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Comparative evaluation of periodontal status and Porphyromonas gingivalis levels in schizophrenia patients and systemically healthy subjects with Periodontitis

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Abstract

Background: One of the chronic mental disorders is schizophrenia, associated with disintegration of emotional responsiveness and thought process. This population is prone for periodontal disease due to poor oral hygiene and nutrition.

Aim: Our study was aimed to compare the clinical parameters and P. gingivalis levels in schizophrenia and systematically healthy patients with periodontitis.

Material & Methods: A total of eighty patients were included in this study. Group I belonged to Schizophrenia patients with periodontitis and Group II were systemically healthy patients with Periodontitis. Clinical parameters such as plaque index (PI), gingival index (GI), probing pocket depth (PPD) and clinical attachment level (CAL)

were recorded and the subgingival plaque samples were obtained to estimate Porphyromonas gingivalis levels.

Result: On comparison of mean values of PI, GI, PPD, CAL and P.gingivalis levels between the two groups showed statistically significant higher levels in group I. On correlation of clinical parameters with P gingivalis levels showed a significant association for all the variables.

Conclusion: In our study P. gingivalis levels were higher in schizophrenia subjects with periodontitis and this periopathogen is incriminated in certain systemic conditions, such as atherosclerotic heart disease. Maintenance of oral health in pshychiatric patients, helps in prevention of comorbid systemic illness.

Keywords : Schizophrenia, Periodontitis, P.gingivalis, pshychiatric disorders

Key Message

Schizophrenia and periodontal disease share a two way relationship. Schizophrenia patients are prone for periodontal disease due to poor oral hygiene and nutrition

Periodontal disease being a inflammatory disease with elevated P.gingivalis and cytokine levels cause schizophrenia by modulating dopamine metabolism. Hence the improper oral health and elevated cytokines due to inflammatory burden in periodontal disease, lead to schizophrenia development.

P.gingivalis is incriminated in certain systemic conditions, such as atherosclerotic heart disease. Maintenance of oral health in pshychiatric patients, helps in prevention of comorbid systemic illness

Introduction

Periodontitis involves the interaction of the microorganisms and host immunoinflammatory response, leading to loss of tooth supporting structures.[1] Periodontal disease is the sixth most prevalent chronic conditions globally, which is the major cause for tooth loss.[2] One of the chronic mental disorders is schizophrenia, associated with disintegration of emotional responsiveness and thought process.[3] Common manifestations are paranoid delusions, disorganized speech and thinking and hallucinations. Worldwide twenty one million people are affected by this mental disorder and the mortality rate is high due to preventable diseases like cardiovascular disease, metabolic disorders and infections.[4] In India, three persons out of thousand people are affected and this disease has greater predilection for males.[5] This population is prone for periodontal disease due to poor oral hygiene and nutrition.[6] The dopamine hypothesis for schizophrenia states that hyperactivity of D2 dopamine receptor located in limbic and subcortical brain regions causes the positive symptoms of schizophrenia and the negative symptoms are associated with dopamine D1 receptor stimulation, which is located in prefrontal cortex.[7]

Porphyromonas gingivalis plays a significant role in the progression of chronic periodontitis and has also been implicated as a contributory factor in the development of systemic diseases such as atherosclerosis.[8] P. ginigivalis is small gram negative, black pigmented anaerobe, considered as a bonafide periodontal pathogen and key stone pathogen in periodontal biofilm.[9] Even low level of colonization by P gingivalis, alters the total number of oral bacteria and changes the commensal bacteria composition. Because of the ability of P gingivalis to inhibit interleukin-8 in the epithelial cells supports the role of P gingivalis as keystone pathogen and the adherence of P. gingivalis in the oral cavity is the initial event in its pathogenicity.

Fawzi et al demonstrated higher prevalence and quantity of salivary P.gingivalis in schizophrenia patients compared to non psychiatric controls.[10] There is paucity in studies, regarding microbial assessment in

Schizophrenia patients with Periodontitis in South Indian Population. Hence our study was aimed to compare the clinical parameters and P. gingivalis levels in schizophrenia and systematically healthy patients with periodontitis.

