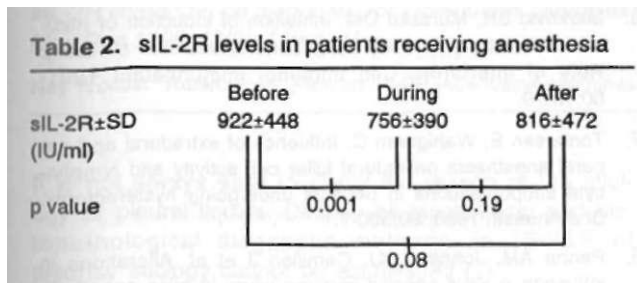
Age (median): 41 (55-66)
Sex: M: 10 F: 15
Surgical intervention and underlying disorder (n):
  •Thyroidectomy
    Euthyroid diffuse goiter (3)
    Nodular goiter (4)
•Cholecycstectomy
    Cholelithiasis (6)
•Mactectomy
    Benign mass (2)
    Fibrocystic disease (1)
    Gynecomastia (1)
•Reconstructive surgery
    Postoperatory hernia (2)
    Vesicoureteral reflux (3)
•Cystectomy
    Cyst Hydatic(1)
•Gastroduodenostomy
    Peptic ulcer (1)
•Nephrolithiasis (1)
Median duration of general anesthesia: 60 minutes (35-120)

Table 2. sIL-2R levels in patients receiving anesthesia

	Before	During	After
sIL-2R±SD (IU/ml)	922±448	756±390	816±472
p value		0.001	0.19
		0.08	

venously with thiopentone (5 mg/kg) followed by tracheal intubation after administering succinylcholine (1 mg/kg). Anesthesia was maintained with 50% nitrous oxide in 50% oxygen and isoflurane (1MAC). Supplementary doses of succinylcholine were given according to the clinical needs of the patients.

Blood Collection: Three consecutive blood samples were obtained from each patient, first half an hour before general anesthesia in the preoperation ward, second after general anesthesia but before first surgical incision and third when the patient was in the recovery room and responding to outer stimuli. All sera was stored at -30°C before assay. sIL-2R levels from

serum were measured by ELISA (T Cell Sciences, Cambridge, USA). All samples were run in duplicate.

Statistical analysis: Patient characteristics are described in medians where possible. All other results are mean values. The probability of existence of significant differences when groups were compared was determined by unpaired Student's t test using a statistical software. Intragroup analysis was done by paired t test. P<0.05 was considered significant.

RESULTS

Statistical analysis revealed a significant decrease in serum sIL-2R levels obtained before induction of general anesthesia and after general anesthesia. SIL-2R decreased from a mean of 922 IU/ml to 756 IU/ml (p=0.001) after the induction of general anesthesia. There was no difference between the mean levels of sIL-2R obtained after general anesthesia (756 IU/ml) and the levels obtained in the recovery room (816 IU/ml) (p-0.19). Also the difference between sIL-2R levels obtained before general anesthesia and levels obtained in the recovery room were not significantly different (p=0.08) (Table 2). To see if the duration of general anesthesia had an effect on SIL-2R levels, patients were divided into two groups. First group consisted of patients receiving general anesthesia for less than 60 minutes. Second group consisted of patients receiving general anesthesia for more than 60 minutes. If the duration of the anesthesia was long the decrease in sIL-2R levels was more impressive but this may be the result of lower levels of initial sIL-2R levels in this group. Although the patients in these two groups were similar in respect to age, diagnosis and type of anesthesia received, preanesthesia sIL-2R levels were slightly different (p=0.04). This difference was constant during and following anesthesia. Intragroup analysis of two groups showed no difference. The results are summarized in Table 3.

DISCUSSION

An increase or decrease in sIL-2R levels may have two important implications. Either it reflects disease activity or it is a part of the immunosupressive state in selected patients. The correlation between disease activity and sIL-2R levels is mainly true for neoplastic disorders such as adult T-cell leukemia, Hairy cell

Table 3. The duration of anesthesia and sIL-2R

SIL-2R	Before anesthesia	P value	During anesthesia	P value	After anesthesia
Duration of anesthesia					
>60min. (n-15)	*766*	0.37	*608*	0.75	659
<60 min. (n=10)	*1172*	0.20	*978*	0.64	7053
P value	0.04		0.03		0.07

*Values in italics represent sIL-2R levels

leukemia and lymphomas (1). Also in non malignant conditions like infectious mononucleosis, cytomegalovirus infection, viral hepatitis and sarcoidosis, sIL-2R levels may increase but this increase is lower than those in malignant disorders (1). The increase in sIL-2R levels is also important in states with immunosuppression such as Hodgkin's disease which is characterized by a defect in cellular immunity (2). In patients receiving general anesthesia, various changes in immune system are demonstrated but it is unclear whether this has any strong influence on the overall immune response of patients. In this study it is clear that general anesthesia causes a profound decrease In sIL-2R levels but this decrease is of short duration and sIL-2R levels return to normal in the recovery room. Shorter duration of anesthesia does not prevent this effect. The release of plasma **Cortisol** during anesthesia can bring an explanation for this sIL-2R level depression (3,10). Cortisol is an inhibitor of monocyte macrophage system and inhibits the release of various cytokines such as IL-2. As IL-2 plays a key role on various parts of the immune system, this finding may be an explanation for the immunodepression related to anesthesia. Whether this short lasting but significant decrease of sIL-2R has a profound effect on patient outcome needs to be clarified.

Genel anestezi alan hastalarda çözünür IL-2R düzeyleri

İnterlökin-2 (IL-2) etkisini interlökin-2 reseptörü (IL-2R) olarak adlandırılan bir hücre membraın reseptörü aracılığıyla gösterir. Bu reseptörün çözünür formunun (SİL-2R) artması immün sistemde bazı değişikliklere neden olabilmektedir. Genel anestezinin hasta immün sisteminde zararlı olabilecek bazı değişiklikleri uyarabildiği gösterilmiştir. Bu çalışma genel anestezi alan 25 hastada yapılmıştır. Genel anesteziden önce, anestezi sırasında ve sonrasında ELISA ile SİL-2R düzeyleri ölçüldü. Bu çalışma genel anesteziden sonra SİL-2R düzeylerinin belirgin olarak azaldığını göstermektedir (p-0.001). Bu azalma, genel anesteziden sonra immün sistemde izlenen değişikliklere katkıda bulunan önemli bir faktör olabilir.
[Türk J Med Res 1995, 13(3): 116-118]

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