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EFFICACY AND SAFETY OF HYALURONIC ACID SUPPOSITORIES (CIKATRIDINA®) IN THE TREATMENT OF VAGINAL ATROPHY IN BREAST CANCER PATIENTS INDUCED BY HORMONE TREATMENT OR CHEMOTHERAPY

Summary

Efficacy and safety of hyaluronic acid (Cikatridina) in breast carcinoma patients suffering from vaginal atrophy induced by hormone treatment or chemotherapy: In an open post-marketing study on 100 patients, the effects on symptom reduction, quality of life and sexuality have been evaluated. Almost all symptoms showed significant reduction, especially atrophy. The tolerability was stated as very good.

Summary

In a therapeutic observational study of 100 patients, who had received chemotherapy or home and treatment after being diagnosed with breast carcinoma, and as a result of which were suffering from vaginal atrophy, the effect of hyaluronic acid suppositories was examined on the progression of the complaint, the quality of life and sexuality. The results showed a significant improvement in almost all symptoms. The symptom "atrophy" was particularly strongly reduced. The tolerability was assessed as being extremely good.

Introduction

Cancer patients receiving chemotherapy or hormone treatment are affected by numerous side-effects such as nausea, hair loss and fatigue. One of the less serious side effects is dryness of the vagina, which is nevertheless an additional source of stress affecting the quality of life and the sex life negatively. Oestrogen suppositories and lubricants are available to relieve these symptoms.

Suppositories containing hyaluronic acid as their main ingredient have enriched the therapeutic options available for vaginal atrophy, particularly for cancer patients. Of the pharmacological effect of hyaluronic acid in regenerative processes in tissues and in wound healing has been well-documented [1].

In the present therapeutic observational study, the efficacy and tolerability of hyaluronic acid suppositories will be examined for vaginal atrophy among cancer patients induced by chemotherapy and hormone treatment.

Patients and Methods

Over the period from November 2004 to January 2006, as part of therapy observation at the Special Gynaecology Department of the University Gynaecology Clinic in Vienna, the efficacy and safety of hyaluronic acid suppositories (Cikatridina) were studied for vaginal atrophy consequent to hormone treatment or chemotherapy among patients diagnosed with breast carcinoma.

A total of 100 patients were recruited and the dates of treatment were recorded. On average, the patients were 59 years old (standard deviation 11.2, median 62 years); the youngest patient was 36 years old and the oldest was 84. 20% of the patients had received chemotherapy, and 78.9% had received hormone therapy (tables 1 and 2).

Table 1: Chemotherapy

Medication	No.
FEC	8
ET	7
Caelyx	1
FEC + irradiation	1
FEC + Herceptin	1
Navelbine	1
No details	1

The investigation consisted of two treatment phases and three visits. The first visit was for recruitment, recording and assessment of the severity of the following symptoms using an evaluation scale from 0 (= none) to 10 (= very strong): dryness, burning, fissures, pain, sensation of heat, tension, redness, inflammation. Furthermore, the patients were asked during the recruitment phase to answer questions about their quality of life. They were asked about effects on their quality of life as a result of vaginal dryness and problems due to vaginal dryness during sexual intercourse, evaluated on a scale from 0 to 10. In addition, there are also questions about the fear of pain and the fear of injury during sexual intercourse, evaluated using an ordinal scale of slight, moderate, severe, and very severe. There was also a yes/no question about avoidance of sexual intercourse at all because of these fears. Visit 1 was followed by a 20-day initial period of therapy, in which the test preparation was introduced into the vagina once a day, before going to bed. During the second visit, changes in the progress of the complaint as a result of the initial treatment were documented. There was then a 10-week maintenance therapy period, during which the preparation was applied twice weekly; the end of this period was also completed their participation. The test preparation was an extract in suppository form (Cikatridina vaginal suppositories containing 5mg of the sodium salt of hyaluronic acid, marketed in Austria by CSC Pharmaceuticals Handels GesmbH).

