Oral Oncology 91 (2019) 128

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Letter to the editor

Can topical 5-fluorouracil be used as a viable treatment option for oral premalignant lesions and tumors?

5-Fluorouracil (5-FU), an antimetabolite drug is used in the treatment of various cancers. It exerts its cytotoxic effects by inhibiting thymidine synthase, leading to depletion of nucleotides required for DNA synthesis and repair. The rate-limiting enzyme in the pathway is dihydropyrimidine dehydrogenase (DPD). Common side effects include diarrhoea, stomatitis, palmar-plantar erythema, bone marrow suppression, hyperpigmentation, nausea. In topical consideration, photosensitivity, erythema, ulceration, and rarely hyperpigmentation are the common side effects. Disadvantages like severe side effects due to topical use of 5-FU have been reported too [1]. Still in high-grade vaginal dysplasia, use of 5-fluorouracil (FU) has been proved to reduce the recurrence rate [2] whereas topical 5-FU is universally accepted for the treatment of dermatological conditions like actinic keratosis, melanoma, squamous cell carcinoma, and basal cell carcinoma [3,4]. Weinstock et al, recently concluded thru their trial that fluorouracil cream does reduce surgery chances for squamous cell carcinoma for 1 year [5]. Even for keratoacanthomas, short-contact topical 5% 5-FU has provided excellent cosmetic results and well-tolerated by the patients [6].

"When a thing ceases to be a subject of controversy it ceases to be subject of interest".

It's a recognized information that 5-FU has 90% success rate in treating potentially malignant lesions of skin. In context to oral lesions, literature search revealed a report as late in 1989, suggested the use of topical 5-FU and carbon dioxide laser for management of oral squamous cell carcinoma in situ revealing good result [7]. Later in 2014, 5-FU in orabase form too presented as a resource in treating potentially malignant oral lesions [8].

In context to oral tumors, Ledderhof et al, stated that "keratocystic odontogenic tumor" (KCOT) treated with enucleation, peripheral ostectomy and 5-FU presented with lower recurrence rates and less morbidity compared to Carnoy's solution [9]. Though KCOT's were earlier categorised as odontogenic keratocyst (OKC), in 2017 it was again reverted to the WHO classification of odontogenic developmental cysts, reconstituting with the original terminology "OKC" [10]. Singh et al., in 2016 too had concluded that aggressive treatment should be reserved for selective cases, in contrary to other authors, who believe that all OKCs behave as a tumor and should be treated aggressively making the recent reclassification a requisite [11]. Pinheiro et al., treated a case of OKC with marsupialization and 5-FU intralesional and observed exuberant bone neoformation, mainly in the basilar region of the mandible [12].

On searching various databases for research details ministering the use of 5-FU in preventing transformation in premalignant lesion, we came crossways with just two reports in the journal OOOO, in almost three decades. Among the challenges to overcome the malignant transformation blockades of premalignant lesions and the possibility of chemopreventive approaches for the treatment of premalignant lesions so as to prevent secondary pre-malignant lesions and their progression to cancer is to be considered on priority basis. Therefore we the authors sturdily voice for more studies and research to be taken up for understanding the role of 5-FU in oral premalignancy and tumors to lower the rate of malignant transformation and recurrence.

References

[1] Kishi P, Price CJ. Life-threatening reaction with topical 5-fluorouracil. Drug Saf Case Rep 2018;12:5(1):4.
[2] Fiascone S, Vitonis AF, Feldman S. Topical 5-fluorouracil for women with high-grade vaginal intraepithelial neoplasia. Obstet Gynecol 2017;130(6):1237–43.
[3] Prince GT, Cameron MC, Fathi R, Alkousakis T. Topical 5-fluorouracil in dermatologic disease. Int J Dermatol 2018;57(10):1259–64.
[4] Haeusler KA, Hall JR, Seykora CM, Abuzeid MJ, Dalton SR. Melanoma or pseudomelanoma? Change in a pigmented lesion after application of topical 5-Fluorouracil. J Cutan Pathol 2018;45(1):97–8.
[5] Weinstock MA, Thwin SS, Siegel JA, Marcolivio K, Means AD, Leader NF, et al. Chemoprevention of basal and squamous cell carcinoma with a single course of fluorouracil, 5%, cream: a randomized clinical trial. JAMA Dermatol 2018;154(2):167–74.
[6] Thompson BJ, Ravits M, Silvers DN. Clinical efficacy of short contact topical 5-Fluorouracil in the treatment of keratoacanthomas: a retrospective analysis. J Clin Aesthet Dermatol 2014;7(11):35–7.
[7] Barbara B, Maxson BB, Scott RF, Headington JT. Management of oral squamous cell carcinoma in situ with topical 5-fluorouracil and laser surgery. OOO 1989;68(1):44–8.
[8] Da Costa GBF, Cavalcanti FDGB, DE Almeida ER, De Castro JFL. Evaluation of the effects of 5-fluorouracil-orabase on potentially malignant lesions of mouse oral mucosa induced by 4-nitroquinoline-1-oxide. OOOO 2014;117(2).
[9] Ledderhof NJ, Caminiti MF, Bradley G, Lam DK. Topical 5-fluorouracil is a novel targeted therapy for the keratocystic odontogenic tumor. J Oral Maxillofac Surg 2017;75:514–24.
[10] Speight P, Devilliers P, Li TJ, Odell EW, Wright JM. World Health Organization classification of tumours. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, editors. Title. Lyon: IARC Press; 2017. p. 235–6.
[11] Singh HP. Need to reclassify keratocystic odontogenic tumor into cyst and neoplasm. Natl J Maxillofac Surg 2016;7(1):111.
[12] Pinheiro GL, Almeida N, Miceli AL, Noce C, Kuzsminszky E, Venturi QGB. Five-fluouracil for odontogenic keratocyst treatment: a case report. J Den Craniofac Res. http://doi.org/10.21767/2576-392X-C1-003.

Samapika Routray (MDS)*
Department of Dentistry, All India Institute of Medical Sciences, Bhubaneshwar, India
E-mail address: drroutray.samapika@gmail.com.

Punit S. Dikhit (MDS)
Ex Senior Resident, All India Institute of Medical Sciences, Bhubaneswar, India
Fellow Oral Oncosurgery, Kidwai Memorial Institute of Oncology, Bangalore, India

Rajani B.C. (MDS)
Department of Oral Oncology, Kidwai Memorial Institute of Oncology, Bangalore, India

Mohd. Musab Khan
Department of Oral and Maxillofacial Surgery, Kothiwal Dental College and Research Centre, Moradabad, India

* Corresponding author.

https://doi.org/10.1016/j.oraloncology.2019.02.009
Received 30 January 2019; Received in revised form 6 February 2019; Accepted 8 February 2019
Available online 15 February 2019
1368-8375/