



## Prognostic Implication of Selective Serotonin Reuptake Inhibitors in Osseointegration of Dental Implants: A 5-year Retrospective Study

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### ABSTRACT

**Aim:** Dental implants are the preferred treatment modality in the present edentulous era. Selective serotonin reuptake inhibitors (SSRIs) have detrimental effect on bone density. The present study was conducted to determine the effect of SSRIs on the success rate of dental implants.

**Materials and methods:** The present study was conducted on 352 patients of both genders with 680 dental implants. History of depression and SSRI medication was retrieved. Patients were divided into two groups. Group I (110 patients, 230 dental implants) patients were on SSRI, while group II (242 patients, 450 dental implants) patients were non-SSRI. In all patients, the implant failure rate was recorded.

**Results:** In group I, 35 patients were >50 years, while 75 were <50 years of age. In group II, 60 patients were >50 years, while 182 were <50 years of age. The difference was significant ( $p < 0.05$ ). Group I had 45 males and 65 females, while group II comprised of 105 males and 137 females. Group I showed 25 implant failures and group II had 21 implant failures. Age group >50 years showed 12 implant failures while <50 years

had 13 in group I compared with 10 in patients >50 years and 11 in patients with <50 years of age; 56% smokers had implant in group I as compared with 60% failure in group II. In group I, 27% diabetic patients had failures as compared with 13.4% in group II. The difference was significant ( $p < 0.05$ ). Group I showed maximum failures in terms of loosening of screw (8) followed by fracture of implant (7), peri-implantitis (6), and fracture of screw (4), whereas in group II, 7 cases were of loosening of screw, 6 cases were of fracture of screw, 5 cases of fracture of implant, and 3 cases of peri-implantitis. The difference was nonsignificant ( $p > 0.05$ ).

**Conclusion:** Selective serotonin reuptake inhibitors cause increased osteoclastic activity, leading to bone loss and implants placed in patients with history of depression are more prone to failures.

**Clinical significance:** Failure rates of dental implants are significantly increased in patients taking SSRIs due to depression. Careful case analysis and history of depression may minimize the failure rates.

**Keywords:** Dental implants, Selective serotonin reuptake inhibitors, Smokers.

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### INTRODUCTION

Dental implants are one of the treatment modalities for missing teeth. This has gained fame over the past few years. The popularity can be judged by the fact that in spite of high treatment cost of the dental implant, patients prefer it. Prosthetic rehabilitation of the patient demands replacement of edentulous area. Removable partial denture (RPD), which was earlier considered the

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preferred treatment modality for replacing few teeth, had several disadvantages also. The effect of clasp on the supporting teeth and on soft tissue was deleterious. Tooth mobility of adjacent teeth was quite common, ultimately leading to tooth loss.<sup>1</sup>

Fixed partial denture (FPD) became popular because it diminished all the possible drawbacks of RPD. There was no need of placing clasps in FPD. Moreover, the repeated insertion and removal step was eliminated too. The only limitation was that for replacing single teeth, two supports were required both anteriorly and posteriorly. Patients often experienced sensitivity to cold and hot which put this option into suspicion.<sup>2</sup>

Dental implant insertion is devoid of all these steps. It is inserted directly into the bone and it unites with it through the process of osseointegration. Better the osseointegration, higher the success rate of dental implant. Apart from its frequent use in dentistry, there are few contraindications, such as smoking, diabetes, and hypertension. Obsolete contraindication includes epilepsy, osteoradionecrosis, etc.<sup>3</sup>

Depression is characterized by a person's low mood which affects behavior, thought, feeling, etc. The person feels sad and negative thoughts prevails in mind. The curiosity to interact with people is decreased and the person can commit suicide. The learning power and concentration decrease and there are considerable failures in life. The overall performance is affected significantly. An estimated >300 million people worldwide are suffering from depression. Selective serotonin reuptake inhibitor is a widely used medication which boosts up the mind with positive thoughts and happiness. The harmful effect of SSRI is that it has negative effects on osteoblasts leading to bone loss.<sup>4</sup> Under the light of above-mentioned data, we planned the present study to assess the success rate of dental implant in patients on SSRIs.

