INTRODUCTION

Immunosuppressive chemotherapy and bone marrow transplantation have been increasingly used to treat and, in some cases, cure numerous malignant conditions. The systemic sequelae as a result of these immunosuppressive techniques induce many oral and dental complications. The direct and indirect stomatotoxic effects are associated with the development of ulcerative, hemorrhagic, or infectious complications. As a consequence, all these problems can potentially cause increasing mortality and morbidity.

Intensive chemoradiotherapy damages the mucosal barrier of the mouth and throat and it is often associated with severe oral inflammation and infection, including herpes simplex, candidiasis, mucositis, and gingivitis. In addition, these oral complications interfere with patients’ comfort, nutrition and may lead to a systemic infection originated in the mouth.

The increased risk for systemic fungal infection and the potential fatal consequences of disseminated candidiasis in patients receiving bone marrow transplants or cytotoxic antineoplastic therapy...
therapy has originated several studies about prophylaxis of candidiasis, mucositis, ulceration, hemorrhage or infection\textsuperscript{1,5-7,17,18}.

The oral health status of hospitalized children suffering from leukemia or other cancers is generally poor\textsuperscript{7}. They should be considered as high risk patients for oral complications, a situation which requires both suitable dentist and medical teams\textsuperscript{4,20}. However, in some cases, patients undergoing cytotoxic chemotherapy and radiation therapy often experience severe oral complications during and after treatment despite the supervised oral hygiene and conventional antimicrobial regimens\textsuperscript{9}.

A variety of chemical substances has been used for the prevention and treatment of chemotherapy-induced oral complications, such as chlorhexidine\textsuperscript{5,7,9,12-14,16}, vitamin E\textsuperscript{18}, itraconazole\textsuperscript{10}, fluconazole\textsuperscript{7}, oral sucralfate suspension\textsuperscript{15}, and low energy helium-neon laser\textsuperscript{11}.

The chlorhexidine mouthwash has been widely used for the aforementioned purpose. The main reason for the use of this drug is the fact that it represents an antimicrobial compound and an effective topical prophylactic agent against oral mucositis and candidiasis\textsuperscript{5}. The relevant literature presents conflicting results with respect to the prophylactic use of chlorhexidine in patients with leukemia or those who have a bone marrow transplant\textsuperscript{5,7,9,12-16}.

The aim of this study was to assess the effectiveness of a preventive oral protocol using chlorhexidine mouthrinses in preventing chemotherapy-induced oral mucosal complications in children receiving intensive chemotherapy for acute lymphoblastic leukemia (ALL) before initiating a wider intervention study.

**MATERIALS AND METHODS**

Fourteen children, two to ten years of age (mean = 7 years), receiving intensive chemotherapy for treatment of acute lymphoblastic leukemia were evaluated. These children were admitted to the Varela Santiago Hospital Service, Natal, Rio Grande do Norte, Brazil. They received an identical intensive chemotherapy regimen for a six-week period. The intensive therapy consisted of 6-mercaptopurine (an oral dose of 50 mg/m\textsuperscript{2} per day during six weeks), methotrexate (an intravenous dose of 2 mg/m\textsuperscript{2} in continuous infusion for 24 hours on days 1, 15, 30 and 45), leucovorin (an oral dose of 15 mg/m\textsuperscript{2} four times per day, on days 2, 3, 16, 17, 31, 32, 46 and 47) and MADIT intrathecal (a combination of methotrexate 12 mg + cytosine arabinoside 70 mg + dexamethasone 2 mg/m\textsuperscript{2}) on days 1, 15, 30 and 45. The protocol and informed consent were reviewed and approved by the ethical review board, Federal University of Rio Grande do Norte, Brazil. The informed consent was obtained from the parents or guardians of all children.

No children had any clinical signs of oral or esophageal candidiasis nor any other oral complications on the mucosa before initiating the preventive oral protocol and the intensive chemotherapy. The chemotherapy regimen employed for the intensive period was identical in all patients. Younger children were included in the control group.

