

A survey of the incidence of chapped lips and cold sores during cytotoxic chemotherapy, and the perceived effectiveness of self medicated lip salves

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ABSTRACT

Objectives: This study evaluated the prevalence and severity of chapped lips and cold sores during chemotherapy, and the perceived effectiveness of self-medicated lip salves.

Methods: One hundred and five consecutive patients receiving chemotherapy were given a specifically designed questionnaire between 2nd July and 31st October 2008, at the Primrose Oncology Unit, Bedford Hospital.

Results: One hundred (95%) were returned. Twenty eight percent reported regular sore lips before chemotherapy as opposed to 69% during chemotherapy. Sixty six percent of these used lip salves, but 82% of these reported little or no benefit. Of these, eighty three percent used petroleum-based creams, and of these, 9% reported that they were helpful. Seventeen used natural oil-based creams, and of these, 63% reported that they were helpful. Patients were 2.5 times more likely to have cold sores if they had chapped lips.

Conclusion: As the incidence of chapped lips more than doubles during chemotherapy, preventative lifestyle advice has been included in our patient information leaflets and website (cancernet.co.uk). This survey suggests a potential association between chapping and cold sores, and a difference in effectiveness between petroleum and natural oil-based creams. This will now be investigated in a forthcoming double-blind, randomised study comparing a natural oil-based cream (Nature-Medical lip balm) against a petroleum-based control.

KEYWORDS

chapped lips, cold sores, chemotherapy, salves.

INTRODUCTION

Chapped lips refer to a common condition in which the lips become dry, cracked and sore. If marked, this can lead to bleeding and secondary infection.^{1,2} In a general population there are a number of other factors which contribute to its incidence and severity. These include overexposure to the sun or cold wind, dehydration particularly associated with alcohol intake, and drugs which cause oral dryness including codeine, opiates, anti cholinergics and aromatase inhibitors.^{3,4,5} Other medical conditions associated with sore lips include malnutrition, particularly vitamins C and B deficiency, systemic sclerosis, eczema, Cushing's Syndrome or long-term steroid intake.⁶ Some people can also irritate their lips by habitually licking them.



Lip soreness during chemotherapy is an understated symptom. Despite being common, it is generally regarded as a trivial condition, and is rarely mentioned in patient information materials or recorded in chemotherapy studies.⁷ Likewise, there is very little advice on how to prevent or alleviate soreness, or the associated visual distress. The purpose of this survey was to record the incidence and severity of sore lips during chemotherapy, find out which over-the-counter remedies are used by patients, and which are perceived to be helpful.

Methods

This study was conducted at the Primrose Oncology Unit, Bedford Hospital, involving patients receiving cytotoxic chemotherapy between 2nd July and 31st October 2008. A lip health questionnaire (Figure. 1) was administered to all available patients by their oncology nurse following a brief verbal explanation. When 100 questionnaires were completed, the survey was stopped, and this resulted in 105 being handed out, with a 95% return rate.

The questionnaire

As sore lips have rarely been evaluated in this setting, there were no specific questionnaires

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A survey of the incidence of chapped lips and cold sores during cytotoxic chemotherapy and the perceived effectiveness of self medicated lip salves

Table 1: Lip health questionnaire results (100 patients).

	Numbers (%)	
	Yes	No
Chapped lips:		
Chapped lips before chemotherapy	28 (28%)	72 (72%)
Regularly used lip creams pre chemotherapy	17 (17%)	83 (83%)
Chapped lips after chemotherapy	69 (69%)	31 (31%)
Used lip creams after chemotherapy	66 (66%)	34 (34%)
Cold sores:		
History before chemotherapy	29 (29%)	71 (71%)
Acute episode during chemotherapy*	19 (19%)	81 (81%)

*Average duration of chemotherapy at the time of completing the questionnaire; 3.8 months.

