The use of Minoxidil to attempt to prevent alopecia during chemotherapy for gynecologic malignancies

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Summary: Minoxidil 2% topical solution applied twice a day is known to induce hair growth and prevent hair loss in normal male pattern baldness. Based on this potential, this pilot study tested the effect of Minoxidil on hair loss during chemotherapy for gynecologic cancers. Ten women about to start alopecia-inducing chemotherapy protocols were entered into this non-randomized prospective trial. By study design, each patient served as her own control, as only a portion of the scalp was treated with Minoxidil. Four of the ten patients were unevaluable for failing to comply with the twice-a-day Minoxidil application schedule. Of the six evaluable patients, five experienced complete or severe symmetrically diffuse hair loss, all of which occurred within four weeks of initiating chemotherapy. One patient had no hair loss in either the treatment or control area. Application of the topical Minoxidil in all ten patients had no untoward side effects, skin changes or hypotension. Thus, in this pilot study, 2% Minoxidil was non-toxic but showed no benefit in the prevention of chemotherapy-induced alopecia.

Key words: Minoxidil; Alopecia; Chemotherapy.

INTRODUCTION

In addition to the many stresses imposed by cancer, patients receiving chemotherapy must also cope with the physical side effects and body-image changes caused by the chemotherapeutic agents themselves. Particularly devastating for female patients is the common side effect of drug-induced alopecia. If the balding caused by chemotherapy could be prevented or lessened, the ordeal of cancer treatment would be reduced for all patients. Unfortunately, approaches toward this end, such as iced headcaps, have proven unsuccessful ([1, 2, 3, 4]) and consequently, a preventative remedy for alopecia is still needed.

Minoxidil was originally developed as a potent oral anti-hypertensive agent which works by exerting a direct vasodilatory effect, primarily on the arterioles. As more hypertensive patients were treated with Minoxidil, a common but curious adverse drug reaction observed was hypertrichosis (excessive growth of hair) ([5, 6]). Patients began reporting a general and unpredictable hyperstrichosis of their facial and body vellus hair. Indeed, a number of males who were going bald prior to initiating treatment for high blood pressure with Minoxidil experienced noticeable

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stimulation of terminal hair growth in both length and thickness ([7]). Further studies suggested that the incidence of hypertrichosis among Minoxidil users was between 30 and 50% for males and 50 to 85% for females ([8, 9]).

Exploring the hair-growing potential of Minoxidil, the drug was studied as a topical solution for the prevention and treatment of male pattern baldness. In these studies, 2% Minoxidil applied twice a day resulted in a statistically significant increase in the hair count as compared to placebo ([10]). Hair growth occurred in the absence of serious side effects or systemic absorption of the drug. This data recently led to FDA approval of topical Minoxidil for the management of male pattern baldness. As this was the only pattern of hair loss officially studied and presented to the FDA, it was the only balding pattern for which Minoxidil use was approved. In hopes of employing the hypertrichosis effect and Minoxidil's purported prophylaxis against hair loss, we conducted a pilot study using the drug in patients undergoing chemotherapy for gynecologic cancers.

MATERIAL AND METHODS

This pilot study was designed to evaluate Minoxidil's ability to prevent drug-induced alopecia in a limited number of patients who were to undergo chemotherapy for gynecologic malignancies. There was particular interest in the effect of Minoxidil on patients receiving the most alopeciagenic chemotherapies such as adriamycin-containing combinations. To be eligible, patients had to be enrolled in the study and begin the twice-a-day 2% Minoxidil application prior to receiving their first course of chemotherapy. Ideally, this meant that Minoxidil solution was applied twice a day for one to two weeks prior to instituting their first treatment cycle. In some cases, because the diagnosis was sudden and unexpected (and so as not to delay the cancer therapy), less lead time was available for treatment with Minoxidil before starting chemotherapy. Whatever their lead time, all patients continued the Minoxidil application until completion of chemotherapy or until a definitive hair loss pattern could be established.

