PRELIMINARY EVALUATION OF A NEW PROTOCOL FOR THE ACTINO-THERAPEUTICAL TREATMENT OF UTERINE CERVIX CARCINOMA IN STAGES II AND III

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SUMMARY

This study concerns 89 patients affected by uterine cervicocarcinoma at stage II or III, hospitalized at the Obstetric and Gynecological Clinic of Genoa University and subjected to transcutaneous (cobalt) and intracavitary (cesium^{137}) actinotherapy.

One year after the treatment end, the Authors observed and compared post-actinic troubles in a group of patients who had undergone a classic actinic treatment and in those subjected to a new therapeutical protocol based on dose fractionation.

The latter showed a higher incidence of immediate troubles, but a lower percentage of cerviconeoplasia persistence.

INTRODUCTION

The uterine cervicocarcinoma treatment has undergone many changes concerning both surgical and actinic therapies.

The discovery of Radium properties and capability to treat some neoplastic forms led, between 1920 and 1930, to a remarkable development of endocavitary therapies, for example in the uterine tumour treatment, according to various methods (Paris; Manchester; Stockholm).

Subsequently, the transcutaneous actinotherapy was modified with the introduction of the Cobalt bomb, Betatron and the linear accelerators.

The remote-after-loading method was introduced in endocavitary therapies ([1, 2, 3, 4, 5]).

Particularly, in the cervical cancer radiotherapeutical treatment, it has been commonly accepted that high-energy external therapy must be carried out throughout the pelvis during the first phase, in rather high doses (4000-5000 rad over 4/5 weeks, or biologically equivalent doses).

The endocavitary therapy is to be kept as a 'booster' for the central area, more resistant and requiring higher doses. This sequence has been adopted because if the endocavitary Curietherapy follows a more or less significant reduction of the tumour mass by external radiotherapy, the residual tumour, made up of a lower number of hypoxic cells and therefore more prepared for complete sterilization, is more likely to be covered with a sufficient dose.

Thus the concept of 'dose-fractionation' was introduced to obtain rapid and significant changes in neoplasia cells, during the first phase of the treatment. These changes make it possible to carry through the radiotherapy under conditions of higher radiosensitiveness ([6, 7, 8]).

The elements of this 'dose-fractionation' that determine radiobiological responses, are the large initial fractions and the intervals. Intervals are adequately modu-

lated to obtain different responses from tumour or healthy tissues, clearly favouring the latter.

MATERIAL AND METHODS

We examined 89 patients hospitalized at the Obstetric and Gynecological Clinic of Genoa University, suffering from portio tumour in stages II and III subjected to transcutaneous and endocavitary radiotreatment.

Patients were divided into two groups. The first included 65 cases of cervical neoplasia treated, between 1978 and 1980, with endouterine and vaginal cesiotherapy, with the remote-afterloading technique and Curietron.

This treatment was followed or preceded by Cobalto-therapy cycles, according to classical schemes.

The second group included 24 patients who, between 1980 and April 1981, underwent combined radiotherapy according to a new therapeutical protocol, based on dose fractionation (table 1).

This treatment programme envisages telecobaltotherapeutical irradiation throughout the small pelvis, with facing fields or four converging fields, according to protocol A (envisaging a more traditional fractionation) or protocol B, characterized by large initial individual fractions, followed after a 3-week interval, by a supplementary dose.

After a 7-day interval all patients underwent endo-uterine and vaginal Curietherapy, in doses never exceeding 2000/2500 rad at the rectum.

Up to April 1981, 17 cases were treated following protocol A and 7 following protocol B.

Table 2 reports the studied clinical cases divided according to the period of treatment and the percentage of cases controlled at least 12 months after the end of the therapy.

Table 1.

Treatment A
- 250 rad 3 times per week totalling 4000 rad over 5 weeks
- one week of interval
- endouterine-vaginal cesiotherapy in 48-72 hours (max 2500 rad at the rectum)

Treatment B
- split: 850 rad-48 hours of rest-850 rad
- interval of three weeks
- 250 rad three times per week totalling 2000 rad over 3 weeks
- endouterine-vaginal cesiotherapy in 48 hours (max 2000 rad at the rectovaginal sect).

Table 2.

