All-on-four rehabilitation in patient with type II diabetes mellitus: case report and literature review

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Abstract

AIM: **The increase in the average age of the population leads to an increasing incidence of many different systemic diseases, often associated with partial or total edentulism. In particular, diabetes plays a significant role in patients' implant-prosthetic rehabilitation, as it has a direct effect on the oral cavity. The aim of this case report is to illustrate the rate of implant survival, marginal bone loss and any intra- and post-operative complications in patients with type II diabetes, undergoing fixed prosthetic rehabilitation according to the All-on-Four method, in a two-years of follow-up.**

Keywords: All-on-Four, systemic diseases, immediate loading, diabetes, hyperglycemia.

Materials and methods

The patient, suffering from type II diabetes, presented edentulous regions and compromised residual teeth in both arches. Considering the need for a fixed rehabilitation and, on the other hand, a severe bone loss in the posterior maxillary and mandibular sectors, we opted for a rehabilitation based on a reduced number of implants, according to the "All-on-Four" method. Follow-up examinations, aiming at assessing implant survival and marginal bone loss, were performed one week after surgery, after six months and then once a year for the following 24 months. Any intra- and postoperative complications were noted to evaluate and monitor the patient. Professional hygiene was performed every four months after surgery.

Results

No implants were lost during the follow-up period. The marginal bone loss was comparable to literature results related to implant-retained prosthetic rehabilitations in healthy patients. No intra- and postoperative complications were reported.

Conclusion

Maintaining a good glycemic control, able to favor the compensation of diabetes, the insertion of implants can be considered a safe procedure. The constant monitoring of the patient and his adherence to a strict hygiene protocol are fundamental to promote implant survival and early identification of complications.

Introduction

The increase in the average age of the population leads to an increase in the incidence of various systemic diseases such as diabetes. At the same time fixed rehabilitation of partial or total edentulous patients with systemic diseases, associated with the increase in the average age, could be increasingly required (1, 2).
Diabetes mellitus is a complex metabolic disease, defined by the ADA (American Diabetes Association) as a group of metabolic diseases characterized by elevated blood glucose levels (hyperglycemia) that result from the body's inability to produce or use insulin (3). There are four types of diabetes: type I diabetes, an autoimmune disease characterized by an absolute deficiency of insulin, caused by destruction of pancreatic ß-cells, that affects approximately 5-10% of the population and tends to occur at a young age; type II diabetes, caused by the association between a peripheral resistance to the action of insulin and an inadequate secretory response of pancreatic ß-cells ("relative insulin deficiency"), represents the majority of cases of late-onset diabetes; drug- or chemical-induced diabetes; and gestational diabetes (4). Diabetes has a direct effect on the oral cavity, manifesting itself through microangiopathy, altered immune response and changes in salivary composition (5). In cases of implant rehabilitations, diabetes, could interfere with the normal processes of osseointegration, as the state of hyperglycemia has a negative effect on osteoblastic regulation and BIC (Bone Implant Contact) values (6, 7).
The diabetic patient's treatment may exhibit two different types of complications: the intra operative and the post-operative ones. The former group includes hypoglycemic crisis, while the latter includes mucositis, peri-implantitis, lack of implant osseointegration and poor wound healing (8). Hypoglycemic crisis is defined as an acute consequence of diabetic disease and usually occurs when the patient had not taken their medi-

cations regularly and had not adequately eaten before the appointment (9). Mucositis and peri-implantitis are defined as inflammatory lesions of the tissues surrounding an implant. Peri-implant mucositis is defined as an inflammatory lesion limited to the surrounding mucosa of an implant, whereas peri-implantitis is defined as an inflammatory lesion of the mucosa affecting the supporting bone resulting in a loss of osseointegration, thus causing a likely decrease in implant success (10). The failure to osseointegrate the implant is another occurring post-operative complication. Osseointegration implies a firm, direct, and lasting connection between the vital bone and the titanium implants (11). In conclusion, we recall the incomplete soft tissue healing, caused by high blood glucose levels and non-enzymatic protein glycation, leading to AGE formation (12) which alters the permeability of the endothelium, releases inflammatory cytokines and growth factors, and increases the expression of adhesion molecules and chemokines, thus leading to delayed wound healing (13,14).

The aim of this case report was to illustrate implant survival rate, marginal bone loss and possible intra- and post-operative complications in patients with type II diabetes undergoing fixed prosthetic rehabilitation, according to the All-on-Four method, at two years follow-up.

Case report

A 60-year-old woman came to the Department of Dentistry of the IRCCS San Raffaele Hospital with the wish to have an implant-prosthetic rehabilitation of the lower arch. The patient was submitted to an anamnestic questionnaire which showed that she suffered from type II diabetic pathology. To assess the state of the disease, it was decided to perform laboratory tests in which the values of Hba1c 7% (glycosylated haemoglobin) and glycaemic levels <180 mg/dl were analysed. The tests' results were normal and her diabetes resulted to be under control, making the patient an excellent candidate for implant therapy. The frontal view of the patient's smile can be observed in Figure 1. Intraoral examination revealed the presence of an incongruous prosthesis anchored to dental elements that functioned as prosthetic abutments (Fig. 2). Among the various treatment options, given the presence of edentulous areas, the placement of implants according to the "All-on-Four" method was considered the most valid. After the signing of the informed consent and the implant-prosthetic treatment, the patient was made aware of the possible intra- and post-operative complications, determined by her general state of health. A professional oral hygiene session was carried out during the preoperative phase; subsequently, conventional impressions were taken for the study models; these were also used for the prosthetic component of the treatment. This was followed by radiographic investigations including an OPT (orthopantomography, a first level examination) which allowed an overall assessment of the jaws (Fig. 3). But, only after performing a CBCT (Cone Beam Computed Tomography, second level examination), it was possible to evaluate the bone volume of the maxilla. After carefully classifying the patient's bone density, defined as D3, and attentively performing all preoperative procedures, surgery could be scheduled. One hour before surgery, 2g of Amoxicillin and Clavulanic Acid (Augmentin, GlaxoSmithKline, Brussels, Belgium) were administered as a preventive measure. The surgical phase was performed under local anaesthesia (Optocaine 20 mg/ml with adrenaline 1:80,000; Molteni Dental, Florence, Italy). Some dental elements considered hopeless were avulsed (Fig. 4).

