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Prospective evaluation of the systemic inflammatory marker C-reactive protein in patients with end-stage periodontitis getting teeth replaced with dental implants: a pilot investigation

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Abstract

Objectives: Serum C-reactive protein (CRP) has been shown to be a risk predictor for cardiovascular disease. Periodontal treatment reduces elevated CRP levels. The aim of this pilot investigation was to evaluate if dental implants placed after extractions in patients with end-stage periodontitis affect the serum CRP levels.

Material and methods: Serum CRP levels in 10 subjects with end-stage periodontitis were measured prior to tooth extraction and placement of dental implants, and at 3-month intervals for a year post-operatively. Univariate repeated measures analysis of variance was used to estimate and test the changes in CRP levels over time.

Results: Mean CRP levels decreased significantly following tooth extraction and replacement with dental implants from 3.45 to 1.55 mg/dl after 12 months ($P<0.01$). Six-, 9-, and 12-month post-implant placement mean CRP values were statistically significantly different from the mean pre-operative CRP value ($P<0.01$).

Conclusions: The pilot data suggest that extraction of advanced periodontally involved teeth and their replacement with dental implants lead to a decrease in CRP levels, and dental implant placement does not change the lowered CRP levels over a 12-month period.

Periodontitis is a chronic inflammatory disease characterized by an inflammatory host response to the bacteria of the dental plaque biofilm (Page 1991). Recent investigations suggest that periodontal disease may affect systemic health (Mattila et al. 1989; Offenbacher et al. 1996; Beck & Offenbacher 2001).

Serum C-reactive protein (CRP), an acute phase reactant produced by the liver, may be a good indicator of the general inflammatory status of individuals. Elevated CRP levels may predict the risk for cardiovascular events, both primary as well as secondary (Ridker et al. 1998; Pepys & Hirschfield 2001). CRP levels have been found to be elevated according to disease severity in periodontitis patients, with reduction in CRP levels following periodontal therapy (Noack et al. 2001).

The hypotheses of this pilot investigation were:

1. Patients who have all their advanced, end-stage, periodontally compromised teeth extracted and restored with dental implants will experience a decrease in serum levels of CRP.
2. Patients restored with dental implants following extractions of such teeth will

have serum CRP levels that remain within the normal range over an extended period of time.

Material and methods

Over a 12-month period, 10 patients, six males and four females, 54–74 years of age (median age 64 years), with advanced chronic periodontitis, and no other significant medical history were recruited in a private practice in Pakistan. All patients signed a consent form stating that the study was in accordance with the Helsinki Declaration of 1975, as revised in 1983. Patients who had taken antibiotics in the preceding 60 days were excluded. Patients having CRP levels above 1 mg/dl, and a minimum of 10 teeth with generalized, severe chronic periodontitis were enrolled in the study.

All surgical procedures were performed under intravenous sedation. A pre-operative dose of 2 g of Amoxicillin was given prior to surgery. After extractions of all infected teeth, the sockets were curetted to remove all granulation tissue. A minimum of five ITI implants were placed in each patient. Operative sites were sutured using 4:0 black silk sutures. Post-operatively, all patients were prescribed Amoxicillin 500 mg t.i.d. for 7 days and for pain Ibuprofen 400 mg t.i.d. as needed. Chlorhexidine 0.2% mouth rinse was recommended for 30 days. All patients were seen 1 week post-operatively and sutures were removed. Definitive removable prostheses anchored on the implants were inserted 8–10 weeks post-operatively. Patients did not receive any non-steroidal anti-inflamatory drugs or systemic antibiotics subsequent to the post-operative dose during the 12-month follow-up period.

Peripheral blood was examined for CRP levels prior to surgery and at approximately 3-month intervals for 12 months at Agha Khan University Hospital in Karachi, Pakistan, using the Sinchore Cermid Turbidity (SCT) test (which is not a high sensitivity CRP (hsCRP) test). The test sensitivity was 0.3 mg/dl. The normal value of serum CRP in the US population is less than or equal to 1 mg/dl (Beckman Coulter Bulletin 9157BB). The range of serum CRP values for the Pakistani population in the pertinent age group has not been established.