Table 2: Hormone treatment

Medication	No.
Novaldex	37
Arimidex	18
Novaldex + Zoladex	9
Femara	6
Aromasin	1
Arimidex + Zoladex	1
Novaldex + Arimidex	1
Novaldex (Arimidex > Jun-05)	1
No details	1

	Mean value on Recruitment (Visit 1)	Mean value at final examination	Significance ($p < 0.01$)	
Dyspareunia	2.87	1.42	0.000001	high
Pain	0.33	0.09	0.042225	tendency
Flushing	0.68	0.27	0.010547	tendency
Dryness	5.65	1.64	0.000000	high
tension	0.92	0.19	0.000209	high
Burning sensation	1.74	0.59	0.000001	high
Itching	1,67	0.25	0.000000	high
Fissures	0.92	0.2	0.000259	high
Redness	0.65	0.14	0.005315	high
Inflammation	1.13	0.15	0.000052	high

Table 3: Changes in the symptoms during the course of treatment

Any side effects were recorded at the first checkup and at the end date. The end date also included a subjective assessment of the efficacy and tolerability by the physician and the patient, evaluated on an ordinal scale as excellent, good, moderate or poor.

The data was analysed statistically using a t-test.

RESULTS

Patient population

There were five cases among the 100 patient questionnaires for which it was not possible to be certain that the test preparation had been regularly applied; these were excluded from the analysis. There were nine cases in which the treatment was discontinued after the second visit; these cases were handled using LOCF (last observation carried forward, see figure 1).

Duration of treatment

The planned duration of treatment was 90 days. On average, the first checkup (Visit 2) took place 20.1 days after the start of treatment; the final visit (Visit 3) the place on average 82.1 days after the initial checkup (Visit 2).

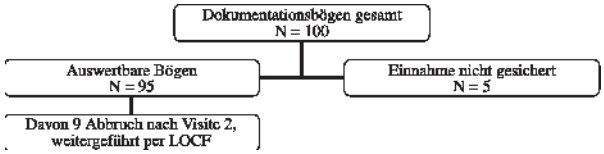
Decrease in symptoms during treatment

All the symptoms monitored during the therapy observation (with the exception of pain and flushing, for which the starting values were already low anyway) showed a highly significant improvement between the initial visit and the final visit. The majority of symptoms showed a highly significant improvement after 20 days. The improvement in the dryness symptom is particularly clear (figure 2 and table 3).

Effect on quality of life and sexuality

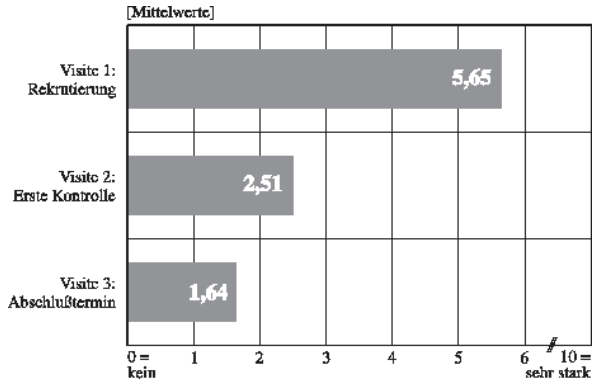
A number of criteria from the quality of life aspect about discomfort during sexual intercourse were only answered by active patients, meaning that correspondingly fewer patients could therefore be included in the analysis.
When asked during the first visit about the effect that vaginal dryness was having on the general quality of life, a mean value of 1.3 was indicated; when asked about the hindrance that these symptoms gave during sexual intercourse, a mean value of 2.47 was given. 12.3% of the patients stated that they were afraid of it being painful; 3.5% said this fear was very strong. 10.7% indicated that they were afraid of injury; 1.8% said this fear was very strong. 21.1% of the patients said that they would avoid sexual intercourse at all because of the fear of injury and pain.
The improvements in the quality of life due to the treatment, assessed using a scale from 0 to 10, gave a mean value of 3; about 5.4% of the patients indicated that their quality of life had been very significantly improved (grade 10), and a further 5.4% saw a subjective but nevertheless very substantial improvement (grades 8 and 9). The improvement in the problems during sexual intercourse resulting from the symptoms yielded a mean value of 1.89 after treatment. 2.8% of the patients indicated that they had observed a very great improvement; a further 8.4% at least experienced a substantial improvement (grades 8 and 9).