Minoxidil was applied to the area of the scalp superior and posterior to the right ear including the superior portion of the right occiput. This region was selected for its ease of identification by the patient allowing consistent placement of the Minoxidil solution. In addition, it is an area which could be cosmetically covered by combing over adjacent hair in the event that the Minoxidil treatment actually worsened or caused permanent hair loss. Finally, this treatment region facilitated analysis of response being accessible for direct visual comparison with its side-by-side contralateral untreated control.

Protocol eligibility required that patients be non-pregnant, have a Karnofsky performance score of 0 to 4 with a life expectancy of greater than four months, have no unlerlying skin or scalp disease, and sign informed consent. Throughout the topical application of Minoxidil, patients were monitored for subjective problems, physical changes, changes in blood pressure and relative hair loss.

RESULTS

Ten patients were entered into this nonrandomixed prospective protocol in which each patient also served as her own nontreatment control. Only six patients were ultimately evaluable. The four unevaluable patients failed to comply with the protocol's treatment schedule. Table 1 summarizes the chemotherapeutic regimens employed for the evaluable patients and the corresponding hair loss observed. In this group, the hair response was identical when the Minoxidil-treated scalp was compared to the untreated (control) areas. Five of the six patients experienced complete or symmetrically diffuse, severe hair loss. Four of five patients who developed alopecia received adriamycin (50 mg/m^2) containing combination chemotherapy. One of six patients experienced no hair loss in either the treatment or control area despite receiving a regimen, which, while not including adriamycin, usually causes significant hair loss.

In this series, no noticeable side effects from the Minoxidil were experienced by any patients, including the four unevaluable patients who had applied the drug

Table 1. – *Chemotherapeutic Regimens Employed and Corresponding Hair Loss.*

Patient	Cancer/Stage	Chemotherapy	Alopecia
1	Cervix IIb recurrent	VcMcP	None
2	Endometrium III	CAP	Diffuse/Severe
3	Ovary IIIc	CAP	Diffuse/Severe
4	Endometrium IV	CAP	Complete
5	Endometrium IV	CAP	Complete
6	Endometrium IV	CAP	Diffuse/Severe
Key:	A: Adriamycin	50 mg/m^2	
	C: Cytoxan	500 mg/m^2	
	P: Cisplatin	50 mg/m^2	
	Vc: Vincristine	1 mg/m^2	
	Mc: Mitomycin C	10 mg/m^2	

regularly, albeit not according to protocol specifications. Neither did this study identify perceivable changes in blood pressure nor increased scalp toxicity associated with the Minoxidil application. The latter potential toxicity was of concern as it was plausible that Minoxidil, by inducing vasodilatation, could result in a higher potentially skin-toxic concentration of chemotherapy in that area.

The greatest single problem encountered in the series, as exemplified by the four unevaluable patients, was compliance with the dosing schedule, i.e., simply remembering to apply the Minoxidil twice a day as prescribed. Of additional note is that most of the patients to whom we offered enrollment into this potentially hair-sparing protocol declined to be entered, apparently feeling that the topical application of Minoxidil would actually add more stress during cancer therapy.

DISCUSSION

This pilot study observed no benefit towards prevention of alopecia by the application of 2% Minoxidil to the scalp of patients undergoing chemotherapy for gynecologic cancers. Although the number of patients studied is small, because each woman represented her own internal control, the limited information takes on more importance. Confounding factors such as patient compliance with application schedule, the varied lead times that the Minoxidil was applied prior to the initiation of chemotherapy, the region of the scalp selected as the treatment area, and concentration of the Minoxidil solution (2%) may have contributed to the failure of this drug to prevent alopecia in this group of women.

Optimistically, because Minoxidil had no apparent toxicity in our pilot study, we will study it further in expanded and modified protocols. In addition, we are evaluating Minoxidil's potential to accelerate the regrowth of the patients' hair after they complete chemotherapy. Certainly, if hair loss could be prevented or, at a minimum, hair regrowth accelerated, the ordeal of chemotherapy would be lessened.

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