

# Management of Oral Hydroxyurea-Related Ulcers: A Cases Series <sup>†</sup>

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<sup>†</sup> Presented at the XV National and III International Congress of the Italian Society of Oral Pathology and Medicine (SIPMO), Bari, Italy, 17–19 October 2019.

Published: 12 December 2019

## 1. Introduction

Hydroxyurea (HU) is an anti-cancer agent commonly used in myeloproliferative Philadelphia negative disorders as polycythemia vera (PV), essential thrombocytosis (ET) and myelofibrosis (MF). Most frequent side effects of HU are skin numbness or purple discoloration, skin ulcers or open sores and low blood cell counts. Using hydroxyurea may increase risk of developing other types of cancer, such as leukemia or skin cancer. Some recent studies underline the possibility of an oral toxicity, but its frequency seems to be quite rare. We present a cases series in which the oral lesions happened in patients in treatment with HU, focusing on their management.

## 2. Methods

A total of 7 patients (3 males, 4 females, mean age 71), arrived from January 2018 to June 2019 to the Oral Medicine section of the Dental school Lingotto, University of Turin, were enrolled in this study. 4 of them were affected by PV, 1 by MF, 2 by ET. Patients were invited to an oral visit by their hematologist. The visit was performed by a doctor expert in oral medicine. When the diagnosis of oral mucosa ulcers was done, the first line treatment was chlorexihidine mouth rinses and a topical cortisteroid applied 3 times daily for 2 weeks (clobetasol 0.05%). Only if this treatment failed or a serious new episode happened, a reduction of HU dose or its suspension were evaluated.

## 3. Results

Results are summarized in Table 1.

**Table 1.** Characteristics of patients and treatments strategies.

Pz	Age	Sex	Haematological Disease	HU Therapy (Years)	HUDose (g/Week)	Jak2	Treatment
1	80	f	PV	3	7	pos	Clobetasol, HU suspension
2	70	m	PV	6	9	pos	Clobetasol
3	70	f	PV	5	7	pos	Clobetasol, HU reduction
4	88	m	MF	5	3	pos	Clobetasol
5	64	m	PV	14	9	pos	Clobetasol, HU suspension
6	61	f	ET	2	6	neg	Clobetasol
7	64	f	ET	2	9	neg	Clobetasol

PV = polycythemia vera, ET = essential thrombocytosis, MF = myelofibrosis HU = hydroxyurea.



The clinical presentation of oral lesions was aphthous-like ulcers. None of the patients had a previous history of recurrent aphthous stomatitis. Oral toxicity appeared after a mean period of 5.2 years. A complete resolution of oral ulcers was observed in 4/7 patients (57.2%), 3 patients had no response or new episode that lead to suspension of HU (2 pz, 28.5%) or its dose reduction (1 pz, 14.2%).

#### 4. Discussion

This condition is considered an early complication, mainly within the first year [1,2]. Previous studies reported that from 0.8 to 1.8% of all patients treated with HU developed oral aphthous ulcers [2,3]. Our study, with a median period of 5.2 years of HU, presents a later onset of the oral toxicity. Other authors [3] suggest a therapy based on mouthwashes with folic acid and vitamin A. In our practice, topical corticosteroids and chlorhexidine mouth rinses seem to be a good treatment for oral lesions, but, when failed, the reduction of the HU dose or its suspension are the only way to solve the problem. Good prospective could arrive from the new cytostatic agents (e.g., ruxolitinib, anagrelide).

**Conflicts of Interest:** The authors declare no conflict of interest.

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