Clinical Experiences With Intravenous Colchicine in Inoperable Bronchogenic Carcinoma

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Introduction

The markedly increasing incidence of cancer of the lung observed during the past two decades has emphasized the urgent need for its early diagnosis. It is probably a fair estimate that by and large approximately 60 per cent or more of patients with pulmonary malignancy are inoperable on admission. Of the remainder that are explored, about one-half have a non-resectable lesion; and of the group that is resected, the five year survival rate ranges approximately between 5 to 25 per cent. It is obvious, therefore, that at present palliative measures are the fate for most patients with bronchogenic carcinoma. Especially intriguing and potentially fruitful is the area of current research for new chemotherapeutic and anti-mitotic agents.

Purpose

Colchicine, used primarily in clinical medicine for the treatment of gout, has long been known to have cytotoxic, anti-mitotic and antitumor properties on the basis of in vitro and in vivo experimental studies. However, published experiences relative to its application in human cancer have been few. Recent access to a new intravenous preparation of Colchicine (1.0 mg. per 2 cc. ampoule) prompted our clinical investigation into the possible efficacy and toxicity of the drug in inoperable cases of bronchogenic carcinoma.

Method

Twenty patients with inoperable pulmonary cancer were divided into the following categories:

Group I: These patients were treated with colchicine intravenously without associated supplementation of x-ray therapy. The alkaloid was given in the following dosage according to body weight; (a) 2.0 mg. (per injection) for patients below 130 lbs.; (b) 4.0 mg. for patients 130-150 lbs.; (c) 8.0 mg. for patients above 150 lbs. This group was subdivided into two classes according to the frequency of administration of colchicine:

(A) Five patients received the above dosage weekly for three consecutive injections. This was followed by a three week rest period; colchicine therapy was then resumed as mentioned above for three more weekly injections. The total amount of colchicine given per patient ranged from a minimum of 12 mg. to a maximum of 30 mg. with an average of 18 mg.

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This investigation was supported by a grant from Eli Lilly and Company. The colchicine was also supplied by the same company.
TABLE 1—RESPONSE TO THERAPY
COMPOSITE OF GROUP IA and IB (COLCHICINE TREATED)
TOTAL — 10 CASES†

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number</th>
<th>E</th>
<th>M</th>
<th>S</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest Pain</td>
<td>8</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Productive Cough</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Weight Loss</td>
<td>7</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Wheezing</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Feeling of “Well Being”</td>
<td>4</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Superficial Nodes</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Osteoarthropathy</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Chest X-ray Film Findings</td>
<td>9*</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>8</td>
</tr>
</tbody>
</table>

*Chest X-ray Film of patient who had pneumonectomy prior to institution of this regimen but later had clinical evidence of mediastinal involvement — not included in this evaluation.

**E=excellent; M=moderate; S=slight; N=no response

Excellent: Significant improvement maintained for at least 3 months.
Moderate: Significant improvement maintained between 1–3 months.
Slight: Significant improvement maintained for less than 1 month or minimal improvement over a longer period of time.

†Evaluation made as of September 1, 1958.

(B) Five patients received colchicine intravenously in the same dosage as above, three times weekly for four weeks, then twice weekly for four weeks, followed by one injection weekly for four doses unless intolerance developed or death intervened. The total amount of colchicine administered per patient ranged from 18 to 48 mg. with an average of 32.8 mg.

The average amount per patient for the total group of 10 cases was 25.4 mg.

Group II: A total of ten patients received both colchicine and conventional x-ray therapy. The latter was administered in the dosage of 2000-3000 roentgens in air over each port; six had three ports and four had two. These cases were also divided into two classes:

(A) Eight patients received colchicine (as per body weight cited above) at two week intervals for three doses. After a rest period of three
TABLE 2—RESPONSE TO THERAPY

<table>
<thead>
<tr>
<th></th>
<th>Group 2 — 10 CASES†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
</tr>
<tr>
<td>Chest Pain</td>
<td>7</td>
</tr>
<tr>
<td>Productive Cough</td>
<td>10</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>5</td>
</tr>
<tr>
<td>Weight Loss</td>
<td>6</td>
</tr>
<tr>
<td>Wheezing</td>
<td>1</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>1</td>
</tr>
<tr>
<td>Feeling of “well being”</td>
<td>4</td>
</tr>
<tr>
<td>Superficial Nodes</td>
<td>3</td>
</tr>
<tr>
<td>Osteoarthropathy</td>
<td>2</td>
</tr>
<tr>
<td>Chest X-ray Film Findings</td>
<td>9*</td>
</tr>
</tbody>
</table>

* Chest X-ray Film of patient who had lobectomy prior to institution of this regimen not included in this evaluation (See text).
† Evaluation made as of September 1, 1958.

weeks, irradiation was instituted. After completion of x-ray therapy, another three week rest period ensued and then colchicine intravenously was resumed in the same manner. The average dose was 19.5 mg. per patient.