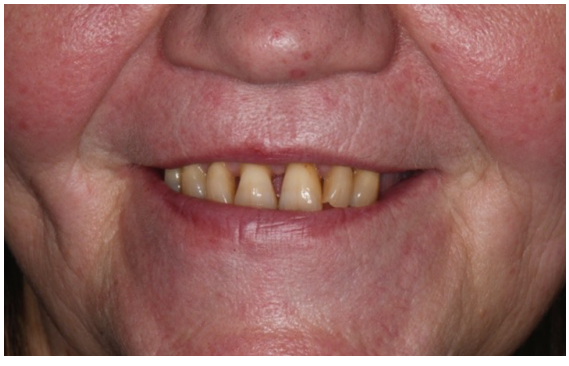

Figure 1. Extraoral photo.

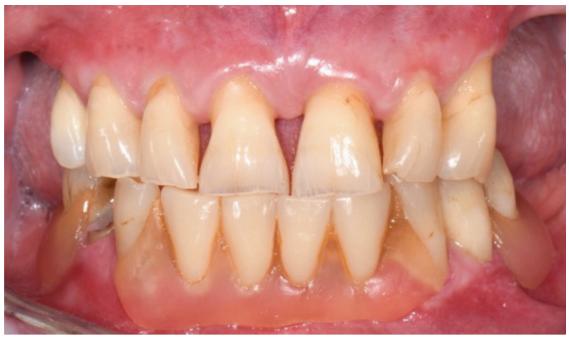

Figure 2. Intraoral photo: presence in the mandible of an incogruous prosthesis anchored to dental elements.

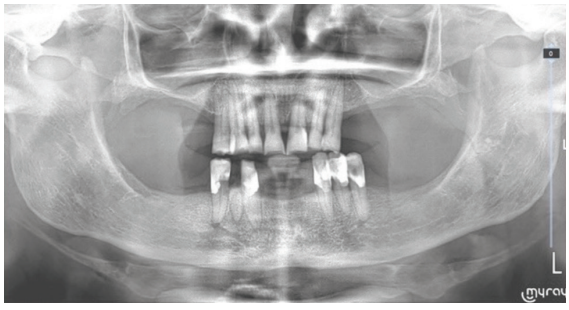

Figure 3. Orthopantomography that shows the condition of the jaw bones and residual elements.

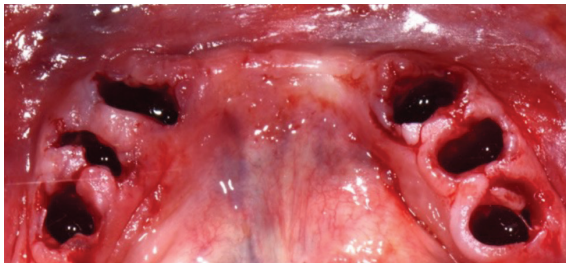

Figure 4. Post-extractive socket.

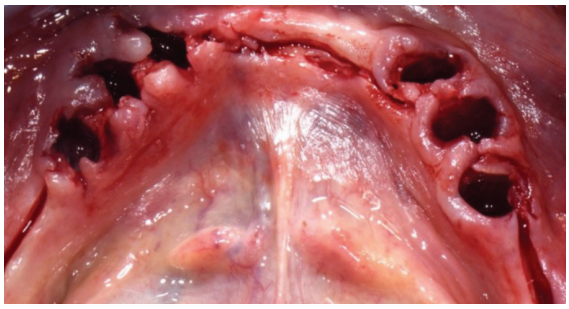

Figure 5. Crestal incision and bilateral release incisions.

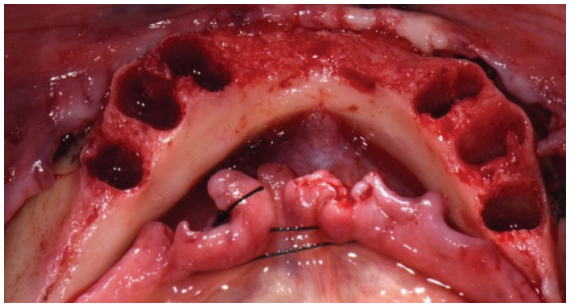

Figure 6. Full-thickness buccal flap.

The mandibular edentulous ridge was incised with a crestal incision and bilateral release incisions from the first molar region to the contralateral side and a subperiosteal dissection was performed on the lingual and buccal surfaces (Fig. 5). A full-thickness buccal flap was then lifted to expose the buccal bone wall and to get an optimal view of the mental foramen (Fig. 6).

Once the incisions had been made and the flaps lifted, implant placement was possible. In the mandible, the two posterior implants (dimensions length and diameter) (TTx, Winsix, Biosafin, Ancona, Italy) were placed bilaterally immediately anteriorly to the mental foramen (Fig. 7). It is important to underline that, following the All-on-Four protocol, the posterior implants are inserted following an inclined trajectory of about 25-30 degrees with respect to the occlusal plane. In fact, they emerge at the level of the second premolar, in order to decrease the length of the cantilever and maintain a large distance between the implants. The central implants, on the other hand, are inserted following a trajectory perpendicular to the occlusal plane (Fig. 8).