Materials And Methods

A total of eighty patients with age group between 30 – 50 years were included in this study. Group I belonged to Schizophrenia patients with periodontitis and Group II were systemically healthy patients with Periodontitis. Ethical clearance was obtained from the ethical committee of our institution. Written informed consent were obtained from the patients. Group I patients diagnosed with schizophrenia were selected from Dr. Fernandez home for schizophrenia. Schizophrenia patients, who had history of this disease for a period of three years and with similar positive and negative syndrome scale were included in this study. Group II subjects were selected from Department of Periodontics. The inclusion criteria for periodontitis subjects were probing pocket depth (PPD) of ≥ 5mm, interproximal clinical attachment loss (CAL) of ≥ 3mm and radiographic evidence of bone loss in > 30% sites.[11] The exclusion criteria included patients having medical disorders, smokers, learning disability and those at risk of harming themselves. Clinical parameters such as plaque index (PI), gingival index (GI), probing pocket depth (PPD) and clinical attachment level (CAL) were recorded and the subgingival plaque samples were obtained to estimate Porphyromonas gingivalis levels. Plaque index was recorded at four sites (midbuccal, mesiobuccal, distobuccal and palatal sites) in each tooth.[12] The facial, lingual, mesial and distal gingival areas were examined for gingival index.[13] PPD and CAL were recorded at six sites in each tooth and expressed in millimetres.[14,15]

Subgingival plaque was collected using curette and it was transferred to sterile tubes containing 500 µl of sterile phosphate buffered saline (pH 7.8) and the samples were stored at −80° till assay. For P.gingivalis estimation, genomic DNA was isolated according to the instructions given by the manufacturers, using a QIAamp DNA Mini kit (QIAGEN Inc., USA, 9300 Germantown Road, Germantown, MD 20874). The species specific primer with the sequence of Forward:5'-AGG CAG CTT GCC ATA CTG CG-3', Reverse: 5'-ACT GTT AGC AAC TAC CGA TGT-3' with 172 base pair was selected according to Becerik et al.[16] Quantitative real time polymerase chain reaction (RT-PCR) was carried out with C1000 touch thermal cycler real time PCR. Relative amount of gene was calculated by using comparative cycle threshold (CT) method. Cycle threshold unit is inversely proportional to the amount of bacteria.

Results & Discussion

Data was analysed using SPSS software, version 21. Forty subjects per group were selected to get the study power of 80%. Mann-Whitney U test was used to assess the mean difference in clinical parameters and P. gingivalis levels between the groups. Spearman correlation was used to find the correlation of clinical parameters with P.gingivalis levels. On comparison of mean values of clinical parameters like PI, GI, PPD and CAL between the two groups showed statistically significant difference and higher levels were observed in group I. Statistically significant difference in P.gingivalis levels were also observed between the groups and higher P.gingivalis levels were observed in group I. On correlation of clinical parameters with P gingivalis levels showed a significant association for all the variables.

Evidence from the previous studies showed a bidirectional relationship between schizophrenia and periodontal disease.[17,18,19] Xerostomia related to the medications, poor oral health due to mental disorder and neglect of dental treatment in schizophrenia patients lead to poor oral

health. Periodontal disease being a inflammatory disease with elevated P.gingivalis and cytokine levels cause schizophrenia by modulating dopamine metabolism.[20] Hence the improper oral health and elevated cytokines due to inflammatory burden in periodontal disease, lead to schizophrenia development..

