Role of TNF alpha and IL-6 in Inflammatory Process after Tooth Extract in Children Under 12 Years

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Abstract

A cross-sectional study was carried out in Kirkuk city from of November 2018 to March 2019. The number of children after tooth extraction under study were 55 children ages were between 5-12 years old. These patients admitted to private clinics of dentists. The control group who were matched to the children with tooth extraction studied, included 35 healthy children. Three ml of blood was collected by vein puncture using Vacutainer tubes from each patient enrolled in this study for determination the level of IL-6 and TNF-α by using ELISA technique. The study showed that the highest mean level of TNF-α was found in children after tooth extraction comparing with healthy control group(36.8±13.4 v.s. 13.5 ±2.9 pg/ml) (P: ≤0.05). The highest mean level of IL-6 was found in children after tooth extraction comparing with control (88.1±15.7 v.s. 21.7±7.13 pg/ml) (P: ≤0.05). The study showed that the highest mean level of TNF-α was found in children after tooth extraction in the first week of after tooth extraction (33.2±9.1 pg/ml) and the level was still decreased to be the lowest level after one month tooth extraction of children (20.18±2.9 pg/ml), the result was significant (P: ≤0.05). The study showed that the highest mean level of IL-6 was found in children in the first week of after tooth extraction (92.1±15.8 pg/ml) and the level was still decreased to be the lowest level was after one month of tooth extraction (67.9±9.81 pg/ml), the result was significant (P: ≤0.05).

Keywords: *TNF; IL-6; Tooth extraction; Inflammation.*

Introduction

Current clinical practices show that health care providers and parents tend to underestimate children's pain when compared with children's self-reports[1] . This incongruity results from the inability of young children to fully understand, verbalize, and express their experiences [2]. in conjunction with adults being unable to adequately detect and identify signs of pain in the pediatric population. Given that pain in children is inherently difficult to assess, pain may be unrecognized or undiagnosed resulting in a mistaken belief that infants and children suffer less than adults or do not feel pain [3] . The International Association for the Study of Pain acknowledges that the "inability to communicate verbally does not negate the possibility that an individual is experiencing pain and (is) in need of appropriate pain management." [1] . Dental extractions of primary teeth have been, and very often still are, carried out without any pain relief medication in the belief that children do not experience significant amounts of pain [4] . Studies conducted to describe dentists' knowledge of and attitudes towards procedural pain in children have revealed that dentists downplay procedural pain [5] . Pain is likely the most significant morbidity associated with dental extractions. [6]. However, for unknown reasons, the impact of these studies has been slow to permeate into clinical knowledge and translate into clinical intervention. Postoperative pain is often a new experience for young children. The complexity of interpreting and verbalizing pain may be convoluted further by unfamiliar postoperative sensations from general anesthesia (GA), surgical site discomfort, and disorientation. The recovery period after surgery may require formal assessments of pain in this population. Interleukin 6 (IL-6) is a proinflammatory cytokine, which is produced by a number of immune system cells; fibroblasts, macrophages, T and B Lymphocytes, endothelial cells, keratinocytes and tumor cells [7]. Interleukin 6 (IL-6), as major mediator of the inflammatory response, plays a primary role in the inflammatory reaction [8]. Based on these data, the inhibition of the IL-6/IL-6 receptor interaction with specific antibodies has been proposed as a support treatment of inflammation after tooth extratction [9]. The cytokines interleukin-6 (IL-6), tumor

necrosis factor alpha (TNF alpha) and interleukin-1 beta (IL-1beta) are critical mediators of the inflammatory response [10] . So the aim of the study was to estimate the level of TNF alpha and IL-6 in children after tooth extraction

Materials and Method

A cross-sectional study was carried out in Kirkuk city from of November 2018 to March 2019. The number of children after tooth extraction under study were 55 children ages were between 5-12 years old. These patients admitted to private clinics of dentists. The control group who were matched to the children with tooth extraction studied, included 35 healthy children. Three ml of blood was collected by vein puncture using Vacutainer tubes from each patient enrolled in this study for determination the level of IL-6 and TNF-α by using ELISA technique (Koma-biotech USA Co).