The insertion torque was between 30 and 40 Ncm before final implant placement, thus achieving high primary stability and immediate functionality.

To compensate for the lack of parallelism between the posterior implants and the prosthetic screw, angled abutments (Extreme Abutment, EA Winsix, Biosafin) were placed at 30°. The anterior implants, on the other hand, were fixed at 17° to allow optimal access for the prosthetic screw ((Fig. 9). After these steps, which were essential for the prosthetic part, the previously lifted flap was repositioned and adjusted with 4-0 nonabsorbable suture (Vicryl; Ethicon, Johnson & Johnson, New B runswick, NJ, USA), ((Fig. 10). Immediately after surgery, an OPT was performed to verify the correct placement of the implants ((Fig. 11).

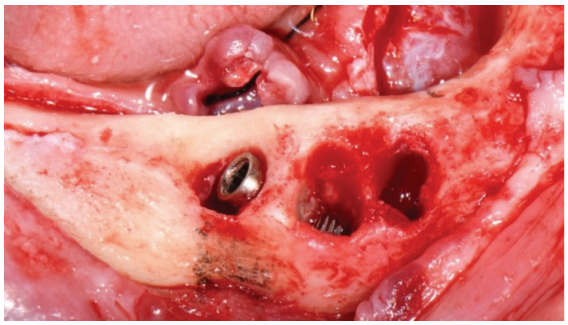

Figure 7. Tilted implant.

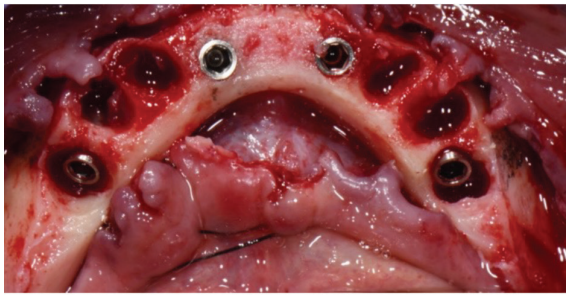

Figure 8. Axial and tilted implants.

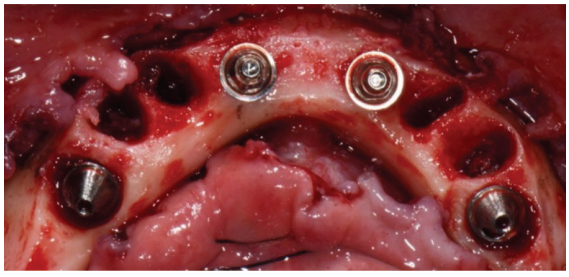

Figure 9. Placement of abutments.

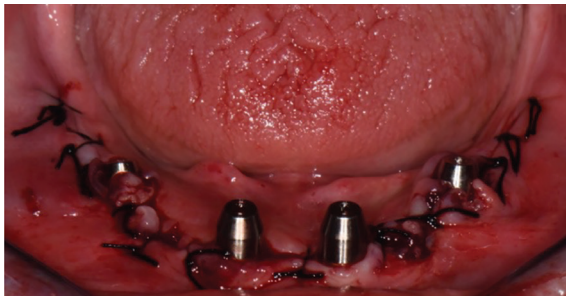

Figure 10. Flap repositioning and suture.

Then the prosthetic phase started, which included the delivery of a provisional prosthesis and the taking of impressions for the fabrication of the definitive one: a few hours after surgery, a screw-reinforced, metal-reinforced, acrylic provisional prosthesis with ten teeth was delivered (no cantilevers were used in the provisional prostheses).

The torque for the tightening the prosthetic screws was 20 N. Eventually the screw access holes were covered with temporary resin (Fermit, Ivoclar Vivadent, Naturno, Bolzano, Italy) ((Fig. 12).