24-79). Analysis of the results showed that 28% described regular episodes of sore lips in the three months prior to the start of chemotherapy. Sixty nine percent of patients experienced sore lips during chemotherapy (Table 1), 37% had grade 1-2 and 32% grade 3-4. Of these, 66% self-medicated with lip salves, but 82% of these reported little or no benefit (Table 2). Eighty three percent (55/66) used petroleum-based creams, and of these, only 9% reported that they were moderately or very helpful. On the other hand, of the 17% (11/66) who used non petroleum-based natural salves (mainly beeswax), 63% reported that they were moderately or very helpful (Table 2).

Table 3: Prevalence of chapped lips during individual chemotherapy regimens.

Regimen (Number)	All grades	Grade 1-2	Grade 3-4
Capecitabine (16)	11	5	6
FEC(14)	9	8	4
Oxaliplatin and capecitabine (12)	9	4	8
Taxotere (11)	6	3	3
Irinotecan (10)	8	4	4
ECX (5)	4	1	3
Chop (4)	2	2	0
Gemcitabine and cisplatin (4)	3	1	2
Chop and Mabthera (3)	2	1	1
Taxol (3)	2	2	0
Gemcitabine and carboplatin (3)	2	2	0
Other (15)	11	4	1
Total (100)	69 (69%)	37 (37%)	32 (32%)

The range of chemotherapy regimens that patients received is listed in Table 3. Sore lips occurred in all of them. In view of the small numbers involved, it was not possible to associate a particular regimen with a higher risk of soreness, although there was a trend with a higher number on the oral fluoropyrimidine capecitabine, with 55% reporting grade 3-4 soreness.

Cold sores were reported by 29% of patients during the four months prior to chemotherapy, and the prevalence was

Table 2: Commonly used self medicated salves and perceptions of benefit.

Type of lip salve	Users	No help	Slight Help	Moderate Help	Major Help
Non-petroleum based:					
Beeswax	9	1	3	3	2
Other	2	0	0	1	1
Total non-petroleum based (% of 11)	11	1 (10%)	3(27%)	4(36%)	3 (27%)
Petroleum based:					
Vaseline	15	11	3	1	0
E-45	6	4	1	0	1
Nivea Chapstick	7	6	1	0	0
Lipsticks	10	7	3	0	0
Original Chapstick	10	9	0	2	0
Other	6	4	1	1	0
Total petroleum based (% of 55)	55	41(75%)	9(16%)	4(7%)	1(2%)
All salves (% of 66)	66	42 (64%)	12 (18%)	8(12%)	4(6%)

Of the 19 individuals who experienced a cold sore during chemotherapy, 13 self medicated with acyclovir before oral acyclovir medication was prescribed.

A survey of the incidence of chapped lips and cold sores during cytotoxic chemotherapy, and the perceived effectiveness of self medicated lip salves

Table 4: Association between cold sores and sores lips.

Cold sores	Chapped lips	
	Yes	No
History of cold sores before chemotherapy (29)	23 (79%)	6 (21%)
Cold sores during chemotherapy (19)	16 (82%)	3 (18%)

slightly lower (19%) during their chemotherapy (Table 4). The average time on chemotherapy, up to the time of completing the questionnaire, was 3.8 months. There appeared to be an association between sore lips and cold sores; Sixteen of 19 patients who had cold sores during chemotherapy also had sore lips (82%). Likewise, 72% of patients who had cold sores pre-chemotherapy also had a history of chapped lips, more than 2.5 times the prevalence of the whole group (28%) (Table 4). Although the prevalence of cold sore episodes was not different, the individual episodes appeared to be more marked during chemotherapy; All patients could recall how many individual cold sore lesions they had during an episode, both in the 4 months pre-chemotherapy (17 had one, 7 had 2, 4 had three, 1 had four lesions; average 1.6), and during chemotherapy (5 had one, 5 had two, 7 had three and 2 had four lesions; average 2.3). The trend was confirmed by the question regarding overall severity; 10 (84%) indicated that their episode(s) was (were) worse during chemotherapy than a typical episode pre-treatment, 2(11%) reported no change and 1(5%) better.