Neoplasia location	Stage	II A	III A	III B
Period: 1978-1980				
Portio		34	15	7
Cervical canal		4	5	
48 out of 65 (73.8%) controlled				
Period: 1980-1981				
Neoplasia location				
Portio		12	1	9
Cervical canal		2		
20 out of 24 (83.3%) controlled				

Table 3.

	within 30 days	within 6 months
Cases treated between 1978 and 1980 (48 controls out of 65 cases)		
Rectocolitical troubles	7 (14.5%)	7 (14.5%)
Urinary troubles	4 (8.3%)	8 (8.3%)
Variation of haematic crasis	3 (6.2%)	
Cases treated between 1980 and 1981 (20 controls out of 24 cases)		
Rectocolitical troubles	7 (35%)	1 (5%)
Urinary troubles	6 (30%)	
Variations of haematic crasis	12 (60%)	

Table 4.

Patients treated between 1978 and 1980:	within	between 1980-1981
Cases of death: 6 months	3 (6.2%)	
Cases of death: 1 year	1 (2.0%)	1 (5%)
Cases of death: 2 years	1 (2.0%)	
Neoplastic persistence	19 (39 %)	7 (35%)
Clinical sterilization	24 (50.4%)	12 (60%)

Table 3 reports troubles relating to the actinic treatment, divided into early (within 30 days) and late (within 6 months) troubles.

48 out of the 65 cases treated during the first period with the traditional technique, and 20 out of the 24 patients who followed the new protocols were controlled.

Finally, table 4 reports cases of death, neoplastic persistency and tumour sterilization.

Though perfectly aware of the inadequacy of our study to evaluate the outcome of this therapy with regard to survival, we felt that a table comparing the results of the two treatments, after 12 months could provide useful indications and orientations.

RESULTS

The incidence of post-actinic early troubles is clearly higher in patients treated with protocols A and B than in those who followed the usual therapy (tab. 3).

Vesical and rectolitical troubles developed to the same extent in patients who underwent treatment A and treatment B. But the latter presented a more developed astenia, particularly after the first irradiation, and temporary inappetence.

The changed values of the haematic crasis (anemia, leukopenia) widely differed in the patients of the first group vis-à-vis those of the A and B protocols.

Probably, the erythrocytic value is closely related to other factors (besides the radiotreatment), like haematic losses, food deficit, age and the better longitudinal control of protocol-A patients.

A similar medullary damage was never observed in protocol-B patients, but this could be due to an insufficient control of the haematic crasis during the 3-week therapeutical interval, in non-hospitalized women.

They showed no remarkable cenesthesic trouble during that period.

The rectolitical and urinary damages were less severe than the stenosis of the descending colon developed in a patient subjected to protocol B (stenosis did not exist prior to the therapy, as proven by a previous barium enema).

This consequence caused the patient to be hospitalized again and again at our institute. At present, after a year since the end of the therapy, canalization troubles persist, though in a lighter form.

In this patient, the diagnostic evaluation showed a tumoural regress (uterus mobilization without noteworthy parametrial metastatic involvement, no genital haemorrhagia, negative pap-test).

But both the double-contrast barium enema and the optic-fybre rectosigmoidoscopy confirmed the presence of a stenosis, so tight as to prevent the endoscopy of the upper colon and with atrophic mucosa (as biopsy confirmed).

Table 4 reports data concerning death, neoplastic persistence and clinical sterilization, a year after the treatment conclusion.

On this basis, we can only note an improvement of the outcome in patients subjected to the new protocols vis-à-vis a similar sample of patients treated with the usual therapy.

CONCLUSION

Although the end of these treatments is not yet very far, a few conclusions can be drawn, which need support by other data, long-term and more complete experiences.

Treatments envisaging dose fractionation appear to be responsible for more severe early post-actinic damages, but not for late consequences, with the exception of the one and only case described.

The clinical and radiologic control of the urinary tract revealed no pathologic picture, when these were not present before the treatment.

In fact, the developing tumour causes lesions of the urinary tracts; moreover the cicatricial retraction of the irradiated tissues can subsequently prove a mere iatrogenic damage, like in the cases treated during the first two years, presenting late damages of the urinary apparatus too.

From the point of view of the clinical evaluation of neoplastic sterilization or persistence, one year (the period since the

conclusion of the various radiotreatments) is too short a time to enable us to express a reliable opinion on the survival aspect.

However, the data suggest greater and more optimistic chances for the future.

The frequent synechiae in the vaginal upper third can certainly distort the clinical response and the outcome of the cytologic examinations, as the persisting activity of tumoural masses could be mistaken for a cicatricial reaction.

Nevertheless, the often dramatic parametrial improvement is absolutely indisputable.

The adoption of new medical methods always entails a comparison of their advantages and disadvantages.

We think that the examined radiotherapeutical method, though increasing some immediate post-actinic troubles, can prove useful in cases for which the effectiveness of the usual treatment cannot exceed its present static limits.

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