



ORIGINAL RESEARCH

ORAL MUCOSITIS IN PEDIATRIC ONCOLOGY PATIENTS TREATED WITH ANTINEOPLASTIC DRUGS: THE ROLE OF THE DENTAL TEAM IN THE PREVENTION AND TREATMENT

Morini M.¹, Nori A.², D'Amario M.¹, Chiacchia M.¹, Marchetti A.¹, Pizzolante T.¹, Botticelli G.¹, Rastelli S.¹, Mummolo S.¹

¹Department of Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, Italy

²Department of Surgical and Special Odontostomatology, Umberto I General Hospital, Ancona, Italy

Corresponding author: Prof. Stefano Mummolo, DDS, PhD Dept. of Life, Health and Environmental Sciences University of L'Aquila Dental Clinic, via Vetoio, Ed. Delta 6 67100 L'Aquila – Italy Phone: +390862433715 Fax: +390862433826 Mobile: +393382690451 email: stefano.mummolo@univaq.it

Received: Aug 27, 2025; **Accepted:** Sep 30, 2025; **Published:** Oct 18, 2025

Abstract

Background: In pediatric oncology population, oral mucositis as a consequence of chemotherapy is a highly prevalent complication which strongly affects both the quality of life and treatment possibilities of the patients. Still, the role of a dental team (dentist and hygienist) is not yet central and always present during diagnosis, recovery and follow up of these patients. The aim of this study is to assess the efficacy of dental team role in prevention and treatment of oral mucositis in pediatric oncology patients.

Materials and Methods: A dental team composed by a Dentist and two hygienists has been established to be disposable once a week rotating to the SOSD Oncoematologia Pediatrica of Azienda Ospedali Riuniti Presidio G. Salesi from the first of September 2022 till June 2024. The members of the team carried out visits and provided instructions of oral hygiene and tested different types of products for oral mucositis in 120 patients based on WHO grading and Wong-Baker faces pain rating scale. At the end by a dichotomous questionnaire was asked to all 120 patients' parents if the role of dental team in this study was appreciated and useful in prevention and treatment of oral mucositis.

Results: Pediatric oncology patients and their parents appreciated the constant presence of a member of the dental team. Information and oral hygiene were crucial preventing mucositis and continuous follow up allowed timely management of this complication showing function improvement in 65.1% of cases and pain reduction in 87.15%.

Conclusions: Our experience highlights that dental team interventions positively impact. These findings suggest that dental team role should be developed to provide better cancer care for parents and their children.

Keywords: pediatric oncology, malignant tumor, oral mucositis, chemotherapy, radiotherapy, immunotherapy

INTRODUCTION

In Italy the annual incidence of malignant tumor in the pediatric population aged between 0 and 14 years is 1400 cases, while 800 in 15 to 19 years population. In the last 40 years the mortality rate of pediatric tumors has changed significantly and it is in sharp decline. Children and teenagers who die for cancer are increasingly fewer: in 2008 the deaths were about a third of those recorded in the early Seventies, and today over 80% of patients recover¹⁻².

In the last 15 years the research has made huge steps about the treatment of these tumors, in fact the 5-years survival rate after diagnosis is about 82% in patients aged between 0-14 years and 86% in 15-19 years; statistics show that 3/4 of them are cured. Even if the study of more effective treatments based on the analyses of cancer genome without side effect is the object of modern researches, today the most used therapies are chemotherapy³, radiotherapy and immunotherapy⁴.

However, these are associated with various side effects such as oral complications that can occur during and after antineoplastic treatment in 30% to 100% of cases ⁵⁻⁸. These include oral mucositis, bacterial and mycotic opportunistic infections during chemotherapy ⁹ or reactivation of herpes simplex post-radiotherapy ¹⁰, salivary gland dysfunction, dysgeusia, trismus ¹¹, bleeding, dentofacial anomalies, GVHD (graft versus host disease) ¹². The severity of these side effects is highly variable and in the most severe cases can lead to a delay or even suspension of antineoplastic therapy ¹³⁻¹⁴.

Oral mucositis is one of the most frequent and disabling complications for pediatric patients ^{5,7}; it affects 20-40% of subjects undergoing conventional chemotherapy and 80% of high-dose chemotherapy as preliminary treatment to hematopoietic stem cell transplantation, in addition, almost all subjects receiving head and neck radiation develop some degree of mucositis ¹⁵. Pediatric patients are more susceptible to develop OM (oral mucositis) due to their intense cell turnover ¹⁶. Historically, the terms stomatitis and mucositis have been interchangeably in the literature, but not reflect the same process. The definition of mucositis emerged in the late 1980s and describes inflammation of the oral mucosa induced by chemotherapeutic and radiotherapy agents, while stomatitis refers to any inflammatory condition of the mouth, including teeth and periodontal tissues. Clinically oral mucositis can present a very heterogeneous pattern: from a tingling sensation to a severe burning pain that prevents same vital function like eating, drinking, speaking and swallowing. At the beginning the inflammation consists of an epithelial atrophy associated with erythema and bleeding, then ulcerations appear. The most severe forms present pseudomembranes and the possibility of mucosal damage dissemination to the pharynx and all gastrointestinal tract; in these cases the risk of secondary opportunistic infection is higher, especially in neutropenic patients undergoing hematopoietic stem cell transplantation who may develop sepsis or systemic compromise, needing total parenteral nutrition (TPN) and analgesic therapy with opioids. Anyway the severity and the width of mucosal damage strictly depend on general condition of the patient (age, neutrophil count, presence of systemic pathology) ¹⁷ and above all on type of medication, administration way, dose and frequency ¹⁸.

Biopathology

Oral mucosa is composed of non-keratinized epithelial cells which reproduce each 7-14 days and the biopathological mechanism underlying the damage is complex. Over time, the theory proposed by Sonis et al. in 1998 ¹⁹ including only the basal layer in

damaging induced by chemo and radiotherapy with impossible cell replication and consequent reduction, atrophy and ulceration has been influenced by new molecular and histological knowledge. Therefore, a new theory born, in which not only the epithelium but the interaction of all mucosa's element, including extracellular matrix, contributing to the damage ²⁰.

Consisting of 5 stages:

1. INITIAL TISSUE INJURY PHASE: chemotherapy and radiotherapy damage cell's DNA directly or indirectly producing ROS (Reactive Oxygen Species).
2. PRODUCTION AND HYPER-REGULATION OF MESSAGE SIGNALS: the expression of genes like c-jun, c-fos and Erg-1 active nuclear factors transcription like NF-kB or vascular adhesion molecules and consequently the up regulation of genes responsible of pro-inflammatory cytokines production such as IL1 and TNFα which lead to apoptosis.
3. SIGNAL AMPLIFICATION: cytokines collecting in tissues induce damage directly or indirectly. Changes in oral mucosa are visible 5-10 days after myoablative treatment and is like atrophy with severe erythema. This phase precedes clinically the mucositis.
4. ULCERATION: loss of integrity of mucosal barrier with painful and possible bacterial colonization after 7-11 days. Typically localized on non-keratinized mucosa in particular mouth's floor, buccal mucosa, labial mucosa and tongue ²¹.
5. HEALING: scarring and tissue healing thanks to fibroblasts when the pharmacological insult stopped and when neutropenia resolve.

Role of dental team

In spite of mucositis can compromise pediatric patients' quality of life, the "Halo Effect" is unfortunately increasing in their parents. This effect is represented by the fact that cancer diagnosis has a such strong and shocking emotional impact on them and for that reason they focus all attention on medical aspects related to antineoplastic treatments, underestimating any side effects in other areas of body like oral cavity ²²⁻²³⁻³⁹⁻⁴⁰.

Dentist and hygienist role is not always central nor present during phases of diagnosis, antineoplastic treatment and follow up of oncology pediatric patients, but due to correlation between chemo-radiotherapy and mucositis and above all the great negative impact of that in patients' lives ²⁴, is essential to inform parents, try to prevent or treat this complication. Despite the lack of literature data, is evident that oral preventive treatment

reduces incidence of complications like mucositis ²⁵.

Italian guidelines of the Ministry of Health of February 2018 shows dental protocols that allow monitoring and treating this type of patients from cancer diagnosis ²⁶. A first dental visit is essential before starting antineoplastic therapy to maintain a good level of oral hygiene and prevent oral complications. Furthermore all patients have to receive adequate oral education in order to acquire the ability to properly clean their teeth and mucosa. Sealings and fluoride prophylaxis are proposed as preventive measures while odontology treatments includes fillings carious elements, endodontic therapy, extraction of compromised teeth, decontamination of orthodontic appliance. In presence of oral complications deriving from antineoplastic therapy like mucositis treatment protocols could be followed; Dental team can collaborate with oncologists in order to improve patients' standard of living and guarantee closeness to their families ²⁷.

For that reason, the aim of this study is to evaluate the effectiveness of dental team the SOSD of Pediatric Oncohematology of G. Salesi University Hospital in Marche (Italy) from 1 September 2022 till June 2024 about prevention and treatment of oral mucositis in pediatric oncology patients.

MATERIALS AND METHODS

A dental team composed by a dentist and two hygienists has been established to be disposable once a week rotating to the SOSD Oncoematologia Pediatrica di Azienda Ospedali Riuniti Presidio G. Salesi from the first of September 2022 until June 2024. All patients read and signed the informed consent to participate in the study and the guidelines outlined in the Declaration of Helsinki for human experimentation were followed.