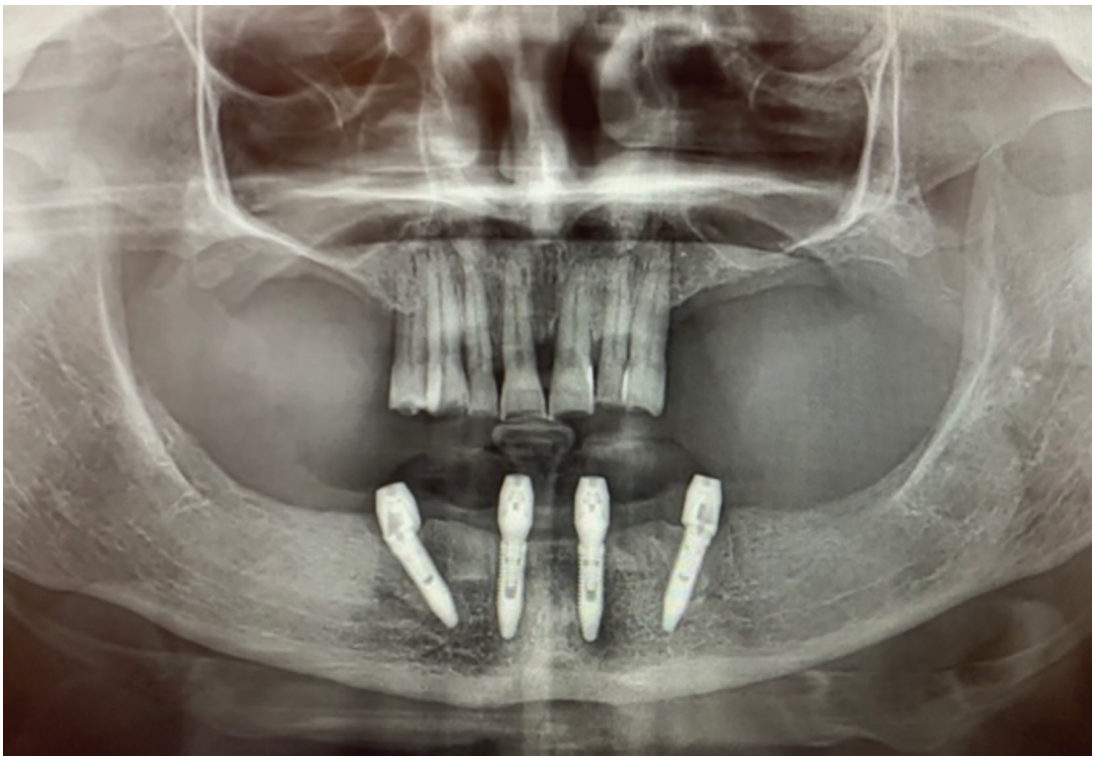

Figure 11. OPT to check implants placement.

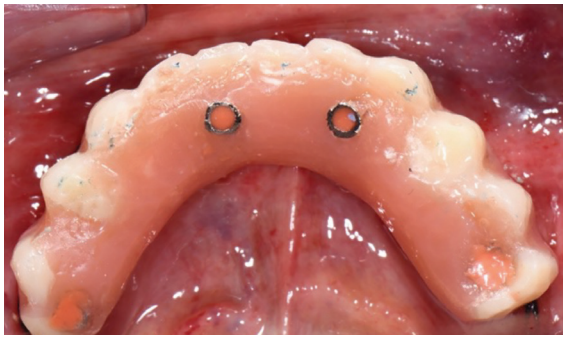

Figure 12. Provisional prosthesis.

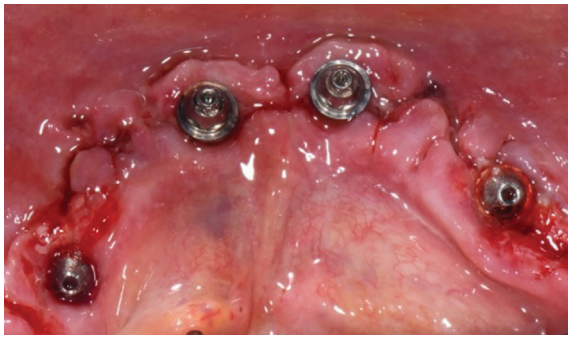

Figure 13. Mucosa after suture removal.

Approximately four months after surgery, the definitive prosthesis will be delivered and, unlike the provisional prosthesis, the latter will have an occlusion reproducing the patient's natural dentition, i.e. it will have a cantilever distal to the first molar.

Post-surgical indications included the use of a post-surgical dressing and rinsing with a solution containing chlorhexidine digluconate (0.12% or 0.2%), twice a day for 10 days. In addition, the use of 1 g Amoxicillin and Clavulanic Acid (Augmentin, GlaxoSmithKline) twice daily for 7 days after surgery and non-steroidal anti-inflammatory drugs (Ibuprofen 600 mg, Brufen, Abbott Laboratories, Chicago, IL, USA) was recommended should it be deemed necessary. Lastly, the patient was advised to eat a liquid diet and to avoid any brushing trauma to the surgical site, as well as smoking. The patient underwent a follow-up visit after one week and the sutures were removed at the same time (Fig. 13).

Follow-up

Follow-up visits, aimed at clinical and radiographic examination, were performed one week after implant placement. Subsequently, at three months, six months and then annually until a two-year follow-up was attained. The patient was instructed, by a dental hygienist, in mechanical plaque control using an electric or manual toothbrush, interproximal brushes and Super Floss (Oral B, Procter & Gamble, Cincinnati, OH, USA). While, professional oral hygiene procedures were performed every three months, after implant placement.

Parameters evaluated

Implants survival rate. Implant survival rate is based on the number of implants that were not lost or removed, during the follow-up period (15).

Marginal bone loss. Intra oral radiographs, using the parallel cone technique, were taken after implant placement, at three, six, twelve months and once a year for the following two years of follow-up. To evaluate marginal bone progression, the measurements were performed using Digora 2.5 software (Soredex, Tuusula, Finland). First, the instrument was calibrated (pixel/mm), using the diameter of the implants as the unit. Then, changes in the height of the peri-implant marginal bone with respect to the most coronal part of the implant fixture and the contact point between the implant fixture and the marginal crest were measured. To evaluate bone, a line passing over the shoulder of the implant was considered as a reference point for measurement from which a straight line was drawn parallel to the long axis of the implant to the most coronal point where the bone made contact with the fixture, both mesially and distally. The software automatically provided the distance between the two points measured in millimeters. To reduce human error, this measurement was made by different operators, and the mean of the three measurements was considered.
Then, to calculate the marginal bone level, a mesial measurement was taken, a distal measurement was taken and then the average of the mesial, distal and the average between the two values of a single implant site was calculated.

Intra-operative and post-operative complications.

Intra-operative complications	Post-operative complications
Hypoglycaemic crisis	Mucositis and peri-implantitis
	Lack of osseointegration
	Insufficient wound healing

Results

Implant survival rate. In the clinical case presented, the diabetic patient who received implant rehabilitation, presented laboratory tests appropriate for implant insertion. No implants were lost during the follow-up period. It is stated that the survival rate, two years after surgery, was 100% (16,17).

Marginal bone loss. Both axial and tilted implants showed marginal bone loss comparable to that of the healthy patient (17-19).