Figure 1: Patient population



Total number of questionnaires recorded: N = 100
Assessable questionnaires: N = 95
Patient compliance uncertain: N = 5
of which 9 discontinued after Visit 2, extrapolated using LOCF

Figure 2: Significant reduction in the “dryness” symptom ($p < 0.001$)



[mean value]	
Visit 1: recruitment	*5.65*
Visit 2: first checkup	*2.51*
Visit 3: completion	*1.64*

0 = none
10 = very strongly

Dr. Muy-Kheng Maria Tea

Born in 1979 in Sageo, Thailand. Studied Human Medicine at Vienna University from 1998 to 2004. Doctorate and dissertation in 2004 at the Special Gynaecology Department of the University Clinic for Gynaecology at the Vienna Academic Hospital on the prevalence and penetration of the L1420F ATM mutation in Austrian families with breast and ovarian cancer. 2003 to 2004: member of the scientific staff at the Special Gynaecology Department of the University Clinic for Gynaecology, Vienna. Since 2004, she has been working at the University Clinic for Gynaecology as part of her specialist training.

2005: Diploma - Acupuncture. 2006: Diploma - Clinical trial physician

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Side effects

Side-effects occurred in 7 out of the 95 patients after 20 days (i.e. 7.4%), which led to the treatment being discontinued in three cases. Two of these patients experienced a burning sensation; one patient referred to bleeding after sexual intercourse, although this was due to the sensitivity of the vaginal mucosa and not due to the treatment. Other items not related to the treatment were hair loss and menstruation. The other seven cases of side-effects were slight itching and slight burning sensations during the first three days.

Side-effects could still be observed after the final visit in just two patients, i.e. 3.1%.

Tolerability and estimation of the efficacy

Both physicians and patients gave a good report on the effectiveness of the test preparation, with 70% of each group rating it as very good. The tolerability was rated even better: 85% of the physicians and 76% of the patients rated the product being tested as very good.

DISCUSSION

In the present treatment observation study, 95 patients were treated with hyaluronic acid suppositories, documenting the changes in the progress of the complaint, and the effective on the quality of life and sexuality, as well as the tolerability of the test product. The results show a significant improvement in all the symptoms, with the exceptions of pain and hot sensations. The improvement in the main symptom, vaginal atrophy, was particularly clear. It should be noted here that a significant reduction of the symptoms was obtained in the initial phase, i.e. during the first 20 days of treatment, and further clear improvements were also obtained during the maintenance phase.

Cikatridina proved to be very well tolerated. The side-effects that did occur were generally mild and could sometimes not be causally related to the treatment with Cikatridina.

When discussing the quality of life and sexuality, it should of course be noted on the one hand that the underlying disease is seen as affecting the quality of life are more strongly than the vaginal atrophy. Sexuality is a sensitive issue and people were therefore not always particularly ready to impart information. Of the average age of 59 may also be playing an essential role in the patients' openness to such questioning. Against this background, it is still possible to see a slight improvement in the quality of life overall after the treatment, as well as a slight improvement in the problems with sexual intercourse.

The results show that Cikatridina vaginal suppositories are effective and well-tolerated for treatment of vaginal atrophy in this vulnerable group of patients and can improve the symptoms rapidly and permanently. Patient satisfaction was very high. For instance, 85% of the patients would rate Cikatridina vaginal suppositories as highly recommended, and many of them wanted to continue using the test preparation after the investigations were completed.

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