120 patients aged between 0-14 years affected by different type of tumor like 46% LLA (acute lymphoblastic leukemia), 16% Lymphoma, 13% SNC Malignant Tumor (Glioma), 8% SNA Tumor (Neuroblastoma), 7% Soft Tissue Sarcoma, 5% Kidney cancer, Bone cancer, retina, thyroid and rare forms have been considered.

At the moment of tumor diagnosis, the dental team carried out a first visit and the medical history folder was completed (Fig. 1).

SCHEDA ANAGRAFICA ED ANAMNISTICA

COGNOME _____ NOME _____

SSISD: M-I-P-O-ETMA _____

DATA E LUOGO DI NASCITA _____

INDIRIZZO via _____

cap _____ Prov _____

INFERM: data di nascita _____

MADRE: data di nascita _____

DIAGNOSI D'INGRESSO _____

ANAMNESI PATOLOGICA ODONTOSTRICA

Precedenti esperienze odontostomatologiche _____

ANAMNESI FAMILIARE

Mai. Ereditaria _____

Mai. Neuromuscolari _____

Mai. Cardiovascolari _____

Mai. Metaboliche _____

ANAMNESI FISIOLOGICA

Allergologie _____

Fisiologia _____

Attività fisica: ☐ No ☐ Moderata ☐ Intensa

Alimentazione: ☐ Naturale ☐ Artificiale

ANAMNESI PATOL. REMOTA

Allergie _____

Mai. Spettiche _____

Mai. Cardiovascolari _____

Spertensione arteriale _____

Mai. Respiratorie _____

Mai. Renali e urinarie _____

Mai. Endocrine e metaboliche _____

Mai. Osteoarticolari muscolari _____

Mai. Della coagulazione _____

Mai. Autoimmunitarie reumatiche _____

Mai. Psichiatriche e neurologiche _____

Progressi interventi chirurgici _____

Progressi ricoveri ospedalieri _____

Mai. Infettive _____

Patologie intercorrenti _____

Deficit sensoriali uditivi e visivi _____

ANAMNESI FARMACOLOGICA

Tempi attuali _____

Tempi attuali _____

ALTRI

VALUTAZIONE DI IGIENE ORALE

Grado di collaborazione

1 Collaborante ☐ 2 Collaborante ☐ 3 Collaborante ☐ 4 Collaborante ☐ 5 Collaborante ☐ 6 Collaborante ☐ 7 Collaborante ☐ 8 Collaborante ☐ 9 Collaborante ☐ 10 Collaborante ☐ 11 Collaborante ☐ 12 Collaborante ☐ 13 Collaborante ☐ 14 Collaborante ☐ 15 Collaborante ☐ 16 Collaborante ☐ 17 Collaborante ☐ 18 Collaborante ☐ 19 Collaborante ☐ 20 Collaborante ☐ 21 Collaborante ☐ 22 Collaborante ☐ 23 Collaborante ☐ 24 Collaborante ☐ 25 Collaborante ☐ 26 Collaborante ☐ 27 Collaborante ☐ 28 Collaborante ☐ 29 Collaborante ☐ 30 Collaborante ☐ 31 Collaborante ☐ 32 Collaborante ☐ 33 Collaborante ☐ 34 Collaborante ☐ 35 Collaborante ☐ 36 Collaborante ☐ 37 Collaborante ☐ 38 Collaborante ☐ 39 Collaborante ☐ 40 Collaborante ☐ 41 Collaborante ☐ 42 Collaborante ☐ 43 Collaborante ☐ 44 Collaborante ☐ 45 Collaborante ☐ 46 Collaborante ☐ 47 Collaborante ☐ 48 Collaborante ☐ 49 Collaborante ☐ 50 Collaborante ☐ 51 Collaborante ☐ 52 Collaborante ☐ 53 Collaborante ☐ 54 Collaborante ☐ 55 Collaborante ☐ 56 Collaborante ☐ 57 Collaborante ☐ 58 Collaborante ☐ 59 Collaborante ☐ 60 Collaborante ☐ 61 Collaborante ☐ 62 Collaborante ☐ 63 Collaborante ☐ 64 Collaborante ☐ 65 Collaborante ☐ 66 Collaborante ☐ 67 Collaborante ☐ 68 Collaborante ☐ 69 Collaborante ☐ 70 Collaborante ☐ 71 Collaborante ☐ 72 Collaborante ☐ 73 Collaborante ☐ 74 Collaborante ☐ 75 Collaborante ☐ 76 Collaborante ☐ 77 Collaborante ☐ 78 Collaborante ☐ 79 Collaborante ☐ 80 Collaborante ☐ 81 Collaborante ☐ 82 Collaborante ☐ 83 Collaborante ☐ 84 Collaborante ☐ 85 Collaborante ☐ 86 Collaborante ☐ 87 Collaborante ☐ 88 Collaborante ☐ 89 Collaborante ☐ 90 Collaborante ☐ 91 Collaborante ☐ 92 Collaborante ☐ 93 Collaborante ☐ 94 Collaborante ☐ 95 Collaborante ☐ 96 Collaborante ☐ 97 Collaborante ☐ 98 Collaborante ☐ 99 Collaborante ☐ 100 Collaborante ☐ 101 Collaborante ☐ 102 Collaborante ☐ 103 Collaborante ☐ 104 Collaborante ☐ 105 Collaborante ☐ 106 Collaborante ☐ 107 Collaborante ☐ 108 Collaborante ☐ 109 Collaborante ☐ 110 Collaborante ☐ 111 Collaborante ☐ 112 Collaborante ☐ 113 Collaborante ☐ 114 Collaborante ☐ 115 Collaborante ☐ 116 Collaborante ☐ 117 Collaborante ☐ 118 Collaborante ☐ 119 Collaborante ☐ 120 Collaborante ☐ 121 Collaborante ☐ 122 Collaborante ☐ 123 Collaborante ☐ 124 Collaborante ☐ 125 Collaborante ☐ 126 Collaborante ☐ 127 Collaborante ☐ 128 Collaborante ☐ 129 Collaborante ☐ 130 Collaborante ☐ 131 Collaborante ☐ 132 Collaborante ☐ 133 Collaborante ☐ 134 Collaborante ☐ 135 Collaborante ☐ 136 Collaborante ☐ 137 Collaborante ☐ 138 Collaborante ☐ 139 Collaborante ☐ 140 Collaborante ☐ 141 Collaborante ☐ 142 Collaborante ☐ 143 Collaborante ☐ 144 Collaborante ☐ 145 Collaborante ☐ 146 Collaborante ☐ 147 Collaborante ☐ 148 Collaborante ☐ 149 Collaborante ☐ 150 Collaborante ☐ 151 Collaborante ☐ 152 Collaborante ☐ 153 Collaborante ☐ 154 Collaborante ☐ 155 Collaborante ☐ 156 Collaborante ☐ 157 Collaborante ☐ 158 Collaborante ☐ 159 Collaborante ☐ 160 Collaborante ☐ 161 Collaborante ☐ 162 Collaborante ☐ 163 Collaborante ☐ 164 Collaborante ☐ 165 Collaborante ☐ 166 Collaborante ☐ 167 Collaborante ☐ 168 Collaborante ☐ 169 Collaborante ☐ 170 Collaborante ☐ 171 Collaborante ☐ 172 Collaborante ☐ 173 Collaborante ☐ 174 Collaborante ☐ 175 Collaborante ☐ 176 Collaborante ☐ 177 Collaborante ☐ 178 Collaborante ☐ 179 Collaborante ☐ 180 Collaborante ☐ 181 Collaborante ☐ 182 Collaborante ☐ 183 Collaborante ☐ 184 Collaborante ☐ 185 Collaborante ☐ 186 Collaborante ☐ 187 Collaborante ☐ 188 Collaborante ☐ 189 Collaborante ☐ 190 Collaborante ☐ 191 Collaborante ☐ 192 Collaborante ☐ 193 Collaborante ☐ 194 Collaborante ☐ 195 Collaborante ☐ 196 Collaborante ☐ 197 Collaborante ☐ 198 Collaborante ☐ 199 Collaborante ☐ 200 Collaborante ☐ 201 Collaborante ☐ 202 Collaborante ☐ 203 Collaborante ☐ 204 Collaborante ☐ 205 Collaborante ☐ 206 Collaborante ☐ 207 Collaborante ☐ 208 Collaborante ☐ 209 Collaborante ☐ 210 Collaborante ☐ 211 Collaborante ☐ 212 Collaborante ☐ 213 Collaborante ☐ 214 Collaborante ☐ 215 Collaborante ☐ 216 Collaborante ☐ 217 Collaborante ☐ 218 Collaborante ☐ 219 Collaborante ☐ 220 Collaborante ☐ 221 Collaborante ☐ 222 Collaborante ☐ 223 Collaborante ☐ 224 Collaborante ☐ 225 Collaborante ☐ 226 Collaborante ☐ 227 Collaborante ☐ 228 Collaborante ☐ 229 Collaborante ☐ 230 Collaborante ☐ 231 Collaborante ☐ 232 Collaborante ☐ 233 Collaborante ☐ 234 Collaborante ☐ 235 Collaborante ☐ 236 Collaborante ☐ 237 Collaborante ☐ 238 Collaborante ☐ 239 Collaborante ☐ 240 Collaborante ☐ 241 Collaborante ☐ 242 Collaborante ☐ 243 Collaborante ☐ 244 Collaborante ☐ 245 Collaborante ☐ 246 Collaborante ☐ 247 Collaborante ☐ 248 Collaborante ☐ 249 Collaborante ☐ 250 Collaborante ☐ 251 Collaborante ☐ 252 Collaborante ☐ 253 Collaborante ☐ 254 Collaborante ☐ 255 Collaborante ☐ 256 Collaborante ☐ 257 Collaborante ☐ 258 Collaborante ☐ 259 Collaborante ☐ 260 Collaborante ☐ 261 Collaborante ☐ 262 Collaborante ☐ 263 Collaborante ☐ 264 Collaborante ☐ 265 Collaborante ☐ 266 Collaborante ☐ 267 Collaborante ☐ 268 Collaborante ☐ 269 Collaborante ☐ 270 Collaborante ☐ 271 Collaborante ☐ 272 Collaborante ☐ 273 Collaborante ☐ 274 Collaborante ☐ 275 Collaborante ☐ 276 Collaborante ☐ 277 Collaborante ☐ 278 Collaborante ☐ 279 Collaborante ☐ 280 Collaborante ☐ 281 Collaborante ☐ 282 Collaborante ☐ 283 Collaborante ☐ 284 Collaborante ☐ 285 Collaborante ☐ 286 Collaborante ☐ 287 Collaborante ☐ 288 Collaborante ☐ 289 Collaborante ☐ 290 Collaborante ☐ 291 Collaborante ☐ 292 Collaborante ☐ 293 Collaborante ☐ 294 Collaborante ☐ 295 Collaborante ☐ 296 Collaborante ☐ 297 Collaborante ☐ 298 Collaborante ☐ 299 Collaborante ☐ 300 Collaborante ☐ 301 Collaborante ☐ 302 Collaborante ☐ 303 Collaborante ☐ 304 Collaborante ☐ 305 Collaborante ☐ 306 Collaborante ☐ 307 Collaborante ☐ 308 Collaborante ☐ 309 Collaborante ☐ 310 Collaborante ☐ 311 Collaborante ☐ 312 Collaborante ☐ 313 Collaborante ☐ 314 Collaborante ☐ 315 Collaborante ☐ 316 Collaborante ☐ 317 Collaborante ☐ 318 Collaborante ☐ 319 Collaborante ☐ 320 Collaborante ☐ 321 Collaborante ☐ 322 Collaborante ☐ 323 Collaborante ☐ 324 Collaborante ☐ 325 Collaborante ☐ 326 Collaborante ☐ 327 Collaborante ☐ 328 Collaborante ☐ 329 Collaborante ☐ 330 Collaborante ☐ 331 Collaborante ☐ 332 Collaborante ☐ 333 Collaborante ☐ 334 Collaborante ☐ 335 Collaborante ☐ 336 Collaborante ☐ 337 Collaborante ☐ 338 Collaborante ☐ 339 Collaborante ☐ 340 Collaborante ☐ 341 Collaborante ☐ 342 Collaborante ☐ 343 Collaborante ☐ 344 Collaborante ☐ 345 Collaborante ☐ 346 Collaborante ☐ 347 Collaborante ☐ 348 Collaborante ☐ 349 Collaborante ☐ 350 Collaborante ☐ 351 Collaborante ☐ 352 Collaborante ☐ 353 Collaborante ☐ 354 Collaborante ☐ 355 Collaborante ☐ 356 Collaborante ☐ 357 Collaborante ☐ 358 Collaborante ☐ 359 Collaborante ☐ 360 Collaborante ☐ 361 Collaborante ☐ 362 Collaborante ☐ 363 Collaborante ☐ 364 Collaborante ☐ 365 Collaborante ☐ 366 Collaborante ☐ 367 Collaborante ☐ 368 Collaborante ☐ 369 Collaborante ☐ 370 Collaborante ☐ 371 Collaborante ☐ 372 Collaborante ☐ 373 Collaborante ☐ 374 Collaborante ☐ 375 Collaborante ☐ 376 Collaborante ☐ 377 Collaborante ☐ 378 Collaborante ☐ 379 Collaborante ☐ 380 Collaborante ☐ 381 Collaborante ☐ 382 Collaborante ☐ 383 Collaborante ☐ 384 Collaborante ☐ 385 Collaborante ☐ 386 Collaborante ☐ 387 Collaborante ☐ 388 Collaborante ☐ 389 Collaborante ☐ 390 Collaborante ☐ 391 Collaborante ☐ 392 Collaborante ☐ 393 Collaborante ☐ 394 Collaborante ☐ 395 Collaborante ☐ 396 Collaborante ☐ 397 Collaborante ☐ 398 Collaborante ☐ 399 Collaborante ☐ 400 Collaborante ☐ 401 Collaborante ☐ 402 Collaborante ☐ 403 Collaborante ☐ 404 Collaborante ☐ 405 Collaborante ☐ 406 Collaborante ☐ 407 Collaborante ☐ 408 Collaborante ☐ 409 Collaborante ☐ 410 Collaborante ☐ 411 Collaborante ☐ 412 Collaborante ☐ 413 Collaborante ☐ 414 Collaborante ☐ 415 Collaborante ☐ 416 Collaborante ☐ 417 Collaborante ☐ 418 Collaborante ☐ 419 Collaborante ☐ 420 Collaborante ☐ 421 Collaborante ☐ 422 Collaborante ☐ 423 Collaborante ☐ 424 Collaborante ☐ 425 Collaborante ☐ 426 Collaborante ☐ 427 Collaborante ☐ 428 Collaborante ☐ 429 Collaborante ☐ 430 Collaborante ☐ 431 Collaborante ☐ 432 Collaborante ☐ 433 Collaborante ☐ 434 Collaborante ☐ 435 Collaborante ☐ 436 Collaborante ☐ 437 Collaborante ☐ 438 Collaborante ☐ 439 Collaborante ☐ 440 Collaborante ☐ 441 Collaborante ☐ 442 Collaborante ☐ 443 Collaborante ☐ 444 Collaborante ☐ 445 Collaborante ☐ 446 Collaborante ☐ 447 Collaborante ☐ 448 Collaborante ☐ 449 Collaborante ☐ 450 Collaborante ☐ 451 Collaborante ☐ 452 Collaborante ☐ 453 Collaborante ☐ 454 Collaborante ☐ 455 Collaborante ☐ 456 Collaborante ☐ 457 Collaborante ☐ 458 Collaborante ☐ 459 Collaborante ☐ 460 Collaborante ☐ 461 Collaborante ☐ 462 Collaborante ☐ 463 Collaborante ☐ 464 Collaborante ☐ 465 Collaborante ☐ 466 Collaborante ☐ 467 Collaborante ☐ 468 Collaborante ☐ 469 Collaborante ☐ 470 Collaborante ☐ 471 Collaborante ☐ 472 Collaborante ☐ 473 Collaborante ☐ 474 Collaborante ☐ 475 Collaborante ☐ 476 Collaborante ☐ 477 Collaborante ☐ 478 Collaborante ☐ 479 Collaborante ☐ 480 Collaborante ☐ 481 Collaborante ☐ 482 Collaborante ☐ 483 Collaborante ☐ 484 Collaborante ☐ 485 Collaborante ☐ 486 Collaborante ☐ 487 Collaborante ☐ 488 Collaborante ☐ 489 Collaborante ☐ 490 Collaborante ☐ 491 Collaborante ☐ 492 Collaborante ☐ 493 Collaborante ☐ 494 Collaborante ☐ 495 Collaborante ☐ 496 Collaborante ☐ 497 Collaborante ☐ 498 Collaborante ☐ 499 Collaborante ☐ 500 Collaborante ☐ 501 Collaborante ☐ 502 Collaborante ☐ 503 Collaborante ☐ 504 Collaborante ☐ 505 Collaborante ☐ 506 Collaborante ☐ 507 Collaborante ☐ 508 Collaborante ☐ 509 Collaborante ☐ 510 Collaborante ☐ 511 Collaborante ☐ 512 Collaborante ☐ 513 Collaborante ☐ 514 Collaborante ☐ 515 Collaborante ☐ 516 Collaborante ☐ 517 Collaborante ☐ 518 Collaborante ☐ 519 Collaborante ☐ 520 Collaborante ☐ 521 Collaborante ☐ 522 Collaborante ☐ 523 Collaborante ☐ 524 Collaborante ☐ 525 Collaborante ☐ 526 Collaborante ☐ 527 Collaborante ☐ 528 Collaborante ☐ 529 Collaborante ☐ 530 Collaborante ☐ 531 Collaborante ☐ 532 Collaborante ☐ 533 Collaborante ☐ 534 Collaborante ☐ 535 Collaborante ☐ 536 Collaborante ☐ 537 Collaborante ☐ 538 Collaborante ☐ 539 Collaborante ☐ 540 Collaborante ☐ 541 Collaborante ☐ 542 Collaborante ☐ 543 Collaborante ☐ 544 Collaborante ☐ 545 Collaborante ☐ 546 Collaborante ☐ 547 Collaborante ☐ 548 Collaborante ☐ 549 Collaborante ☐ 550 Collaborante ☐ 551 Collaborante ☐ 552 Collaborante ☐ 553 Collaborante ☐ 554 Collaborante ☐ 555 Collaborante ☐ 556 Collaborante ☐ 557 Collaborante ☐ 558 Collaborante ☐ 559 Collaborante ☐ 560 Collaborante ☐ 561 Collaborante ☐ 562 Collaborante ☐ 563 Collaborante ☐ 564 Collaborante ☐ 565 Collaborante ☐ 566 Collaborante ☐ 567 Collaborante ☐ 568 Collaborante ☐ 569 Collaborante ☐ 570 Collaborante ☐ 571 Collaborante ☐ 572 Collaborante ☐ 573 Collaborante ☐ 574 Collaborante ☐ 575 Collaborante ☐ 576 Collaborante ☐ 577 Collaborante ☐ 578 Collaborante ☐ 579 Collaborante ☐ 580 Collaborante ☐ 581 Collaborante ☐ 582 Collaborante ☐ 583 Collaborante ☐ 584 Collaborante ☐ 585 Collaborante ☐ 586 Collaborante ☐ 587 Collaborante ☐ 588 Collaborante ☐ 589 Collaborante ☐ 590 Collaborante ☐ 591 Collaborante ☐ 592 Collaborante ☐ 593 Collaborante ☐ 594 Collaborante ☐ 595 Collaborante ☐ 596 Collaborante ☐ 597 Collaborante ☐ 598 Collaborante ☐ 599 Collaborante ☐ 600 Collaborante ☐ 601 Collaborante ☐ 602 Collaborante ☐ 603 Collaborante ☐ 604 Collaborante ☐ 605 Collaborante ☐ 606 Collaborante ☐ 607 Collaborante ☐ 608 Collaborante ☐ 609 Collaborante ☐ 610 Collaborante ☐ 611 Collaborante ☐ 612 Collaborante ☐ 613 Collaborante ☐ 614 Collaborante ☐ 615 Collaborante ☐ 616 Collaborante ☐ 617 Collaborante ☐ 618 Collaborante ☐ 619 Collaborante ☐ 620 Collaborante ☐ 621 Collaborante ☐ 622 Collaborante ☐ 623 Collaborante ☐ 624 Collaborante ☐ 625 Collaborante ☐ 626 Collaborante ☐ 627 Collaborante ☐ 628 Collaborante ☐ 629 Collaborante ☐ 630 Collaborante ☐ 631 Collaborante ☐ 632 Collaborante ☐ 633 Collaborante ☐ 634 Collaborante ☐ 635 Collaborante ☐ 636 Collaborante ☐ 637 Collaborante ☐ 638 Collaborante ☐ 639 Collaborante ☐ 640 Collaborante ☐ 641 Collaborante ☐ 642 Collaborante ☐ 643 Collaborante ☐ 644 Collaborante ☐ 645 Collaborante ☐ 646 Collaborante ☐ 647 Collaborante ☐ 648 Collaborante ☐ 649 Collaborante ☐ 650 Collaborante ☐ 651 Collaborante ☐ 652 Collaborante ☐ 653 Collaborante ☐ 654 Collaborante ☐ 655 Collaborante ☐ 656 Collaborante ☐ 657 Collaborante ☐ 658 Collaborante ☐ 659 Collaborante ☐ 660 Collaborante ☐ 661 Collaborante ☐ 662 Collaborante ☐ 663 Collaborante ☐ 664 Collaborante ☐ 665 Collaborante ☐ 666 Collaborante ☐ 667 Collaborante ☐ 668 Collaborante ☐ 669 Collaborante ☐ 670 Collaborante ☐ 671 Collaborante ☐ 672 Collaborante ☐ 673 Collaborante ☐ 674 Collaborante ☐ 675 Collaborante ☐ 676 Collaborante ☐ 677 Collaborante ☐ 678 Collaborante ☐ 679 Collaborante ☐ 680 Collaborante ☐ 681 Collaborante ☐ 682 Collaborante ☐ 683 Collaborante ☐ 684 Collaborante ☐ 685 Collaborante ☐ 686 Collaborante ☐ 687 Collaborante ☐ 688 Collaborante ☐ 689 Collaborante ☐ 690 Collaborante ☐ 691 Collaborante ☐ 692 Collaborante ☐ 693 Collaborante ☐ 694 Collaborante ☐ 695 Collaborante ☐ 696 Collaborante ☐ 697 Collaborante ☐ 698 Collaborante ☐ 699 Collaborante ☐ 700 Collaborante ☐ 701 Collaborante ☐ 702 Collaborante ☐ 703 Collaborante ☐ 704 Collaborante ☐ 705 Collaborante ☐ 706 Collaborante ☐ 707 Collaborante ☐ 708 Collaborante ☐ 709 Collaborante ☐ 710 Collaborante ☐ 711 Collaborante ☐ 712 Collaborante ☐ 713 Collaborante ☐ 714 Collaborante ☐ 715 Collaborante ☐ 716 Collaborante ☐ 717 Collaborante ☐ 718 Collaborante ☐ 719 Collaborante ☐ 720 Collaborante ☐ 721 Collaborante ☐ 722 Collaborante ☐ 723 Collaborante ☐ 724 Collaborante ☐ 725 Collaborante ☐ 726 Collaborante ☐ 727 Collaborante ☐ 728 Collaborante ☐ 729 Collaborante ☐ 730 Collaborante ☐ 731 Collaborante ☐ 732 Collaborante ☐ 733 Collaborante ☐ 734 Collaborante ☐ 735 Collaborante ☐ 736 Collaborante ☐ 737 Collaborante ☐ 738 Collaborante ☐ 739 Collaborante ☐ 740 Collaborante ☐ 741 Collaborante ☐ 742 Collaborante ☐ 743 Collaborante ☐ 744 Collaborante ☐ 745 Collaborante ☐ 746 Collaborante ☐ 747 Collaborante ☐ 748 Collaborante ☐ 749 Collaborante ☐ 750 Collaborante ☐ 751 Collaborante ☐ 752 Collaborante ☐ 753 Collaborante ☐ 754 Collaborante ☐ 755 Collaborante ☐ 756 Collaborante ☐ 757 Collaborante ☐ 758 Collaborante ☐ 759 Collaborante ☐ 760 Collaborante ☐ 761 Collaborante ☐ 762 Collaborante ☐ 763 Collaborante ☐ 764 Collaborante ☐ 765 Collaborante ☐ 766 Collaborante ☐ 767 Collaborante ☐ 768 Collaborante ☐ 769 Collaborante ☐ 770 Collaborante ☐ 771 Collaborante ☐ 772 Collaborante ☐ 773 Collaborante ☐ 774 Collaborante ☐ 775 Collaborante ☐ 776 Collaborante ☐ 777 Collaborante ☐ 778 Collaborante ☐ 779 Collaborante ☐ 780 Collaborante ☐ 781 Collaborante ☐ 782 Collaborante ☐ 783 Collaborante ☐ 784 Collaborante ☐ 785 Collaborante ☐ 786 Collaborante ☐ 787 Collaborante ☐ 788 Collaborante ☐ 789 Collaborante ☐ 790 Collaborante ☐ 791 Collaborante ☐ 792 Collaborante ☐ 793 Collaborante ☐ 794 Collaborante ☐ 795 Collaborante ☐ 796 Collaborante ☐ 797 Collaborante ☐ 798 Collaborante ☐ 799 Collaborante ☐ 800 Collaborante ☐ 801 Collaborante ☐ 802 Collaborante ☐ 803 Collaborante ☐ 804 Collaborante ☐ 805 Collaborante ☐ 806 Collaborante ☐ 807 Collaborante ☐ 808 Collaborante ☐ 809 Collaborante ☐ 810 Collaborante ☐ 811 Collaborante ☐ 812 Collaborante ☐ 813 Collaborante ☐ 814 Collaborante ☐ 815 Collaborante ☐ 816 Collaborante ☐ 817 Collaborante ☐ 818 Collaborante ☐ 819 Collaborante ☐ 820 Collaborante ☐ 821 Collaborante ☐ 822 Collaborante ☐ 823 Collaborante ☐ 824 Collaborante ☐ 825 Collaborante ☐ 826 Collaborante ☐ 827 Collaborante ☐ 828 Collaborante ☐ 829 Collaborante ☐ 830 Collaborante ☐ 831 Collaborante ☐ 832 Collaborante ☐ 833 Collaborante ☐ 834 Collaborante ☐ 835 Collaborante ☐ 836 Collaborante ☐ 837 Collaborante ☐ 838 Collaborante ☐ 839 Collaborante ☐ 840 Collaborante ☐ 841 Collaborante ☐ 842 Collaborante ☐ 843 Collaborante ☐ 844 Collaborante ☐ 845 Collaborante ☐ 846 Collaborante ☐ 847 Collaborante ☐ 848 Collaborante ☐ 849 Collaborante ☐ 850 Collaborante ☐ 851 Collaborante ☐ 852 Collaborante ☐ 853 Collaborante ☐ 854 Collaborante ☐ 855 Collaborante ☐ 856 Collaborante ☐ 857 Collaborante ☐ 858 Collaborante ☐ 859 Collaborante ☐ 860 Collaborante ☐ 861 Collaborante ☐ 862 Collaborante ☐ 863 Collaborante ☐ 864 Collaborante ☐ 865 Collaborante ☐ 866 Collaborante ☐ 867 Collaborante ☐ 868 Collaborante ☐ 869 Collaborante ☐ 870 Collaborante ☐ 871 Collaborante ☐ 872 Collaborante ☐ 873 Collaborante ☐ 874 Collaborante ☐ 875 Collaborante ☐ 876 Collaborante ☐ 877 Collaborante ☐ 878 Collaborante ☐ 879 Collaborante ☐ 880 Collaborante ☐ 881 Collaborante ☐ 882 Collaborante ☐ 883 Collaborante ☐ 884 Collaborante ☐ 885 Collaborante ☐ 886 Collaborante ☐ 887 Collaborante ☐ 888 Collaborante ☐ 889 Collaborante ☐ 890 Collaborante ☐ 891 Collaborante ☐ 892 Collaborante ☐ 893 Collaborante ☐ 894 Collaborante ☐ 895 Collaborante ☐ 896 Collaborante ☐ 897 Collaborante ☐ 898 Collaborante ☐ 899 Collaborante ☐ 900 Collaborante ☐ 901 Collaborante ☐ 902 Collaborante ☐ 903 Collaborante ☐ 904 Collaborante ☐ 905 Collaborante ☐ 906 Collaborante ☐ 907 Collaborante