## MATERIALS AND METHODS

The present 5-year retrospective study was conducted in the Department of Prosthodontics and comprised of 352 patients of both genders who were rehabilitated with a total of 680 dental implants. All were informed

regarding the study and written consent was obtained. Ethical clearance was obtained prior to the study.

General information, such as age, name, and gender was recorded. History of depression and SSRI medication was retrieved from patient's case history proforma. Considering this, patients were divided into two groups. Group I (110 patients, 230 dental implants) were on SSRI, while group II (242 patients, 450 dental implants) were non-SSRI.

Implants were inserted depending upon the edentulous site, following which prostheses were given on implants. To maintain the uniformity and to avoid bias, a single manufacturer implant (Nobel) was inserted in all patients. In cases where there were pneumatization of maxillary sinus, lifting of sinus was performed and where bone was lacking, vertical or lateral bone grafting was done.

Following implant surgery, all patients were prescribed 0.2% chlorhexidine mouthwash rinse TDS for a week and antibiotic Augmentin 500 mg (amoxicillin + clavulanic acid) thrice daily for 5 days. In all cases, nonabsorbable silk suture was used. Patients were instructed to be on soft diet for at least 1 week. Patients were recalled periodically for follow-up. Factors, such as fracture of implant, prosthesis screw fracture, and loosening of screw, and features of peri-implantitis, such as radiolucency around implant apex and bone loss around implant were considered and recorded as suggested by Nallaswami.<sup>5</sup> Results thus obtained were subjected to statistical analysis using chi-square test;  $p$ -value < 0.05 was considered significant.

## RESULTS

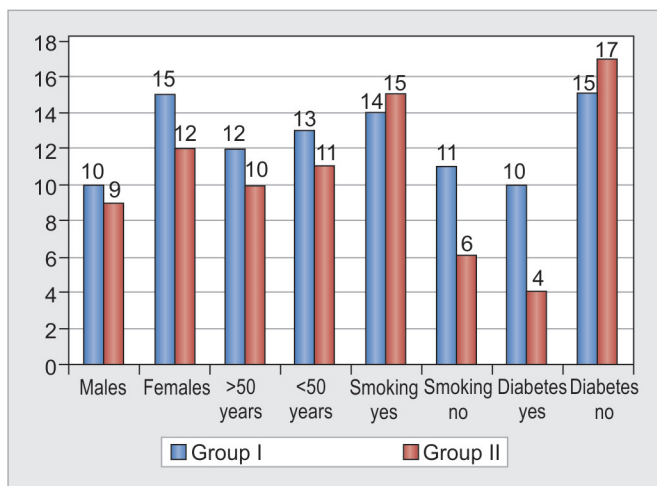
Table 1 shows that group I had 110 patients (230 implants) and group II had 242 patients (450 implants). The difference was significant ( $p < 0.05$ ). Table 2 shows that

**Table 1:** Distribution of patients

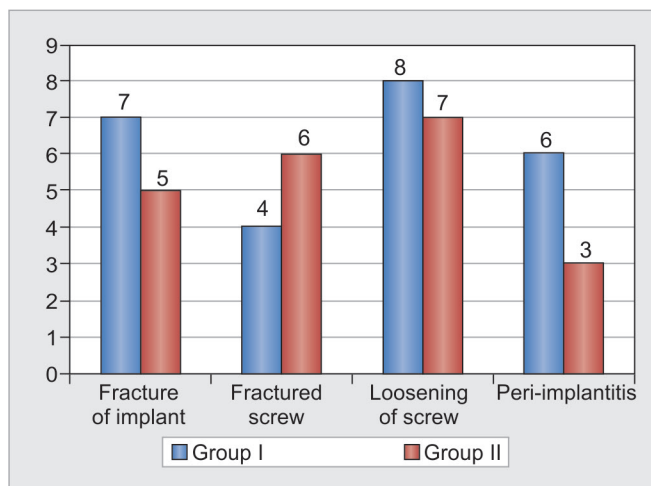
Group	Group I (SSRI)	Group II (Non-SSRI)	p-value
No. of patients	110	242	0.01
No. of implants	230	450	0.001