MARGINAL BONE LOSS	Axial implants	Tilted implants
6 months (mm)	0.61 ± 0.75	0.66 ± 0.58
1 year (mm)	0.85 ± 0.83	0.86 ± 0.91
2 years (mm)	0.86 ± 0.78	0.88 ± 0.64

Intra- and post-operative complications. The patient, thanks to adequate glycemic control (20), did not suffer from hypoglycemic crisis during the surgical procedure. No clinical signs of mucositis and peri-implantitis were observed during the two-year follow-up. This was made possible by the patient's inclusion in a maintenance program of professional oral hygiene and control of the diabetic pathology (21). The literature suggests that mucositis is caused by the accumulation of biofilm that interrupts host-microbe homeostasis at the implant-mucosal interface, resulting in an inflammatory lesion. Mucositis is a reversible condition, so the clinical implication is that optimal biofilm removal is a prerequisite for the prevention and management of mucositis (22). Based on these considerations, it was agreed that periodic clinical and radiographic controls should always be performed after implant placement to allow for the possible diagnosis of mucositis and peri-implantitis. Intra-oral radiographs, taken during the follow-up period, confirmed that osseointegration had taken place. They showed intimate contact between bone and implant, with an apparent absence of interposed fibrous tissue. The osseointegration of the patient's implants was promoted by the correct implant placement, based on the primary stability, which was obtained by an insertion torque of 30 N (23).

Discussion

According with the clinical considerations examined, it will be necessary to follow an adequate diagnostic pathway, to obtain a predictable result of the implant-prosthetic therapy of the diabetic patient. During the first visit, in fact, the general medical and dental history plays a crucial role and allows the clinician to reach an adequate knowledge of the patient's general and dental health status (24). An anamnesis is followed by an extra- and intra-oral examination; the latter paying particular attention not only to the dental elements present in the oral cavity but also to the soft tissues surrounding the tooth or located on the edentulous ridges (25, 26).
Before a diabetic patient undergoes oral surgery, it is necessary to establish the type of diabetes and the degree of glycaemic control. Robertson C et al., in a review of the literature, describe the criteria to establishing the diagnosis of diabetes and to identifying individuals at high risk of developing the disease. They suggest that if patients with controlled diabetes maintain a Hba1c value of <7%, then it will be possible to proceed with surgery (27).
In the literature review, by Ramu C. et al., the indications for antibiotic prophylaxis in dental practice are stated. For patients with uncontrolled diabetes, antibiotic prophylaxis is considered mandatory as they are more susceptible to oral infections. On the other hand, antibiotic prophylaxis is recommended for patients with controlled diabetes, both in the case of minor and major surgery (28). For these reasons, in agreement with the authors, the patient was given 2g of Amoxicillin and Clavulanic acid one hour before surgery, as a preventive measure.
The most serious complication, that a diabetic patient can experience during oral surgery, is a hypoglycemic crisis. To prevent this fact, it is important to make sure that the patient has taken their usual medication and eaten regularly before the appointment (29). If the patient has lost consciousness due to hypoglycemic crisis,

medical assistance should be sought; a solution of 25-30 ml 50% dextrose or 1 mg glucagon should be injected intravenously; glucagon can also be administered intramuscularly or subcutaneously (30). According to Kidambi S. et al., patients receiving oral antidiabetics have a lower risk of developing hypoglycemic crises than those receiving insulin therapy (31).

Holmstrup P. et al. state that, since diabetes mellitus is a systemic inflammatory state, often associated with periodontitis, in case of implant rehabilitation, the patient may have an increased risk of developing mucositis and peri-implantitis (32). In the literature, the correlation between hyperglycemia and the risk of peri-implantitis is still a matter of discussion. Alberti A. et al., in their retrospective study, evaluated the influence of diabetes on peri-implantitis and implant failure. They considered 204 patients, treated with 929 implants. Of these, 19 were diabetic patients and most of them showed good control of their diabetic disease at the time of implant surgery. Among the diabetic patients only one showed peri-implantitis and another one showed increased implant failures. The results of these authors showed no association between peri-implantitis, diabetes mellitus and implant failure (33). In contrast, Rekawek P. et al, in their retrospective cohort study, examined 286 patients treated with 748 implants and found that diabetic patients had an increased risk of peri-implantitis. However, this risk can be counteracted by placing patients on a maintenance regimen with regular visits and professional oral hygiene sessions (34).

Another clinical aspect affected by diabetes is implant osseointegration. In the retrospective case-control study by Sghaireen MG et al. 257 subjects were included, 121 with and 136 without diabetes; diabetes was defined as well controlled with a HbA1c of less than 8%. Implant failure in the osseointegration process was observed in 17 cases in the diabetes group (4.5%) and in 16 cases in the control group (4.4%), so that a non-significant difference ($p = 0.365$) was concluded (35). Schwarz F. et al., in their retrospective cohort study, evaluated immediate loading in a patient with type II diabetes. In 108 diabetic patients, immediately loaded implants showed identical survival to those placed after 3 months (100% each) (36). In diabetic individuals, persistent hyperglycaemia suppresses osteoblastic activity and alters the response of parathyroid hormone which regulates calcium and phosphorus metabolism (37), decreases collagen formation, induces apoptosis in bone lining cells and increases osteoclastic activity resulting in bone loss (38). The reduction in bone-implant contact confirms that diabetes inhibits osseointegration, unless hyperglycemia is therapeutically treated, and normal glucose levels are maintained (39). In the article by Khan N et al. it appears that the authors were not in favour of dental implant placement in patients with diabetes mellitus because of the high failure rate due to poor wound healing and impaired bone metabolism (40). High blood glucose levels and non-enzymatic glycation of proteins lead to the formation of AGEs (advanced glycation end products) (40). AGE alters the permeability of the endothelium, releases inflammatory cytokines and growth factors, increases the expression of adhesion molecules and chemokines, thus leading to micro-vascular complications and delayed wound healing (41).