This in-depth examination allows to evaluate whether the patient is a potential subject at risk of developing more easily mucositis or oral problems (Fig. 1).

Therefore, following the Guidelines of the Italian Ministry of Health of February 2018 ²⁶ adequate oral hygiene education and infective foci decontamination were carried out before starting any antineoplastic therapy especially in those cases, in which profound and prolonged immunosuppression was foreseeable for hematopoietic stem cell transplantation, provided that neutrophil count was $> 10007/\text{mm}^3$ and platelets $> 8000/\text{mm}^3$. Infective foci decontamination consists of all dental procedures that allow restoration of oral health reducing infective risk such as: professional oral hygiene, fillings, endodontic treatment of no vital teeth or with pulp inflammation, extraction of compromised teeth, elimination or decontamination of orthodontic appliances that represented a source of massive plaque colonization, periodontal therapy. These treatments were performed according to oncologists based on the state of the disease at the SOSD of Surgical and Special Dentistry of University Hospital Umberto I Marche (Italy). If there was no collaboration by patients they were underwent to general anesthesia or deep venous sedation; in that case was necessary to expand the available team including a nurse and an anesthetist. Furthermore all 120 patients was prescribed the use of a Galenic Mouthwash (composed by 2 bottle (100ml) of Sodium Bicarbonate 8.4%, 1 bottle of Tantum Verde®, 1 bottle of Mycostatin®) as preventive measure for mucositis used at least 2 rinses per day throughout all antineoplastic treatment.

During weekly follow-ups and after the antineoplastic therapy beginning, mucosal barrier breakdown and consequent mucositis occurred in 109 out of 120 patients (90.8% mucositis). To this 90.8 % of patients with mucositis were assessed and added to anamnestic folder the Clinical Grading of mucositis using two scales, WHO ²⁸ and OMAS ²⁹. The painful symptoms and functional limitations were recorded using the ChIMES classification (Children's International Mucositis Evaluation Sale) ³⁰ which uses the Wong-Baker scale created specifically for pediatric patients.

WHO scale identifies the degree by a visual staging and symptoms, assigning a value from 0 to 4:

- 0 : no symptoms
- 1 : irritation (mild discomfort)+/- erythema, no ulcers
- 2 : erythema, ulcers, solid diet possible
- 3 : erythema, ulcers, liquid diet (solid diet not possible)

- 4 : extended mucositis, diet not possible

OMAS scale combines two parameters (erythema and ulcers/pseudomembranes) giving them a number value and adding together:

-ERYTHEMA :

- 0 no change in mucosa color
- 1 increase mucosal color intensity
- 2 bright blood color mucosa

-ULCERS/PSEUDOMEMBRANES :

- 0 no lesions
- 1 lesion surface area $< 1\text{cm}^2$
- 2 lesion surface area between 1cm^2 e 3cm^2
- 3 lesion surface area $> 3\text{cm}^2$

In presence of clinical mucositis, some therapeutic protocols have been applied used different devices like:

- CURASEPT PREVENT® (Curasept SpA; Saronno; IT) mouthwash with an innovative formula with postbiotics ozonized with olive oil suitable for restoring oral microbiota and increasing mucosal defenses (25 patients)
- VEA LIPSTICK® (Vea Srl; Aprilia; IT) lipgel protective lip balm rich in vitE
- DECA® (sedo-calcio-gola) (Laboratorio chimico Deca; Milano; IT) nutritional supplement spray rich in vitE, wheat bud oil and myrrh extract (24 patients)
- MUCOSYTE® (Biopharm Srl; Milano; IT) protective bioadhesive gel in sachet for regenerate oral mucosa (25 patients)
- AFTASOL® (Healmann Health Care Srl; San Canzian D'Isonzo; IT) strawberry flavoured spray (20 patients)
- NOVOX DROPS® (Novox; Novara; IT) for mucosal lesion treatment, recommended several applications per day for 7-30 days (15 patients)

Every week patients were visited and grading evaluation was repeated, modulating the therapy.

At the end of mucositis therapy was also administered a questionnaire to patients with dichotomous answer (yes/no) about products used. Examines about:

- APPLICATION METHOD
- PAIN REDUCTION AFTER APPLICATION
- PLEASANT FLAVOUR
- FUNCTION IMPROVEMENT (DRINK OR EAT) AFTER APPLICATION

- REDUCTION OF OPIOIDS ANALGESICS REQUIREMENT
- REDUCTION OF ORAL PATHOGENS COLONIZATION (assessed by laboratory-processed oral swabs or biopsies to analyze the presence of superinfections such as Candida, Herpes simplex, Gram -, Pseudomonas, Escherichia coli, Klebsiella, Neisseria)

The dental team effectiveness is evaluated based on three parameters: improvement of vital functions in case of mucositis after treatment, pain reduction after treatment and through degree of appreciation expressed by parents. At first were collected all the answer (pain reduction, pleasant flavor, function improvement, opioids reduction, colonization reduction) given by patients divided in groups according to different device used. If the answer “YES” was given by more than 50% of patients per group the result parameter analyzed is YES, if by less than 50% is NO. Subsequently, were summed the answers of all the groups regarding the analyzed

parameters and final result was obtained using the previous method. In a table (Table 1) were summarized all results about each product for group.

In a different dichotomous questionnaire was asked to all 120 patients’ parents if the role of dental team in this study was appreciated and useful in prevention and treatment of oral mucositis.

Table 1. Results of first questionnaire about each device used by 109 out of 120 patients who developed mucositis

MEDICAL DEVICE	APPLICATION METHOD	PAIN REDUCTION	PLEASANT FLAVOR	APPROVE EATING/ DRINKING	REDUCE OPIOID ANALGESICS NECESSITY	REDUCE ORAL PATHOGENS COLONIZATION	N. PATIENTS
MUCOSYTE	ORAL RINSE	YES (22/25)	YES (22/25)	YES (22/25)	NO (0/25)	NO (0/25)	25
CURASEPT PREVENT	ORAL RINSE	YES (23/25)	YES (23/25)	YES (23/25)	NO (0/25)	NO (0/25)	25
SEDO-CALCIO GOLA	SPRAY	YES (21/24)	YES (21/24)	YES (21/24)	NO (0/24)	NO (0/24)	24
NOVOX	GEL	YES (12/15)	NO (3/15)	NO (3/15)	NO (0/15)	NO (0/15)	15
AFTASOL	SPRAY	YES (17/20)	YES (17/20)	NO (2/20)	NO (0/20)	NO (0/20)	20
TOTAL		95/109 87.15 %	86/109 78.9 %	71/109 65.1 %	0/109 0%	0/109 0%	109

In a different dichotomous questionnaire was asked to all 120 patients’ parents if the role of dental team in this study was appreciated and useful in prevention and treatment of oral mucositis.

RESULTS

For each group of patients undergoing to treatment, some parameters were investigated and for each one the evaluation was reported in a table (Table 1). Each evaluation corresponds to the answers reported by more than 50% of people in each group subjected to a single device. Is highlighted that:

- MUCOSYTE®: YES pain reduction, YES pleasant flavor, YES function improvement, NO reduction of opioids analgesics requirement, NO reduction of oral pathogens colonization
- CURASEPT PREVENT®: YES pain reduction, YES pleasant flavor, YES function improvement, NO reduction of opioids analgesics requirement, NO reduction of oral pathogens colonization
- SEDO-CALCIO-GOLA®: YES pain reduction, YES pleasant flavor, YES function improvement, NO reduction of opioids analgesics requirement, NO reduction of oral pathogens colonization
- NOVOX®: YES pain reduction, YES pleasant flavor, NO function improvement, NO reduction of opioids analgesics requirement, NO reduction of oral pathogens colonization
- AFTASOL®: YES pain reduction, YES pleasant flavor, NO function improvement, NO reduction of opioids analgesics requirement, NO reduction of oral pathogens colonization

From that was possible to deduce that:

- pain reduction in 95 patients out of 109 so 87.15 % of cases regardless of devices used
- Pleasant flavor in 86 patients out of 109 so 78.9 % of cases, NOVOX® is the only device without a good flavor
- Function improvement (eat or drink) in 71 patients out of 109 so 65.1% of cases
- Reduction of opioids analgesics requirement in none 0% cases regardless of device used
- Reduction of oral pathogens colonization in no-one 0% cases regardless of device used

To give more support at the study 5 patients were thoroughly examined, each with a specific tumor, reporting Grading by WHO scale and pain evaluation according to Wong-Baker scale during weekly follow up (Fig.2 to Fig.6).