**Table 2:** Characteristics in both groups

Parameters		Group I	Group II	p-value
Age	> 50 years	35 (50 implants)	60 (135 implants)	0.01
	<50 years	75 (180 implants)	182 (315 implants)	
Gender	Male	45 (95 implants)	105 (180 implants)	0.02
	Female	65 (135 implants)	137 (270 implants)	
Smoking	Yes	12 (25 implants)	25 (60 implants)	0.001
	No	98 (205 implants)	217 (390 implants)	
Diabetes	Yes	10 (37 implants)	15 (30 implants)	0.001
	No	100 (193 implants)	227 (420 implants)	



Graph 1: Failure rates in both groups



Graph 2: Features of implant failures

in group I, 35 patients were >50 years, while 75 were <50 years of age. In group II, 60 patients were >50 years, while 182 were <50 years of age. The difference was significant ( $p < 0.05$ ). Group I had 45 males and 65 females, while group II comprised of 105 males and 137 females. The difference was significant ( $p < 0.05$ ). Twelve patients in group I and 25 in group II had the habit of smoking; 10 patients in group I and 15 in group II had diabetes. The difference was significant ( $p < 0.05$ ).

Graph 1 shows that group I had 25 implant failures (males 10, females 15) and group II had 21 implant failures (males 9 and females 12). The failure rate in group I was 10.8% and in group II, it was 4.7%. In group I, 12 implant failures (24%) were in age group >50 years and 13 (7.2%) were <50 years and in group II; 10 (7.4%) implant failures were in age group >50 years and 11 (3.5%) were <50 years. Out of 25 implants placed in 12 smokers, 14 (56%) had failure in group I, and out of 60 implants placed in 25 smokers, 15 (60%) had failure in group II. In group I, out of 205 implants placed in 98 patients, 11 (5.3%) implants had failure, while in group II, out of 390 implants placed in 217 patients, 6 (1.5%) implants had failure. In group I, out of 37 implants in diabetic patients, 10 (27%) had failure, while in group II, out of 30 implants placed in diabetics, 4 (13.4%) had failure. In group I, out of 193 implants in nondiabetics, 21 (10.9%) had failure and in group II, out of 420 implants in nondiabetics, 17 (4.1%) had failure. The difference was significant ( $p < 0.05$ ). Graph 2 shows that in group I, common failures were fracture of implant (7), fracture of screw (4), loosening of screw (8), and peri-implantitis (6), and in group II, fracture of implant (5), fracture of screw (6), loosening of screw (7), and peri-implantitis (3). The difference was nonsignificant ( $p > 0.05$ ).

## DISCUSSION

Dental implant failures are not uncommon. There are various factors that determine the survival rate

of implant. Systemic conditions, such as diabetes, smoking habit, and hypertension play an important role in the success or failure of dental implant treatment. Depression is a serious condition that may result from various reasons. There can be depression due to poor performance in office, school, college, repeated failures, unemployment, abuse that can be sexual, mental abuse, etc., and menopause. Most of the patients with history of depression are on SSRIs.<sup>6</sup>

The SSRIs are extensively used antidepressants that enhance the activity and availability of serotonin in the brain which boosts the mood. Krishnan and Nestler<sup>7</sup> in their study of the molecular neurobiology of depression suggested that continued supply of serotonin is mandatory in mood elevation and deficiency of it leads to severe depression among people.

Tsapakis et al<sup>8</sup> in their study of the adverse skeletal effects of SSRIs found that SSRI promotes osteoclast activity by inhibiting osteoblasts, thus suggesting that in patients taking SSRI, the chances of dental implant failures are more as compared with those not on it. In the present study, 110 patients were on SSRI (group I) (230 implants) and in group II, 242 patients were non-SSRI users (450 implants). Wu et al<sup>9</sup> conducted a cohort study on SSRIs and the risk of osseointegrated implant failures and classified patients into two groups. Group I was non-SSRI users containing 453 patients (849 implants) and group II was SSRI users having 53 patients and 99 dental implants.