In the retrospective study by Alberti et al., no difference in implant survival (survival rate) after 10 years was shown in patients with diabetes (survival rate 96.5%), compared to patients without diabetes mellitus (survival rate 94.8%) (42). According to the literature review, by Naujokat H. et al., in the first years after implant placement, the survival rate of implants in patients with controlled diabetes does not differ from that of non-diabetics. However, when observed in the long term, about twenty years, the implant survival rate is reduced in patients with controlled diabetes compared to non-diabetic patients (43).

Lorean A et Al., in their retrospective study, reported that patients with high HbA1c values (8.1% to 10.0%) had greater marginal bone loss than those with lower HbA1c values (44). In agreement with this, Souto-Maior JR et al., through a systematic review of the literature, state that it is possible to observe marginal bone loss that affects osseointegration (45). The factors that can contribute to implant failure, as already described, are many. However, according to the scientific review by Mombelli et al., bacterial plaque has a negative role in the health of peri-implant oral tissues; in fact, the basis of a correct management of the bacterial flora is home oral hygiene supported by professional services (46). It is necessary to underline how fundamentally important the synergy between the dental professional and the dental hygienist is in the context of successful implant rehabilitation, which, even more so in the treatment and monitoring of patients with systemic pathologies, must be expressed because of the potential risks of any preoperative, intraoperative, and postoperative complications (47, 48).

Conclusion

This case report could demonstrate that implant-prosthetic rehabilitations in the totally edentulous patient with compensated diabetes could be safely applied. Clinical studies should be performed to confirm this result.

References

1. Tetè G, Polizzi E, D'orto B, Carinci G, Capparè P. How to consider implant-prosthetic rehabilitation in elderly patients: a narrative review. J Biol Regul Homeost Agents. 2021 Jul-Aug;35(4 Suppl. 1):119-126. doi: 10.23812/21-4supp1-11. PMID: 34425667.
2. D'Orto B, Tetè G, Polizzi E. Osseointegrated dental implants supporting fixed prostheses in patients affected by Sjögren's Sindrome: A narrative review. J Biol Regul Homeost Agents. 2020 Nov-Dec;34(6 Suppl. 3):91-93. PMID: 33412784.
3. Sannino G, Bollero P, Barlattani A, Gherlone E. A Retrospective 2-Year Clinical Study of Immediate Prosthetic Rehabilitation of Edentulous Jaws with Four Implants and Prefabricated Bars. J Prosthodont. 2017 Jul;26(5):387-394. doi: 10.1111/jopr.12406. Epub 2015 Nov 30. PMID: 26619306.
4. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. Diabetes Care. 2021 Jan;44(Suppl 1):S15-S33. doi: 10.2337/dc21-S002. Erratum in: Diabetes Care. 2021 Sep;44(9):2182. PMID: 33298413.

5. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020. Diabetes Care. 2020 Jan;43(Suppl 1):S14-S31. doi: 10.2337/dc20-S002. PMID: 31862745.
6. Ternois M. La bouche : un miroir du diabète [The oral cavity: A mirror of diabetes]. Presse Med. 2017 Sep;46(9):822-830. French. doi: 10.1016/j.lpm.2017.04.001. Epub 2017 May 10. PMID: 28502373.
7. Retzepi M, Donos N. The effect of diabetes mellitus on osseous healing. Clin Oral Implants Res. 2010 Jul;21(7):673-81. doi: 10.1111/j.1600-0501.2010.01923.x. Epub 2010 May 3. PMID: 20465554.
8. Mellado-Valero A, Ferrer García JC, Herrera Ballester A, Labaig Rueda C. Effects of diabetes on the osseointegration of dental implants. Med Oral Patol Oral Cir Bucal. 2007 Jan 1;12(1):E38-43. PMID: 17195826.
9. Jiang X, Zhu Y, Liu Z, Tian Z, Zhu S. Association between diabetes and dental implant complications: a systematic review and meta-analysis. Acta Odontol Scand. 2021 Jan;79(1):9-18. doi: 10.1080/00016357.2020.1761031. Epub 2020 May 13. PMID: 32401121.
10. Umpierrez G, Korytkowski M. Diabetic emergencies - ketoacidosis, hyperglycaemic hyperosmolar state and hypoglycaemia. Nat Rev Endocrinol. 2016 Apr;12(4):222-32. doi: 10.1038/nrendo.2016.15. Epub 2016 Feb 19. PMID: 26893262.
11. Figuero E, Graziani F, Sanz I, Herrera D, Sanz M. Management of peri-implant mucositis and peri-implantitis. Periodontol 2000. 2014 Oct;66(1):255-73. doi: 10.1111/prd.12049. PMID: 25123773.
12. Brånemark PI, Hansson BO, Adell R, Breine U, Lindström J, Hallén O, Ohman A. Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. Scand J Plast Reconstr Surg Suppl. 1977;16:1-132. PMID: 356184.
13. Tetè G, D'orto B, Ferrante L, Polizzi E, Cattoni F. Role of mast cells in oral inflammation. J Biol Regul Homeost Agents. 2021 Jul-Aug;35(4 Suppl. 1):65-70. doi: 10.23812/21-4supp1-6. PMID: 34425662.
14. Tetè G, D'Orto B, Nagni M, Agostinacchio M, Polizzi E, Agliardi E. Role of induced pluripotent stem cells (IPSCS) in bone tissue regeneration in dentistry: a narrative review. J Biol Regul Homeost Agents. 2020 Nov-Dec;34(6 Suppl. 3):1-10. PMID: 33386051.
15. Misch CE. Bone classification, training keys to implant success. Dent Today. 1989 May;8(4):39-44. PMID: 2597401.
16. Andrade CAS, Paz JLC, de Melo GS, Mahrouseh N, Januário AL, Capeletti LR. Survival rate and peri-implant evaluation of immediately loaded dental implants in individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Clin Oral Investig. 2022 Feb;26(2):1797-1810. doi: 10.1007/s00784-021-04154-6. Epub 2021 Sep 29. PMID: 34586502; PMCID: PMC8479496.
17. Chrcanovic BR, Albrektsson T, Wennerberg A. Diabetes and oral implant failure: a systematic review. J Dent Res. 2014 Sep;93(9):859-67. doi: 10.1177/0022034514538820. Epub 2014 Jun 13. PMID: 24928096; PMCID: PMC4541101.
18. Souto-Maior JR, Pellizzer EP, de Luna Gomes JM, Dds CAAL, Dds JFSJ, Vasconcelos BCDE, de Moraes SLD. Influence of Diabetes on the Survival Rate and Marginal Bone Loss of Dental Implants: An Overview of Systematic Reviews. J Oral Implantol. 2019 Aug;45(4):334-340. doi: 10.1563/aaid-joi-D-19-00087. Epub 2019 May 1. PMID: 31042455.
19. Lorean A, Ziv-On H, Perlis V, Ormianer Z. Marginal Bone Loss of Dental Implants in Patients with Type 2 Diabetes Mellitus with Poorly Controlled HbA1c Values: A Long-Term Retrospective Study. Int J Oral Maxillofac Implants. 2021 Mar-Apr;36(2):355-360. doi: 10.11607/jomi.8476. PMID: 33909727.
20. de Araújo Nobre M, Maló P, Gonçalves Y, Sabas A, Salvado F. Dental implants in diabetic patients: retrospective cohort study reporting on implant survival and risk indicators for excessive marginal bone loss at 5 years. J Oral Rehabil. 2016 Nov;43(11):863-870. doi: 10.1111/joor.12435. Epub 2016 Sep 27. PMID: 27611605.
21. Robertson C, Drexler AJ, Vernillo AT. Update on diabetes diagnosis and management. J Am Dent Assoc. 2003 Oct;134 Spec No:16S-23S. doi: 10.14219/jada.archive.2003.0368. PMID: 18196669.
22. Smeets R, Henningsen A, Jung O, Heiland M, Hammächer C, Stein JM. Definition, etiology, prevention and treatment of peri-implantitis--a review. Head Face Med. 2014 Sep 3;10:34. doi: 10.1186/1746-160X-10-34. PMID: 25185675; PMCID: PMC4164121.
23. Heitz-Mayfield LJA, Salvi GE. Peri-implant mucositis. J Clin Periodontol. 2018 Jun;45 Suppl 20:S237-S245. doi: 10.1111/jcpe.12953. PMID: 29926488.
24. Villa R, Polimeni G, Wikesjö UM. Implant osseointegration in the absence of primary bone anchorage: a clinical report. J Prosthet Dent. 2010 Nov;104(5):282-7. doi: 10.1016/S0022-3913(10)00146-0. PMID: 20970533.
25. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. Diabetes Care. 2021 Jan;44(Suppl 1):S15-S33. doi: 10.2337/dc21-S002. Erratum in: Diabetes Care. 2021 Sep;44(9):2182. PMID: 33298413.
26. Song YL, Zhang SJ. [Clinical features, diagnosis and treatment key points of dental implant prostheses for diabetic patients]. Zhonghua Kou Qiang Yi Xue Za Zhi. 2021 Dec 9;56(12):1172-1178. Chinese. doi: 10.3760/cma.j.cn112144-20210926-00437. PMID: 34915649.
27. Halpern LR, Adams DR. Medically Complex Dental Implant Patients: Controversies About Systemic Disease and Dental Implant Success/Survival. Dent Clin North Am. 2021 Jan;65(1):1-19. doi: 10.1016/j.cden.2020.08.001. Epub 2020 Oct 9. PMID: 33213704.
28. Robertson C, Drexler AJ, Vernillo AT. Update on diabetes diagnosis and management. J Am Dent Assoc. 2003 Oct;134 Spec No:16S-23S. doi: 10.14219/jada.archive.2003.0368. PMID: 18196669.
29. Ramu C, Padmanabhan TV. Indications of antibiotic prophylaxis in dental practice- review. Asian Pac J Trop Biomed. 2012 Sep;2(9):749-54. doi: 10.1016/S2221-1691(12)60222-6. PMID: 23570007; PMCID: PMC3609373.
30. Turchin A, Matheny ME, Shubina M, Scanlon JV, Greenwood B, Pendergrass ML. Hypoglycemia and clinical outcomes in patients with diabetes hospitalized in the general ward. Diabetes Care. 2009 Jul;32(7):1153-7. doi: 10.2337/dc08-2127. PMID: 19564471; PMCID: PMC2699723.
31. Mealey BL. Impact of advances in diabetes care on dental treatment of the diabetic patient. Compend Contin Educ Dent. 1998 Jan;19(1):41-4, 46-8, 50 passim; quiz 60. PMID: 9533351.
32. Kidambi S, Patel SB. Diabetes mellitus: considerations for dentistry. J Am Dent Assoc. 2008 Oct;139 Suppl:8S-18S. doi: 10.14219/jada.archive.2008.0364. PMID: 18809649.
33. Holmstrup P, Damgaard C, Olsen I, Klinge B, Flyvbjerg A, Nielsen CH, Hansen PR. Comorbidity of periodontal disease: two sides of the same coin? An introduction for the clinician. J Oral Microbiol. 2017 Jun 14;9(1):1332710. doi: 10.1080/20002297.2017.1332710. PMID: 28748036; PMCID: PMC5508374.
34. Alberti A, Morandi P, Zotti B, Tironi F, Francetti L, Taschieri S, Corbella S. Influence of Diabetes on Implant Failure and Peri-Implant Diseases: A Retrospective Study. Dent J (Basel). 2020 Jul 4;8(3):70. doi: 10.3390/dj8030070. PMID: 32635449; PMCID: PMC7559512.
35. Rekawek P, Carr BR, Boggess WJ, Coburn JF, Chuang SK, Panchal N, Ford BP. Hygiene Recall in Diabetic and Nondiabetic Patients: A Periodic Prognostic Factor in the Protection Against Peri-Implantitis? J Oral Maxillofac Surg. 2021 May;79(5):1038-1043. doi: 10.1016/j.joms.2020.12.032. Epub 2020 Dec 29. PMID: 33497648.
36. Sghaireen MG, Alduraywish AA, Srivastava KC, Shrivastava D, Patil SR, Al Habib S, Hamza M, Ab Rahman S, Lynch E, Alam MK. Comparative Evaluation of Dental Implant Failure among Healthy and Well-Controlled Diabetic Patients-A 3-Year Retrospective Study. Int J Environ Res Public Health. 2020 Jul 21;17(14):5253. doi: 10.3390/ijerph17145253. PMID: 32708165; PMCID: PMC7400304.