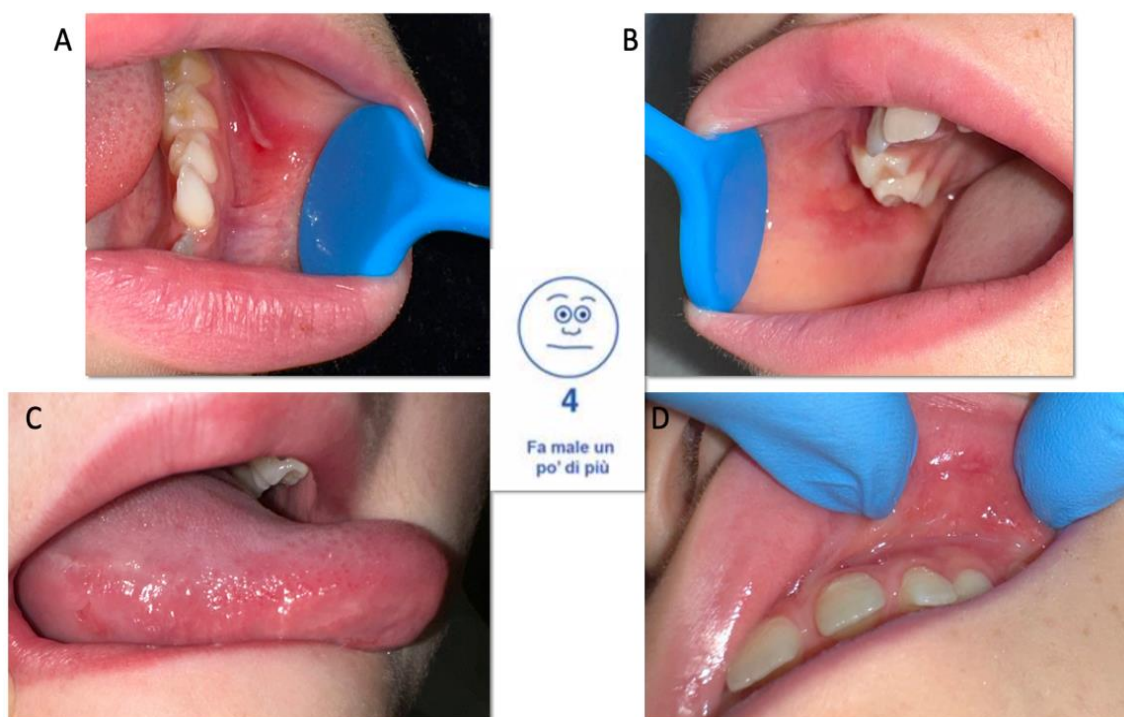


Figure2. Patient affected by LLA-B ; WHO Grading 2; pain grade 4 ;

(A)Intraoral photo III quadrant, (B) intraoral photo I quadrant, (C) intraoral photo right site of tongue, (D) intraoral photo II quadrant



Figure 3. Patient affected by Medulloblastoma; WHO Grading 3;
(A) intraoral photo of right site of tongue initial and pain grade 8 , (B) intraoral photo right site of tongue and pain grade 6

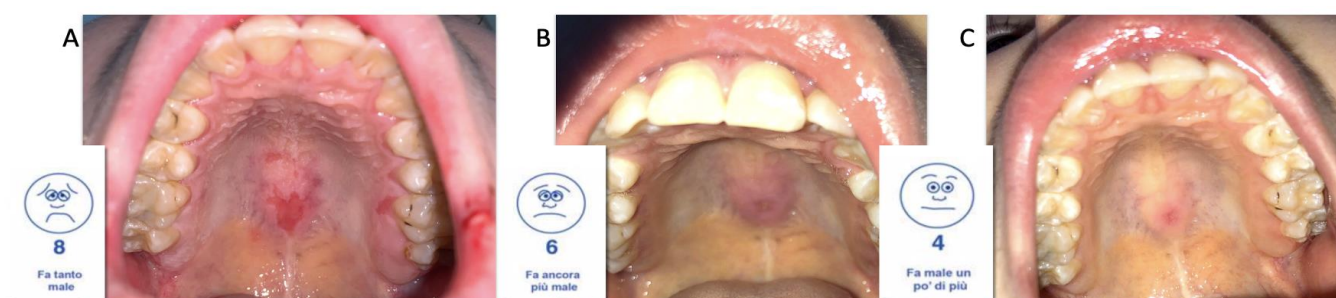


Figure 4. Patient affected by Embryonal Metastatic Rhabdomyosarcoma; WHO Grading 3;
(A) intraoral photo of palate and pain grade 8, (B) intraoral photo of palate and pain grade 6, (C) intraoral photo of palate and pain grade 4

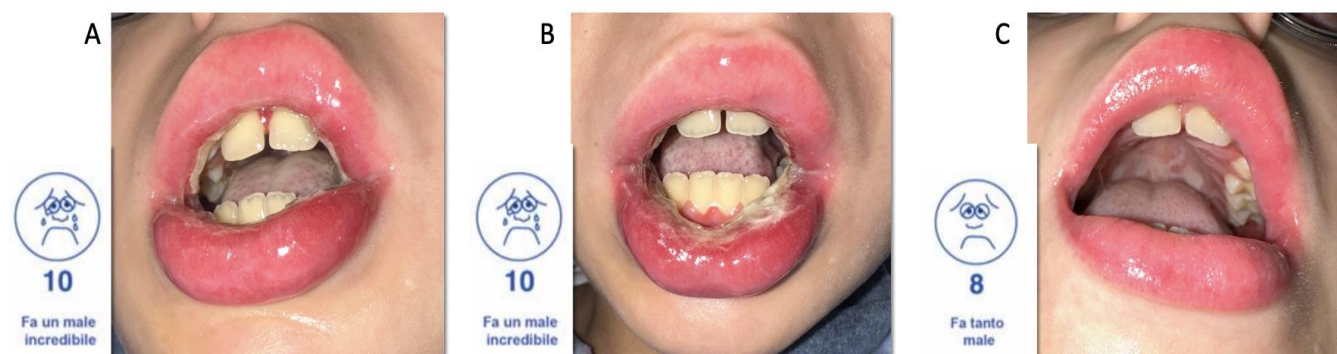


Figure 5. Patient affected by Burkitt Lymphoma ; WHO Grading 4; (A) extraoral photo of mouth and pain grade 10, (B) extraoral photo of mouth and pain grade 10, (C) extraoral photo of mouth and pain grade 8

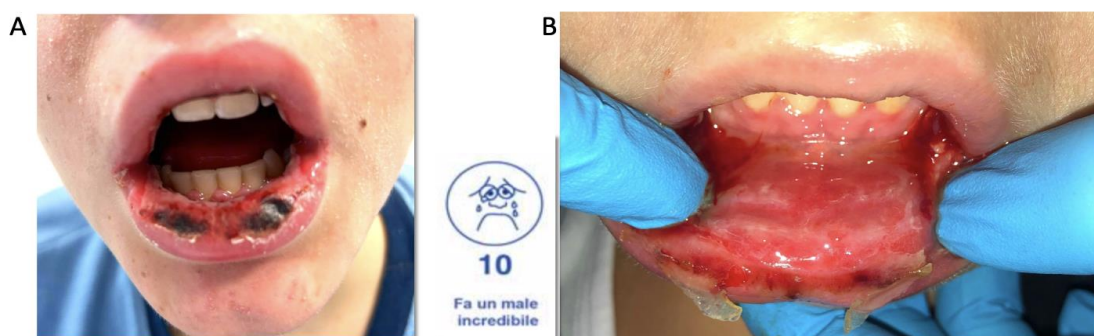


Figure 6. Patient affected by LLA-B; WHO Grading 4;

(A) Extraoral photo of inferior lip and pain grade 10, (B) intraoral photo of inferior vestibule and pain grade 10

Supporting the hypothesis of this study, according to which using devices for mucositis treatment and the proximity of dental team could lead to a better healing and could be helpful for pediatric patients, 5 patients were deeply examined during their follow ups.

- Patient affected by LLA-B, WHO Grading 2 with erythema, ulcers, solid diet possible and pain grade 4 (Fig. 2A,2B,2C,2D) photo of 01/09/23. First methotrexate administration on December 2022: therapy with galenic mouthwash + Vea Oris (liquid diet possible). Second methotrexate administration on January 2023, therapy with Novox (2 per day) is reported a rapid healing of lesions but an unpleasant taste of device
- Patient affected by Medulloblastoma, WHO Grading 3 with erythema, ulcers, liquid diet possible, initial pain grade 8 and final 6 (Fig. 3A and Fig. 3B). First check on 10/10/22 (Fig. 3A): therapy with Contramal for pain (grade 8) + Galenic mouthwash+ Vea Oris (only liquid diet possible). Second check on 24/10/22 (Fig. 3B): after two weeks of treatment pain decreased (grade 6) and solid diet was possible
- Patient affected by Embryonal Metastatic Rhabdomyosarcoma with palatal lesions, WHO Grading 3, initial pain grade 8, at second check 6 and at last 4 (Fig. 4A,4B,4C). First check on 05/09/22 (Fig. 4A) initial mucositis with moderate pain (grade 8) and difficult solid diet; start therapy with galenic mouthwash+ Sedo-calcio-Gola. Second check on 12/09/22 (Fig. 4B): Healing improving after therapy and pain reduction (grade 6). Third check on 19/09/22 (Fig. 4C): healing almost complete and pain improvement (grade 4)
- Patient affected by Burkitt Lymphoma, WHO Grading 4 with extensive mucositis and no diet possible. Initial pain grade 10, second check 10 and at last 8. (Fig. 5A,5B,5C) the only check reported was the last photo of 27/02/23 (Fig. 5C) and the therapy was morphine used before oral hygiene+galenic mouthwash +Film OS+ Novox. Due to severe lesion and pain the only possible diet is parenteral but is still found an improvement of pain after treatment (from grade 10 to grade 8)
- Patient affected by LLA-B, WHO Grading 4 with severe labial lesions, impossible function and pain grade 10 (Fig. 6A and Fig. 6B). The only check reported is the second photo (Fig. 6B) of 07/ 11/22 and therapy was morphine before meals+galenic mouthwash+Vea Oris+Novox

The close collaboration between dental team and pediatric oncologists guarantee an early diagnosis, monitoring and implementation of therapeutic protocols for mucositis treatment finding positive effects for parameters analyzed in particular pain reduction and function improvement. In second questionnaire 100% case (120 patients) appreciated the constant weekly support by a member of dental team and oral hygiene instruction.