In our study the clinical parameters like PI, GI, PPD and CAL were higher in schizophrenia patients with periodontitis compared to systemically healthy subjects with periodontitis. comparable to the study by Arnaiz et al., who had reported poor periodontal health in schizophrenic patients and suggested that impaired mental health might be a contributing factor for poor oral health and associated inflammatory process.[21] Shetty et al have also reported poor periodontal condition in schizophrenic patients evidenced by increase in PI,GI and PPD.[22] Higher PI and GI index in schizophrenic patients with periodontitis, may be due to the negligence of oral hygiene by these patients and xerostomia produced by antipsychotic drugs. Kebede et al. also reported that tooth brushing technique, intake of more sugary foods, type of medication and the duration of illness were associated with periodontal disease in in patients with mental disorders.[23] It is also stated that systemic infections and inflammation can lead to dopamine dysregulation. The key cytokines in periodontal disease such as interleukin-1β and interleukin-6, also affect the neurotransmitter dopamine levels by inhibiting the release of glutamate and enhancing the dopamine survival.[24,25,26] Hence dysregulation of dopamine levels in Schizophrenic patients with periodontal disease, also leads to, elevated proinflammatory cytokines, which is responsible for increased tissue destruction.[27] The negative symptoms and cognitive defects prevailing in schizophrenia patients also would have contributed to poor oral health.[28] Hence it is proved that improper oral health in schizophrenic patients can also modulate the mental conditions.

Polymerase chain reaction is one of the molecular biological techniques, enabled the identification of periopathogens. P.gingivalis levels were expressed in CT units, which is inversely proportional.. In our study P. gingivalis levels were also higher in Schizophrenic patients with periodontitis compared to systemically healthy subjects with periodontitis similar to study by Fawzi et.al.[10] P gingivalis, being a putative periodontal pathogen, modulate responses by inflammatory cytokines. Hence in periodontal disease increased levels of P.gingivalis along with increased levels of proinflammatory cytokines can alter the dopamine metabolism leading to schizophrenia. On correlation of P.gingivalis with clinical parameters showed a statistically significant positive correlation with all the parameters. Fawzi et al reported the correlation of psycopathic symptoms with P.gingivalis levels.[10] In our study we included schizophrenia subjects with similar PANSS score and duration of three years, so we could not correlate the severity of schizophrenia P.gingivalis levels.

Individuals with schizophrenia are also prone for chronic systemic diseases like diabetes, cardiovascular disease and cancer.[29] The periopathogen P. gingivalis is strongly associated with cardiovascular disease. Hence it is stated that periodontal management of schizophrenia patients with periodontitis will reduce the cardiovascular risk among these population.

Conclusion

It may be observed from our study that schizophrenia patients with periodontitis had poor oral hygiene, higher periodontal destruction and harboured increased proportion of P.gingivalis. P. gingivalis is incriminated in certain systemic conditions, such as atherosclerotic heart disease. Maintenance of oral health in pshychiatric

patients, helps in prevention of comorbid systemic illness. In future preventive dental programs will become an integral part of psychiatric management to meet the need of these vulnerable group of population.

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Legends Tables

Table1: Comparison of Clinical Parameters and P gingivalis between two groups.

Variables	Groups	Mean ± SD	Mann whitney U	P-value
PI	Group I	2.55±0.20	216.00	0.001
	Group II	2.35±0.20		
GI	Group I	2.55±0.20	216.00	0.001
	Group II	2.35±0.20		
PPD	Group I	7.52±0.28	0.00	0.001
	Group II	6.52±0.33		
CAL	Group I	7.47±0.26	30.00	0.001
	Group II	6.50±0.39		
P. gingivalis	Group I	22.0±2.82	120.00	0.001

* Level of significance :P<0.05 significant PI –plaque index; GI – Gingival index; PPD – probing pocket depth; CAL – clinical attachment level; *P gingivalis – Porphyromonas gingivalis* P- value – Probability value

Table 2: Correlation of clinical parameters with *P.gingivalis* levels

			P. gingivalis
Spearman's rank	PI	Correlation Coefficient	-.277
		Sig. (2-tailed)	..032
		N	80
	GI	Correlation Coefficient	-.277*
		Sig. (2-tailed)	.032
		N	80
	PPD	Correlation Coefficient	-.573**
		Sig. (2-tailed)	.000
		N	80
	CAL	Correlation Coefficient	-.454**
		Sig. (2-tailed)	.000
		N	80

* Level of significance :P<0.05 significant PI –plaque index; GI – Gingival index; PPD – probing pocket depth; CAL – clinical attachment level; *P gingivalis – Porphyromonas gingivalis*, N- number of sample