37. Schwarz F, Derks J, Monje A, Wang HL. Peri-implantitis. J Clin Periodontol. 2018 Jun;45 Suppl 20:S246-S266. doi: 10.1111/jcpe.12954. PMID: 29926484.
38. Santana RB, Xu L, Chase HB, Amar S, Graves DT, Trackman PC. A role for advanced glycation end products in diminished bone healing in type 1 diabetes. Diabetes. 2003 Jun;52(6):1502-10. doi: 10.2337/diabetes.52.6.1502. PMID: 12765963.
39. Kayal RA, Tsatsas D, Bauer MA, Allen B, Al-Sebaei MO, Kakar S, Leone CW, Morgan EF, Gerstenfeld LC, Einhorn TA, Graves DT. Diminished bone formation during diabetic fracture healing is related to the premature resorption of cartilage associated with increased osteoclast activity. J Bone Miner Res. 2007 Apr;22(4):560-8. doi: 10.1359/jbmr.070115. PMID: 17243865; PMCID: PMC3109431.
40. Kopman JA, Kim DM, Rahman SS, Arandia JA, Karimbux NY, Fiorellini JP. Modulating the effects of diabetes on osseointegration with aminoguanidine and doxycycline. J Periodontol. 2005 Apr;76(4):614-20. doi: 10.1902/jop.2005.76.4.614. PMID: 15857103.
41. Khan N, Bakshi KS, Jaggi AS, Singh N. Ameliorative potential of spironolactone in diabetes induced hyperalgesia in mice. Yakugaku Zasshi. 2009 May;129(5):593-9. doi: 10.1248/yakushi.129.593. PMID: 19420890.
42. Basta G, Schmidt AM, De Caterina R. Advanced glycation end products and vascular inflammation: implications for accelerated atherosclerosis in diabetes. Cardiovasc Res. 2004 Sep 1;63(4):582-92. doi: 10.1016/j.cardiores.2004.05.001. PMID: 15306213.
43. Alberti A, Morandi P, Zotti B, Tironi F, Francetti L, Taschieri S, Corbella S. Influence of Diabetes on Implant Failure and Peri-Implant Diseases: A Retrospective Study. Dent J (Basel). 2020 Jul 4;8(3):70. doi: 10.3390/dj8030070. PMID: 32635449; PMCID: PMC7559512.
44. Naujokat H, Kunzendorf B, Wiltfang J. Dental implants and diabetes mellitus-a systematic review. Int J Implant Dent. 2016 Dec;2(1):5. doi: 10.1186/s40729-016-0038-2. Epub 2016 Feb 11. PMID: 27747697; PMCID: PMC5005734
45. Lorean A, Ziv-On H, Perlis V, Ormianer Z. Marginal Bone Loss of Dental Implants in Patients with Type 2 Diabetes Mellitus with Poorly Controlled HbA1c Values: A Long-Term Retrospective Study. Int J Oral Maxillofac Implants. 2021 Mar-Apr;36(2):355-360. doi: 10.11607/jomi.8476. PMID: 33909727.
46. Souto-Maior JR, Pellizzer EP, de Luna Gomes JM, Dds CAAL, Dds JFSJ, Vasconcelos BCDE, de Moraes SLD. Influence of Diabetes on the Survival Rate and Marginal Bone Loss of Dental Implants: An Overview of Systematic Reviews. J Oral Implantol. 2019 Aug;45(4):334-340. doi: 10.1563/aaid-joi-D-19-00087. Epub 2019 May 1. PMID: 31042455.
47. Mombelli A, Lang NP. The diagnosis and treatment of peri-implantitis. Periodontol 2000. 1998 Jun;17:63-76. doi: 10.1111/j.1600-0757.1998.tb00124.x. PMID: 10337314.
48. Cattoni F, Tetè G, D'orto B, Bergamaschi A, Polizzi E, Gastaldi G. Comparison of hygiene levels in metal-ceramic and stratified zirconia in prosthetic rehabilitation on teeth and implants: a retrospective clinical study of a three-year follow-up. J Biol Regul Homeost Agents. 2021 Jul-Aug;35(4 Suppl. 1):41-49. doi: 10.23812/21-4supp1-4.
49. Polizzi E, D'orto B, Tomasi S, Tetè G. A micromorphological/microbiological pilot study assessing three methods for the maintenance of the implant patient. Clin Exp Dent Res. 2021 Apr;7(2):156-162. doi: 10.1002/cre2.345. Epub 2020 Nov 19. PMID: 33211411; PMCID: PMC8019768.