DISCUSSION

The aim of this study is to highlight the role of dental team in the management of oral complications, in particular mucositis, in pediatric oncology patients undergoing antineoplastic therapy. A dental examination before antineoplastic therapy and the effects of different products were recorded during weekly follow-ups. The winning strategy was to monitor constantly patients, managing their treatments protocols and check the level of oral hygiene weekly.

Oral hygiene serves to prevent formation of biofilm that constituting bacterial plaque on teeth and especially mucosa, helping to maintain integrity of tissue and preventing infections ³¹; has also been suggested that the oral microbiota can potentially exacerbate mucositis leading to delayed healing by enhancing apoptosis and pro-inflammatory proteins ³².

Scientific evidence supports that treatments protocols including information and education on systematic cleaning of teeth and mucosa are the best practice to prevent oral consequences combined with follow up ³³-

³⁴. Moreover oral preventive treatment reduces incidence of complications like mucositis [26]. For that reason, the first step was to frame the patient and his profile of risk, having a greater control for those who presented lack oral hygiene or bad habits already at first visit.

Therefore the continuous follow up on patients allowed to evaluate the evolution of lesions due to antineoplastic therapy, acting promptly in those cases in which vital function were limited and pain was severe. Some protocols were used on all patients to prevent onset of any complications (Galenic mouthwash) others due to severity and grading of mucositis. Results in table 1 show that the use of protocols and follow ups led to a pain reduction in 87.15 % of cases regardless of devices used and function improvement in 78.9 % of cases. These results validate the hypothesis about effectiveness of dental team in oral mucositis management.

To 120 patients' parents was asked by a questionnaire if the weekly presence of a dental team in the management of oral complications was effective and in 100% of cases

the answer was affirmative, also supported by the pain reduction and function improved after therapeutic protocols used.

According to the American Academy of Pediatric Dentistry (AAPD), pediatric dentists play an important role in the diagnosis, prevention, stabilization, and management of oral and dental conditions that can impair a child's quality of life before, during, and after immunosuppressive treatments and/or head and neck radiation^{27, 35}. The study conducted by Nunez et al.³⁶ confirms that professional planned dental treatment during antineoplastic therapy produces an improvement of quality of life in patients highlighting that dentist role is crucial. Professionals are responsible for providing patients with information about the importance of good oral health³⁷ and prevention of radio-chemotherapy complications and for establishing oral hygiene protocols and preventive measures accessible to patients. The literature update written by Ferrández-Pujante et al.³⁸ also shows that the use of standardized protocols based on prevention and treatment from early stages can avoid or minimize oral complications and the side effects of cancer therapies, improving the quality of life of children.

Due to immunosuppression induced by antineoplastic therapy, has been also noted that 100% of subjects with mucositis showed positivity for oral superinfections in swabs or biopsies. In patients with such a compromised immune system and mucosa breakdown the presence of pathogens such as *Candida*, *Herpes simplex*, *Gram -*, *Pseudomonas*, *Escherichia coli*, *Klebsiella*, *Neisseria* is more common⁹⁻¹⁰. Therefore weekly observation allowed monitor mouth because these infections do not have the same clinical appearance as normal ones³⁸ and modulating the therapeutic plans by introducing antibiotics, antifungals and antivirals since the devices used in the study were not effective in resolving superinfection. So thanks to follow-ups conducted by dental team, was possible to prevent problems like sepsis or bacteremia and try to improve the subject's quality of life.

Overall, the presence of a dental team in the management of oral complications in pediatric oncology patients has met with considerable approval among the study participants. First of all because it was possible to reduce problems (pain and limitation of functions) acting promptly on a weekly basis and in second time because having a reference figure to rely on and by whom to be followed during such an important antineoplastic treatment can generate psychological and emotional implications such as tranquility and gratitude. The limits of this study are related to the used of Wong-Baker scale because pediatric patients identify pain level through a smile and not an objective data. However the literature

defines this classification reliable³⁰. The second limit lies in a single question questionnaire regarding the degree of appreciation of dental team only in a qualitative way.

CONCLUSION

This clinical experience highlights that dental team intervention have had a positive impact on pediatric patients and their parents. Would be necessary in future to expand research investigating about the role of dental team and the central importance in improve quality of life. Given the limitations of this study due to use of less objective pain scales, future studies could focus on a quantitative parameters of evaluation dental work and a randomized clinical trial.

DECLARATIONS

Funding

None

Conflict of Interest

None declared

REFERENCES

1. Zecca M, Ferrari A, Quarello P, Rabusin M, Balduzzi A, Buldini B, Rostagno E, Prete A, Favre C, Massimino M, Biondi A, Porta F, Biffi A, Locatelli F, Pession A, Fagioli F. Childhood cancer in Italy: background, goals, and achievements of the Italian Paediatric Hematology Oncology Association (AIEOP). *Tumori*. 2021 Oct;107(5):370-375.
2. Pastore G, De Salvo GL, Bisogno G, Dama E, Inserra A, Cecchetto G, Ferrari A; TREP Group; CSD of Epidemiology Biostatistics, AIEOP. Evaluating access to pediatric cancer care centers of children and adolescents with rare tumors in Italy: the TREP project. *Pediatr Blood Cancer*. 2009 Aug;53(2):152-5.
3. J. A. Garrocho-Rangel, M. Herrera-Moncada, R. Márquez-Preciado, F. Tejeda-Nava, J. J. Ortiz-Zamudio, A. Pozos-Guillén (2018) "Oral mucositis in paediatric acute lymphoblastic leukemia patients receiving methotrexate-based chemotherapy: case series", *European Journal of Paediatric Dentistry*, 19(3), pp239-242.
4. Forrest SJ, Georger B, Janeway KA. Precision medicine in pediatric oncology. *Curr Opin Pediatr*. 2018 Feb;30(1):17-24.
5. Miller MM, Donald DV, Hagemann TM. Prevention and treatment of oral mucositis in children with cancer. *J Pediatr Pharmacol Ther*. 2012;17:340-350.
6. Sonis ST. Oral mucositis in cancer therapy. *J Support Oncol*. 2004 Nov-Dec;2(6 Suppl 3):3-8.
7. Lalla RV, Bowen J, Barasch A, et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer*. 2014;120:1453-1461
8. Sonis ST, Elting LS, Keefe D, et al. Perspectives on cancer therapy-induced mucosal injury: pathogenesis, measurement, epidemiology, and consequences for patients. *Cancer*. 2004;100: 1995-2025.