The preventive oral protocol was performed during the intensive period of the chemotherapy. It started at least one day before initiating the intensive chemotherapy and ended ten days after the end of this period, with an average length of eight weeks. In the experimental group, seven patients received a daily preventive protocol consisting of an oral hygiene care, including twice a day (in the morning and in the evening) teeth brushing, supervised by guardians, parents and/or dentist, and mouthrinses with a non-alcoholic solution of 0.12% chlorhexidine (Ao Pharmacêutico, Natal, RN, Brazil). The seven children of the control group received a daily oral hygiene care, including twice a day (in the morning and in the evening) supervised brushing and mouthrinses with a placebo mouthwash. Both groups were then similarly evaluated daily by the same pediatric dentist for oral mucosal complications during the intravenous and intrathecal drug administration of the intensive therapy.

**Statistical analysis**

The data were analyzed statistically by means of Fisher’s exact test. A p value < 0.05 was considered significant.

**RESULTS**

During the experimental period all the children maintained good oral hygiene. A significant decrease in the incidence of mucositis and ulceration in the children who received the preventive oral protocol using 0.12% chlorhexidine mouthrinses was observed (p < 0.05; Fisher’s exact test). One child (14.3%) of the experimental group and five (71.4%) of the control group developed oral mucositis and ulceration (Figures 1 and 2). No other oral mucosa complication was observed. Mucositis developed between two and four days after the initial administration of the intravenous dose of metho-
tremore, and this was more frequent on the labial and buccal mucosa. The average durations of mu-
cositis and ulceration was ten and sixteen days,
respectively. The severity of the oral lesions and
their duration in the child who received chlorhexi-
dine mouthrinses were lesser compared to the
control group. No toxicity was observed in this
study. Only the child who developed mucositis in
the experimental group reported a burning sensa-
tion in the mouth associated with the chlorhexidi-
ne mouthwash.

**DISCUSSION**

The results of this study confirm previous stu-
dies regarding the usefulness of a preventive oral
protocol using a chlorhexidine mouthrinse for the
prevention of chemotherapy-induced oral compi-
lcations, including oral mucositis and *Candida*
fections, in children with leukemia receiving inten-
sive chemotherapy.9,12-14,16

In the present study, children who were sub-
mitted to a preventive oral protocol including a
chlorhexidine mouthwash exhibited fewer mu-
cositis lesions. Only one (14.3%) of the seven chil-
dren who used chlorhexidine experienced oral mu-
cositis. These findings indicate that oral soft tissue
disease associated with chemotherapy can be dra-
matically reduced if a prophylactic oral protocol is
applied in association with the chemotherapy.

Consistent with the findings of Ferretti *et al.* (1987) the preventive oral protocol using chlorhe-
xidine mouthrinses can reduce both the incidence
and the severity of oral lesions in children suf-
fearing from leukemia receiving chemotherapy. In ad-
dition to its value in protecting severely immuno-
compromised patients from oral mucosa
complications, chlorhexidine also offers a therape-
utic benefit in the resolution of existing therapy-
induced oral soft tissue disease.9

In contrast, other studies5,7 do not support the
use of chlorhexidine mouthrinses for the preventi-
on of mucositis in patients with bone marrow
transplantation or with leukemia receiving che-
motherapy who are able to maintain good oral
hygiene by mechanical means during their illness.

**CONCLUSIONS**

The results obtained in this limited number of
patients are promising. We support that the pre-
ventive oral protocol applied in the present study
may be used as an oral complications prophylaxis
for children with leukemia who are receiving inten-
sive chemotherapy. Besides, it may be justified to
obtain and maintain the best possible oral health
in seriously ill patients, because an improvement
of the oral conditions may diminish their suffering
and prevent the spread of serious infections from
the oral cavity. These results have been used to im-
prove the ongoing larger intervention study.

**ACKNOWLEDGEMENT**

Financial support for this study was provided
by the Conselho Nacional de Desenvolvimento Ci-
entífico e Tecnológico (CNPq).
REFERENCES


10. Foot AB, Veys PA, Gibson BE. Itraconazole oral solution as antifungal prophylaxis in children undergoing stem cell transplantation or intensive chemotherapy for haematological disorders. Bone Marrow Transplant 1999; 24:1089-93.