The longitudinal change in the CRP levels was analyzed using univariate repeated measures analysis of variance. Contrasts between the time periods were performed to estimate and test the differences over time. Level of significance was set at $P = 0.05$. The sphericity test indicated that the covariance structure of the data did not exhibit compound symmetry ($P = 0.0016$) so the P values associated with the Greenhouse–Geisser correction were used (SAS Institute, Cary, NC, USA).

Results

The serum CRP levels for each of the 10 patients during the study period are shown in Figs 1 and 2. CRP levels had decreased at 12 months in eight of the 10 patients. The average CRP level before extraction and dental implant placement was 3.45 mg/dl (SD = 1.89) and decreased over time to 1.55 mg/dl at 12 months (SD = 2.26). This change over time was statistically significant ($P < 0.01$) (Table 1). The pre-operative and 3 month average values were not statistically different ($P = 0.54$) but were significantly different from the later collection periods ($P < 0.01$). The average and the majority of the actual CRP values decreased until 6 months post-operatively and then stabilized (Figs 1 and 2). Neither the difference in mean values from 6 to 9 months nor from 9 to 12 months was statistically significant ($P > 0.1$) (Table 1). All 60 implants integrated.

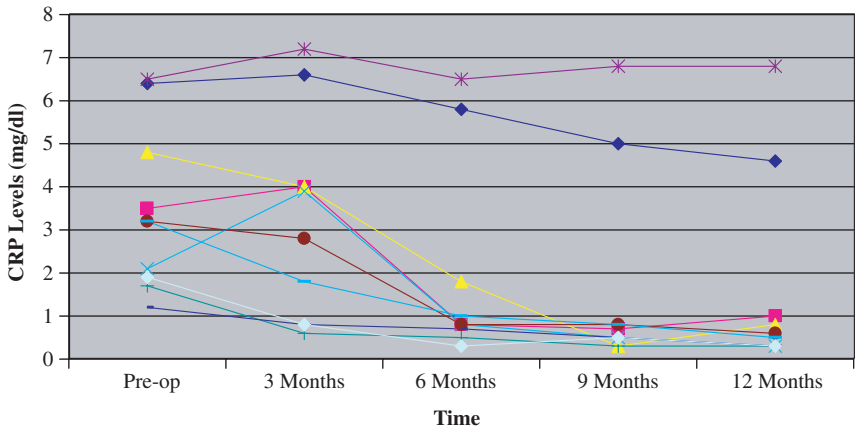

Fig. 1. Actual C-reactive protein (CRP) levels for each subject: pre-operative and every 3 months after extraction and implant placement.

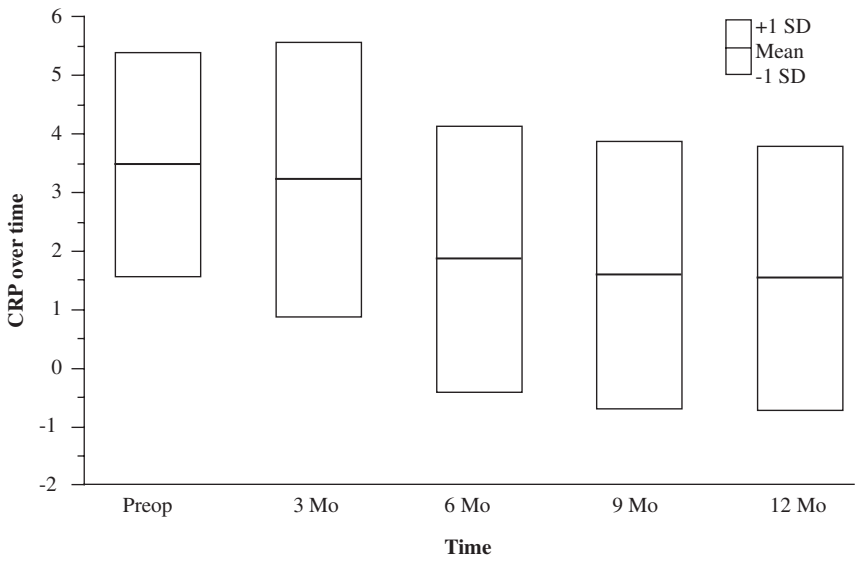

Fig. 2. Mean C-reactive protein (CRP) levels for each subject: pre-operative and every 3 months after extraction and implant placement.