Charcanovic et al<sup>10</sup> conducted a study to appraise the function of SSRIs coupled with an increased risk of dental implant failure on 300 patients (35 failures). There was a 12.5% failure rate in SSRI users and 3.3% in nonusers  $p$ -value  $< 0.05$ . The authors concluded that the intake of SSRIs may not be connected with the higher risk of dental implant failure. In the present study, 10.8% failure rate was seen in group I and 4.7% in group II.

Alsaadi et al<sup>11</sup> conducted a study of impact of local and systemic factors on the incidence of late oral implant loss and found that the greatest dental implant failure was observed in smokers as compared with nonsmokers. The authors concluded that smoking has deleterious effect on wound healing. A similar study by Krall and Dawson-Hughes<sup>12</sup> analyzed the relation between smoking and bone loss among postmenopausal women and found that smoking causes loss of bone mineral density. The chances of implant failure were more in these patients. In our study, 56% implant failure was seen among smokers in group I as compared with 60% in group II.

We found that 24% implant failure was seen in patients >50 years of age and 7.2% <50 years of age in patients on SSRIs as compared with 7.4 and 3.5% on non-SSRI group respectively. This suggests that group I had higher implant failure rate, especially in patients above 50 years of age. Massimiliano Negri et al<sup>13</sup> evaluated the effect of age, gender, and insertion site on marginal bone loss around endosseous implants in a 3-year retrospective study and found that patients >60 years of age had higher marginal bone loss around implants as compared with patients <60 years of age.

Prakash and Victor<sup>14</sup> in their retrospective study of influence of diabetes on dental implants found 13 implant failures among 127 implants in diabetic patients. The authors concluded that high success rate can be achieved in control diabetics. We found that 27% implant failure was observed in diabetics in group I while group II showed 13.4% implant failure. There was a 10.9% dental implant failure rate in nondiabetic in group I as compared with 4.1% failure in group II. This suggests that even in nondiabetics, SSRI drugs have higher failure rate.

Battaglino et al<sup>15</sup> in their study suggested that serotonin regulates osteoclast differentiation through its transporter. This leads to excessive osteoclastic activity which in turn accelerates the mobility of dental implant. Diem et al<sup>16</sup> found that in women there is more calcium loss in bones, especially of hip bone through osteoporosis in patients on SSRIs.

Noda et al<sup>17</sup> in their study evaluated the risk factors of implant failure and found that in females maximum implant failures were seen as compared with males. We observed that in group I, 10 males and 15 females and in group II, 9 males and 12 females had implant failure. Selective serotonin reuptake inhibitors are drug of choice in patients with depression. Widely used drugs are fluoxetine, indalpine, sertraline, etc. It is also useful in patients with anxiety disorders,<sup>18</sup> obsessive compulsive disorders,<sup>19</sup> eating disorder, etc. Common side effects in patients on these drugs are fracture bone due to decreased bone density, excessive bleeding, serotonin syndrome, etc. Kirsch et al<sup>20</sup> in their study observed that the effect

of SSRIs is minimal as compared with placebo in cases of mild and moderate depression respectively, whereas the effect is substantial in patients with very severe depression. A study by Eom et al<sup>21</sup> on SSRIs and risk of fracture found that bone mineral density is considerably reduced in these patients.

Most of the patients with depression are on SSRI. The role of SSRI in depression is well documented. Though it has deleterious effects on the bone in terms of bone resorption which is the biggest drawback, the consideration of need of the patient is of paramount importance.

## CONCLUSION

Selective serotonin reuptake inhibitors are commonly employed antidepressants among adult population. This is found to be effective in correcting the depression, but, in the mean time, it has deleterious effect in bone in terms of excessive osteoporosis. We found more implant failures in patients on SSRI as compared with non-SSRI. The reasons for failures were implant fracture, fracture screw, loosening of screw, and peri-implantitis. However, implant insertion in patients on SSRIs is not strictly contraindicated. Careful systemic evaluation is necessary in implant planning.

## CLINICAL SIGNIFICANCE

There is need to assess the depression in patients requiring dental implants. Proper drug history may help in treatment planning, thus minimizing the failure rates.

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