Statistical Analysis

Computerized statistically analysis was performed using Mintab ver 18.0 statistic program for determination of the *P.* value (P <0.05 considered significant).

Finding

The study showed that the highest mean level of TNF-α was found in children after tooth extraction comparing with healthy control group (36.8±13.4 v.s. 13.5 ±2.9 pg/ml) (P: ≤0.05), Table 1.

Table 1: Level of TNF-α beta in children after tooth extraction and the control group.

TNF-α level pg/ml	Patients	Control group	P. value
Mean	36.8	13.5	≤ 0.05
SD.	13.4	2.9	

The highest mean level of IL-6 was found in children after tooth extraction comparing with control (88.1±15.7 v.s. 21.7±7.13 pg/ml) (P: ≤0.05), Table 2

Table 2: Level of IL-6 beta in children after tooth extraction and the control group.

IL-6	Patients	Control group	P. value
Mean	88.1	21.7	≤ 0.05
SD.	15.7	7.13	≤ 0.05

The study showed that the highest mean level of TNF-α was found in children after tooth extraction in the first week of after tooth extraction (33.2±9.1 pg/ml) and the level was still decreased to be the lowest level after one month tooth extraction of children (20.18±2.9 pg/ml), the result was significant (P: ≤0.05). The study showed that the highest mean level of IL-6 was found in children in the first week of after tooth extraction (92.1±15.8 pg/ml) and the level was still decreased to be the lowest level was after one month of tooth extraction (67.9±9.81 pg/ml), the result was significant (P: ≤0.05), Table 3.

Table 2: comparison among Level of TNF-α and IL-6 levels regarding the duration after tooth extraction

Interleukins levels (Mean±SD) pg/ml	First week	2 week	3 week	1 month	P. value
TNF-α	33.2±9.1	29.8±3.6	26.8±3.8	20.18±2.9	≤ 0.05
IL-6	92.1±15.8	80.6±13.2	77.8±10.8	67.9±9.81	≤ 0.05

Discussion

In this study, serum IL-6 level was evaluated in children after tooth extraction as compared to healthy controls. Interleukin-6 is found to be elevated in various inflammatory and malignant diseases including oral infection and their levels are found to correlate with the extent of the infection [9-11]. It is produced by some types of cancer cells and by normal stromal cells, such as fibroblasts and endothelial cells [5] . By acting as growth factor, IL-6 is able to promote tumor cell proliferation through upregulation of anti-apoptotic and angiogenic proteins in tumor cells. Also IL-6, is a major mediator of the inflammatory response, plays a primary role in the pathophysiology of wound infection[7] . The study results were in agreement with a recent study made by Rhodus et al [12] carried out on 75 children after tooth extraction patients and 15 healthy controls. He found that serum IL-6 level for the patients was significantly higher than normal children and strongly correlated with disease progression. Also Yazid *et al* [13] found that serum level of both IL-6 and IL-8 were found to be higher in patients than in healthy volunteers. Some other studies have mentioned that children after tooth extraction have more elevated levels of IL-6 and TNF alpha and their levels were negatively correlated with time after the process ($p < 0.01$) [6-8]. It was reported that IL-6 antitumor activity was enhanced by induction of induction of T cell and B cell differentiation, stimulation of cytotoxic T cells and help in producing lymphokineactivated killer cells [1] . We thought that This immune response trigger synthesis and release of this cytokine leading to augmentation of its serum level that might be utilized as a marker of immunity status and immune system activation in prognosis and monitoring of the course of infection [4] . This immune response might be attenuated with the progression of disease stage and inflamtory overwhelming which reflect decrease in (IL-6) synthesis [5,6].

Conclusions

There was a highly significant relation of TNF-α and IL-6 with children after tooth extraction and especially in first week after extraction of disease.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Kirkuk health Directorate and all experiments were carried out in accordance with approved guidelines.

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