Table 1. **Statistical comparison of mean CRP levels between pre-operative and each follow-up value and among consecutive 3 monthly follow-up values**

Mean CRP levels comparison	Mean difference	SD	*P*-value
Pre-operative vs. 3 months	0.20	0.997	0.541
Pre-operative vs. 6 months	1.55	1.009	0.001
Pre-operative vs. 9 months	1.83	1.297	0.002
Pre-operative vs. 12 months	1.90	1.159	0.001
3 months vs. 6 months	1.35	1.179	0.006
6 months vs. 9 months	0.28	0.522	0.124
9 months vs. 12 months	0.07	0.279	0.458

CRP, C-reactive protein; SD, standard deviation.

Discussion

This pilot investigation was initiated to evaluate the relationship between serum CRP levels in patients with generalized severe chronic periodontitis before and after extraction and placement of dental implants.

It is known that serum CRP levels increase in patients with periodontal disease (Ebersole et al. 1997) and that CRP levels decrease after periodontal treatment (Mattila et al. 2002). There are no prior reports in the literature with regard to serum CRP levels after extractions and placement of dental implants in patients with end-stage periodontitis. We now report that CRP levels in patients with implant-supported prostheses restored after extraction of all advanced periodontally involved teeth, are lowered and remain so over a 12-month period.

Our data are in agreement with the findings that serum CRP levels decrease after periodontal treatment. The baseline mean CRP level in the current study was more than three times that of the Mattila et al. (2002) study, namely, 3.45 vs. 1.05 mg/l, which might be because of the much more severe disease level in the current study population. The mean CRP level decreased 0.2 mg/l during the first 3 months post-operatively, and Mattila et al. (2002) reported a decrease of 0.34 mg/l 6 weeks after treatment of the infection. In addition, the presence of dental implants did not cause the serum CRP levels to increase after the initial post-operative decrease. The patients are continuing to be monitored and subsequent CRP levels will be reported. The resolution of infection by extraction of all advanced periodontally involved teeth and rehabilitation with dental implant therapy could be a significant factor in improving the overall health of the individual.

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Résumé

La protéine réactive C (CRP) est comme annonciatrice du risque de la maladie cardiovasculaire. Le traitement parodontal réduit les taux élevés en CRP. Le but de cette étude pilote a été d'évaluer si les implants dentaires placés après des extractions chez des patients avec une parodontite en stade final affectaient les niveaux sériques de CRP. Les niveaux sériques de CRP chez dix sujets avec parodontite terminale ont été mesurés avant l'avulsion des dents et le placement des implants dentaires et à des intervalles de trois mois après l'opération durant un an. L'analyse de variance par mesure répétée a été utilisée pour estimer et tester les variations des niveaux CRP dans le temps. Les niveaux CRP moyens diminuaient significativement après les avulsions dentaires et le remplacement des implants dentaires de 3,45 mg/dl à 1,55 mg/dl après douze mois ($P<0{,}01$). Six, neuf et douze mois après le placement des implants, les valeurs CRP moyennes étaient significativement différentes de la valeur CRP moyenne avant l'opération ($P<0{,}01$). Cette étude pilote suggère que l'avulsion des dents chez les patients en parodontite terminale et leur remplacement par des implants dentaires apportent une diminution des niveaux de CRP et que le placement des implants dentaires ne changent pas les niveaux de CRP ainsi diminués sur une période de douze mois.

Zusammenfassung

Eine prospektive Auswertung des systemischen Entzündungsindikators C-reaktives Protein in Patienten mit Parodontitis im Endstadium, bei welchen Zähne durch Implantate ersetzt werden: Eine Pilotstudie

Ziele: Es wurde gezeigt, dass das c-reaktive Protein (CRP) im Serum einen Risikoindikator für kardiovaskuläre Erkrankungen darstellt. Die Parodontaltherapie führt zu einer Reduktion von erhöhten CRP Werten. Das Ziel dieser Pilotstudie war, auszuwerten, ob dentale Implantate, welche bei Patienten mit Parodontitis im Endstadium nach Extraktionen eingesetzt wurden, die Serum CRP-Werte beeinflussen.