9. Whittle SB, Williamson KC, Russell HV. Incidence and risk factors of bacterial and fungal infection during induction chemotherapy for high-risk neuroblastoma. *Pediatr Hematol Oncol*. 2017 Aug;34(5):331-342.
10. Ramirez-Fort MK, Zeng J, Feily A, Ramirez-Pacheco LA, Jenrette JM, Mayhew DL, Syed T, Cooper SL, Linden C, Graybill WS, French LE, Lange CS. Radiotherapy-induced reactivation of neurotrophic human herpes viruses: Overview and management. *J Clin Virol*. 2018 Jan;98:18-27.
11. Assas M, Wiriyakijja P, Fedele S, Porter S, Ní Ríordáin R. Measurement properties of patient-reported outcome measures in radiotherapy-induced trismus. *J Oral Pathol Med*. 2019 May;48(5):351-357.
12. Defabianis P, Braidà S, Guagnano R. 180-day screening study for predicting the risk factors for developing acute oral Graft-versus-Host disease in paediatric patients subjected to allogeneic haematopoietic stem cells transplantation. *Eur J Paediatr Dent*. 2010 Mar;11(1):31-4.
13. Marchetti, E., Ratta, S., Mummolo, S., Pecci, R., Bedini, R. Mechanical Reliability Evaluation of an Oral Implant-Abutment System According to UNI en ISO 14801 Fatigue Test Protocol Implant Dentistry, 2016, 25(5), 613–618
14. Bernardi, S., Mummolo, S., Continenza, M.A., Zeka, K., Pajewski, L. Use and Evaluation of a Cooling Aid in Laser-Assisted Dental Surgery: An Innovative Study Photomedicine and Laser Surgery, 2016, 34(6), 258–262
15. Tecco, S., Gherlone, E.F., Baldini, A., Marzo, G., Giuca, M.R. Frenulectomy of the tongue and the influence of rehabilitation exercises on the sEMG activity of masticatory muscles *Journal of Electromyography and Kinesiology*, 2015, 25(4), 619–628
16. Marchetti, E., Ratta, S., Mummolo, S., Pecci, R., Bedini, R. Evaluation of an endosseous oral implant system according to UNI en ISO 14801 fatigue test protocol Implant Dentistry, 2014, 23(6), 665–671
17. Bernardi, S., Mummolo, S., Marchetti, E., Macchiarelli, G., Varvara, G. Bio-morphological evaluation of periodontal ligament fibroblasts on mineralized dentin graft: An in vitro study. *Journal of Biological Regulators and Homeostatic Agents*, 2019, 33(1), 275–280
18. Quinzi, V., Caggiati, E., Mummolo, S., Tecco, S., Nota, A. Mesial rotation of the upper first molar: Association with anterior dental crowding in mixed and permanent dentition *Applied Sciences Switzerland*, 2020, 10(15), 5
19. Arcuri, C., Petro, E., Sollecchia, G., Mummolo, S., Marzo, G. Laser in periodontal pockets: In vivo and in vitro study *Journal of Biological Regulators and Homeostatic Agents*, 2020,34(3), 139–146
20. Mummolo, S., Marchetti, E., Albani, F., Campanella, V., Tecco, S. Comparison between rapid and slow palatal expansion: Evaluation of selected periodontal indices *Head and Face Medicine*, 2014, 10(1), 30
21. Saccomanno, S., Mummolo, S., Giancaspro, S., Quinzi, V., Mastrapasqua, R.F. Catering work profession and medico-oral health: A study on 603 subjects. *Healthcare Switzerland*, 2021, 9(5), 582
22. Mancini, L., Tarallo, F., Quinzi, V., Mummolo, S., Marchetti, E. Platelet-rich fibrin in single and multiple coronally advanced flap for type 1 recession: An updated systematic review and meta-analysis *Medicina Lithuania*, 2021, 57(2), 1–20, 144
23. Pennazza, G., Santonico, M., Mantini, G., Marzo, G., Paolesse, R. Application of a quartz microbalance based gas sensor array for the study of halitosis *Journal of Breath Research*, 2008, 2(1), 017009
24. Saccomanno, S., Mummolo, S., Marzo, G., Greco, F., Fiasca, F. The digital diagnostic approach to stafne's bone cavity (Sbc): From a review of the literature to the description of a clinical case. *Open Dentistry Journal*, 2021, 15(Special Issue),111–119
25. Memè, L., Bambini, F., Sampalmieri, F., Bianchi, A., Mummolo, S. Evaluation of a single non-surgical approach in the management of periimplantitis: glycine powder air-polishing versus ultrasonic device. *Oral and Implantology*, 2024, 16(2), 67–78
26. Pizzolante, T., Rasicci, P., Saggiomo, A.P., Capogreco, M., Mummolo, S. Buccal Fat Pad Flap and Buccal Advancement Flap for Closure of Oroantral Fistula: A Systematic Review and a Case Report. *Oral and Implantology*, 2024, 16(2),50–61
27. Grilli, F., Pizzolante, T., Capogreco, M., Bambini, F., Sampalmieri, F. Clinical and histomorphometric comparison of autologous dentin graft versus a deproteinized bovine bone graft for Socket Preservation. *Oral and Implantology*, 2024, 16(2), 101–106
28. Memè, L., Bambini, F., Sampalmieri, F., ... Inchingolo, F., Marricco, F. Osteonecrosis of the jaw in patients with metastatic renal carcinoma: systematic review and meta-analysis. *Oral and Implantology*, 2024, 16(2), 79–87
29. Pizzolante, T., Memè, L., Ciccariello, A., Bambini, F., Inchingolo, F. Complications of zygomatic implantology: observational clinical study. *Bulletin of Stomatology and Maxillofacial Surgery*, 2024, 20(4),73–80
30. Botticelli, G., Severino, M., Gatto, R., Franceschini, C., Di Paolo, C. Excision of lower lip mucocele using injection of hydrocolloid dental impression material in a pediatric patient: A case report. *Applied Sciences Switzerland*, 2021, 11(13), 5819

31. Falisi, G., Rastelli, C., Rastelli, S., ... Paolo, C.D., Franceschini, C. Ultrashort Implants, Alternative Prosthetic Rehabilitation in Mandibular Atrophies in Fragile Subjects: A Retrospective Study. *Healthcare*, 2021, 9(2), 1–9
32. Falisi, G., Gatto, R., Monaco, A., ... De Biase, A., Franceschini, C. A Female Psoriatic Arthritis Patient Involving the TMJ. *Case Reports in Dentistry*, 2021, 2021, 6638638
33. Gerardi, D., Bernardi, S., Falisi, G., Botticelli, G., Bruni, A. Characterization and morphological methods for oral biofilm visualization: where are we nowadays? *Aims Microbiology*, 2024, 10(2), 391–414
34. Falisi, G., Botticelli, G., Rastelli, S., Mondragon, M., Di Giacomo, P. Stabilization of the lower denture through the use of fine mini-implants: retrospective study. *European Journal of Musculoskeletal Diseases*, 2024, 13(2), 1–7
35. Guerra, D., Severino, M., Caruso, S., Rastelli, S., Gatto, R. The importance of using physical tridimensional models for the management and planning of extended osseous odontogenic lesions. *Dentistry Journal*, 2021, 9(11), 134
36. Iacomino, E., Rastelli, S., Capogreco, M., ... Gallottini, S.G., Grivetto, F. Pterygoid implants in severe posterior maxillary atrophy: a case report. *Oral and Implantology*, 2024, 16(2), pp. 88–94
37. Rastelli, S., Capogreco, M., D'amario, M., ... Iacomino, E., Severino, M. PTERIGOID IMPLANTS: A viable alternative for the rehabilitation of the posterior sectors of the atrophic maxilla. *Oral and Implantology*, 2024, 16(1), 38–43
38. Scarano, A., Bernardi, S., Rastelli, C., ... Falisi, G., Mortellaro, C. Soft tissue augmentation prior bone volume increase by means of silicon expanders: A case series. *Journal of Biological Regulators and Homeostatic Agents*, 2019, 33(6), 77–84
39. Mazzone, P., Padua, L., Falisi, G., ... Florio, T.M., Scarnati, E. Unilateral deep brain stimulation of the pedunculopontine tegmental nucleus improves oromotor movements in Parkinson's disease. *Brain Stimulation*, 2012, 5(4), 634–641
40. Bernardi, S., Botticelli, G., Marzo, G., ... Mortellaro, C., Lupi, E. Use of electrical field for biofilm implant removal. *European Review for Medical and Pharmacological Sciences*, 2023, 27(3), 114–121
41. Rampello, A., Saccucci, M., Falisi, G., ... Polimeni, A., Di Paolo, C. A new aid in temporomandibular joint disorders' therapy: The universal neuromuscular immediate relaxing appliance. *Journal of Biological Regulators and Homeostatic Agents*, 2013, 27(4), 1011–1019
42. Franco, R., Lupi, E., Capogreco, M., Rosa, A. The Influence of Dental Implant Roughness on Biofilm Formation: A Comprehensive Strategy Dental Hypotheses, 2023, 14(3), 90–92
43. Di Somma, L., Iacoangeli, M., Nasi, D., ... Girotto, R., Polonara, G. Combined supra-transorbital keyhole approach for treatment of delayed intraorbital encephalocele: A minimally invasive approach for an unusual complication of decompressive craniectomy. *Surgical Neurology International*, 2016, 7, 12–16
44. Franco, R., Lupi, E., Iacomino, E., ... Galeotti, A., Santos, J.M.M. Low-Level Laser Therapy for the Treatment of Oral Mucositis Induced by Hematopoietic Stem Cell Transplantation: A Systematic Review with Meta-Analysis. *Medicina Lithuania*, 2023, 59(8), 1413
45. Messi, M., Consorti, G., Lupi, E., ... Valassina, D., Balercia, P. A new operative open-wings technique to correct the frontoforeshead unit in metopic synostosis *Journal of Craniofacial Surgery*, 2015, 26(3), 902–905
46. Singh N, Scully C, Joyston-Bechal S. Oral complications of cancer therapies: prevention and management. *Clin Oncol (R Coll Radiol)* 1996;8:15–24
47. American Academy of Pediatric Dentistry. Dental management of pediatric patients receiving immunosuppressive therapy and/ or head and neck radiation. *The Reference Manual of Pediatric Dentistry*. Chicago, Ill.: American Academy of Pediatric Dentistry; 2024:545-53.
48. Nunez-Aguilar J, Oliveros-Lopez LG, Fernandez-Olavarria A, Torres-Lagares D, Serrera-Figallo MA, Gutierrez-Corrales A, Gutierrez-Perez JL. Influence of dental treatment in place on quality of life in oral cancer patients undergoing chemoradiotherapy. *Med Oral Patol Oral Cir Bucal*. 2018 Jul 1;23(4):e498-e505.
49. Giannattasio A, Poggi E, Migliorati M, Mondani PM, Piccardo I, Carta P, Tomarchio N, Alberti G. The efficacy of Italian guidelines in promoting oral health in children and adolescents. *Eur J Paediatr Dent*. 2015 Jun;16(2):93-8.
50. Ferrández-Pujante A, Pérez-Silva A, Serna-Muñoz C, Fuster-Soler JL, Galera-Miñarro AM, Cabello I, Ortiz-Ruiz AJ. Prevention and Treatment of Oral Complications in Hematologic Childhood Cancer Patients: An Update. *Children (Basel)*. 2022 Apr 15;9(4):566.
51. Mummolo, S., Cirillo, E., Ciribè, M., Manenti, R.J., Galeotti, A. Periodontology. Part 1: Gingivitis in adolescence. Review of the literature and case reports. *European Journal of Paediatric Dentistry*, 2022, 23(1), 79–82
52. Marchetti, E., Pizzolante, T., Americo, L.M., ... Quinzi, V., Mummolo, S. Periodontology Part 4: Periodontal disease in children and adolescents *European Journal of Paediatric Dentistry*, 2022, 23(4), 332–335