DISCUSSION

This study has provided previously unpublished information regarding the prevalence and severity of chapped lips and cold sores during chemotherapy. It has also provided useful feedback for the development of a designated lip health questionnaire, which will be evaluated for construct validity for use in future studies. The patients evaluated in this study have reported that the prevalence of chapped sore lips more than doubles after the start of chemotherapy. This is likely to be caused by chemotherapy damaging the rapidly dividing basal cells in the vermilion boarder.⁸ The majority (96%) of patients used a lip salve, but only 18% felt they were moderately or very helpful. This proportion was higher (63%) in those who used natural ingredients-based creams such as beeswax. This difference, however, in such small numbers, in an open and subjective end point, does not justify statistical calculation, and should be regarded as a trend rather than conclusive. Nevertheless, this observation justifies a further randomised evaluation of petroleum versus non petroleum-based, natural ingredients-based creams. In the meantime, our patient information chemotherapy sheets (available on www.cancernet.co.uk) will be adjusted to include the side effect of sore lips, and include lifestyle advice to help prevent chapping (such as avoid excessive licking and avoiding dehydration).

A number of infective conditions can affect the lips

including bacteria and fungi, but the most common in the community, by far, is the herpes simplex virus (HSV). Acute episodes are characterised by the presence of red swollen areas on the mucous membrane or skin, with fluid-filled blisters which can be disfiguring and painful. The prevalence of cold sore acute episodes was similar before (29%) and after chemotherapy (19%). These figures are similar to previous studies from Wisconsin and France, which have reported that the prevalence of recurrent herpes labialis (>3 acute episodes/year) in the general population was 30%.^{9,10,11} There are anecdotal reports of cold sores being more severe during chemotherapy, and this survey suggested the same increased trend¹² as 16 of 19 (84%) reported that the severity of their cold sores, and the average number of sores per episode, were worse than those typically experienced before chemotherapy. Although not an occurrence in this study, acute episodes have also been reported to have more sinister consequences, especially when associated with neutropenia,¹³ and patients who develop herpes whilst on chemotherapy are required to present urgently for high-dose anti-virals, as there are concerns of system spread.⁹

The HSV, once caught, lies dormant in the facial nerve ganglion.^{13,14} Cold sore episodes occur when the HSV migrates down the nerve to the dermis in and around the lips. The precise triggers for these acute episodes are not certain, but there are associations with iron deficiency, psychological stress and a history of aphthous ulcers.^{12,13} This survey suggests that there is a link between chapped lips and cold sores, as 79-82% of patients with cold sores also suffered from chapped lips, as opposed to 18-21% who did not (Table 4). This association has been alluded to in previous studies as it has been described more frequently following dental treatments, and damage to the lips via wind and sun exposure.¹⁵

Although strategies to prevent an acute episode have so far been unsuccessful,¹³ topical or systemic anti-viral agents such as acyclovir, docosanol, penciclovir or valacyclovir, have been shown to shorten the length of the attack if used early in an episode.^{12,16,17} In patients with a history of cold sores, it may be appropriate to prescribe a supply of these with the first cycle so that patients can apply them as soon as the episodes appear. The association between chapped lips and cold sores also has implications for further research, with the hypothesis that preventing chapping may prevent cold sores.

In view of the high prevalence of chapped lips, the increased severity and serious nature of cold sores during chemotherapy, the lack of benefit of existing commonly used salves and the trend of an increased benefit of natural ingredients, a clinical study is justified. A double-blind, randomised study has been designed to compare the incidence of chapped lips and cold sores amongst individuals using either a petroleum-based salve, or one containing only natural waxes and oils and the available brand which best met this criteria was Nature-Medical lip balm (cancernet.co.uk).¹⁸

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A survey of the incidence of chapped lips and cold sores during cytotoxic chemotherapy, and the perceived effectiveness of self medicated lip salves

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