Material und Methoden: Bei 10 Subjekten mit Parodontitis im Endstadium wurden die Serum CRP-Werte vor der Zahnextraktion und der Platzierung von dentalen Implantaten und während eines Jahres im einem Intervall von drei Monaten gemessen. Zur Abschätzung und Testung der Veränderungen in den CRP-Werten über die Zeit wurden Analysen der Varianz von univariaten wiederholten Messungen durchgeführt.

Resultate: Die mittleren CRP-Werte nahmen nach Zahnextraktion und Einsetzen von dentalen Implantaten von 3.45 mg/dl auf 1.55 mg/dl nach 12 Monaten signifikant ab ($P<0.01$). Es bestanden statistisch signifikante Unterschiede zwischen den mittleren CRP-Werten nach sechs, neun und zwölf Monaten nach Implantation und dem mittleren präoperativen CRP-Wert ($P<0.01$).

Schlussfolgerungen: Die Daten der Pilotstudie lassen vermuten, dass die Extraktion von Zähnen mit fortgeschrittener Parodontitis und deren Ersatz mit dentalen Implantaten zu einer Abnahme der CRP-Werte führt. Die Platzierung von dentalen Implantaten führt über einen Zeitraum von 12 Monaten zu keiner Veränderung der reduzierten CRP-Werte.

Resumen

Objetivos: La proteína C-reactiva sérica (CRP) ha demostrado ser un predictor para enfermedades cardiovasculares. El tratamiento periodontal reduce los niveles elevados de CRP. La intención de esta investigación piloto fue evaluar si los implantes dentales colocados tras extracciones en pacientes con periodontitis en fase Terminal afectaría los niveles de CRP.

Material y Métodos: Se midió el nivel de CRP sérica en diez sujetos con periodontitis en fase Terminal antes de la extracción dentaria y colocación de implantes dentales, y a intervalos trimestrales durante un año tras la operación. Se usó el análisis de la varianza de mediciones repetidas univariadas para estimar y probar los cambios en los niveles de CRP a lo largo del tiempo.

Resultados: Los niveles de CRP medios descendieron significativamente tras la extracción dentaria y sustitución con implantes dentarios de 3.45 mg/dl a 1.55 mg/dl tras 12 meses ($P<.01$). Los niveles medios de CRP a los seis, nueve y doce meses post extracción fueron diferentes estadísticamente significativos a los valores de CRP preoperatorios ($P<.01$).

Conclusiones: Los datos piloto sugieren que la extracción de dientes con periodontitis avanzada y su sustitución con implantes dentales conduce a una disminución en los niveles de CRP y la colocación de implantes dentales no cambia los niveles descendidos de CRP durante un periodo de 12 meses.

要旨

目的：血清C反応蛋白（ＣＲＰ）は心血管病のリスク予知因子として知られている。歯周病の治療は上昇したＣＰＲの濃度を下げる。本パイロット研究の目的は、末期歯周炎の患者において抜歯後のインプラント埋入が血清ＣＲＰ濃度に影響するかどうかを評価することであった。

材料と方法：１０人の患者において、血清ＣＲＰ濃度を抜歯とインプラント埋入の術前及び術後１年間３ヶ月毎に測定した。単一変量反復計測分散解析法を用いて、経時的なＣＲＰ濃度の変化を測定し、検査した。

結果：平均ＣＲＰ濃度は抜歯とインプラント埋入後１２ヶ月後に３．４５ｍｇ／ｄｌから１．５５ｍｇ／ｄｌに有意に減少した（ｐ＜０．０１）。インプラント埋入後６、９、１２ヵ月後の平均ＣＲＰ値は術前の平均ＣＲＰ値と統計学的に有意に異なっていた（ｐ＜０．０１）。

結論：本パイロット･データは、進行した歯周病に罹患した歯牙を抜去し、インプラントを埋入することによってＣＲＰ濃度は減少し、インプラント埋入後の１２ヶ月間減少したＣＲＰ濃度は変化しないことを示唆している。

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