(B) Two patients received colchicine once weekly for three doses concurrently with the initiation of irradiation. The average amount of colchicine given was 12 mg.

TABLE 3—LENGTH OF SURVIVAL

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (Colchicine)</th>
<th>Composite Groups</th>
<th>Group 2 Colchicine and X-ray</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>1A 1B 1A and 1B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (average)</td>
<td>63.4 59.8 61.6 59.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time interval (mos.) from onset of symptoms/signs to onset of palliative Rx</td>
<td>7.8* 10 9 8.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dead</td>
<td>4 (80 per cent) 5 (100 per cent) 9 (90 per cent) 8 (80 per cent)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (average)</td>
<td>61.2 59.8 60.4 61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time interval (mos.) from onset of symptoms/signs to onset of palliative Rx</td>
<td>7.8 10 9 9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>From onset of Rx to death (mos.)</td>
<td>5.5 5.8 5.7 6.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>From onset of symptoms/signs to death (mos.)</td>
<td>13.3 15.8 14.7 15.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living</td>
<td>1 (20 per cent) 0 (per cent) 1 (10 per cent) 2 (20 per cent)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>72 48 and 56 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time interval (mos.) from onset of symptoms/signs to palliative Rx</td>
<td>?* 3 and 13 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>From onset of Rx to Sept. 1958 (mos.)</td>
<td>15 15 and 20 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>From onset of symptoms/signs to Sept. 1958 (mos.)</td>
<td>?* 18 and 33 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Patient was transferred from the Mental Disease Hospital and an accurate determination of duration of symptomatology could not be made.
COLCHICINE IN INOPERABLE BRONCHOGENIC CARCINOMA
The average dose for the entire group of ten patients was 18 mg. with a minimum and maximum range from 12 to 48 mg. Cortisone was administered empirically in these patients in an attempt to minimize radiation pneumonitis, pleuritis and fibrosis. The steroid was given in divided doses, totalling 100 mg. daily during the use of x-ray therapy and for one month after its completion. Concomitantly, the patient received a low salt diet, 3 grams of potassium chloride daily and 300,000 units of penicillin daily (or 2.0 grams daily of Gantrisin if followed in the out-patient department after discharge). When cortisone was terminated, two doses of ACTH-gel (40 units at 12 hour intervals) were given. To lessen the possibility of osteoporosis and for its protein anabolic effect, depo-testosterone (100 mg.) was administered intramuscularly every two weeks.

All of the patients received the colchicine before breakfast and 50 mg. of chlorpromazine was given intramuscularly prior to each injection. Penicillin or a broad spectrum antibiotic was administered during hospitalization to all patients soon after admission. Supportive therapy, including blood transfusions, was employed as indicated. Frequent chest x-ray films, blood counts (including platelet counts) as well as other pertinent procedures, supplemented the clinical notations in the follow-up observation of these patients.

Results

Before commenting on the results of treatment, a few general remarks about the two groups of patients are merited. All of the 20 patients were white men and the average age was similar (61.6 and 59.2, respectively). The two groups were also comparable in that the duration of illness from onset of symptoms to institution of palliative therapy was 6.7 months and 8.6 months, respectively. All 20 patients had a cigarette smoking history, with 16 classified as moderate to heavy smokers.* Cytological studies of the sputum and/or bronchial secretions were positive for cancer cells in 18 (90 per cent). Bronchoscopic

*A moderate smoker is arbitrarily defined as one who average one to two packages daily for at least 20 years. A heavy smoker is one who averages two packages or more daily for at least 10 years.
examinations were performed in 19 patients and gross positive findings were observed in two instances. There was histological confirmation (ante mortem or post mortem) of malignancy in 16 patients and all showed the squamous cell type. In the remaining four, the clinical and roentgenological findings were overwhelmingly consistent with the diagnosis of primary bronchogenic cancer.

The clinical response to therapy is summarized in Tables 1 and 2. Table 3 summarizes survival data in both treated groups and Table 4 relates to the incidence of toxicity and its manifestations.

(1) **Subjective Manifestations**: The improvement in the symptomatology of patients treated with colchicine alone was not significant and of short duration (an average of about two months). It is possible that supportive therapy alone may have contributed to or indeed accounted for these temporary results. (See Table 1).

Superior symptomatic improvement was seemingly obtained in the colchicine-irradiated group. (See Table 2). It is our opinion that the administration of x-ray therapy may have been the most important single factor to account for this difference between the two groups. The ancillary adreno-cortical and androgenic steroid supplements might also have contributed favorably to the results.

(2) **Objective Manifestations**: One must utilize caution in ascribing regressive changes in chest x-ray findings to a specific anti-tumor modality. Experience indicates that when secondary obstructive pneumonitis or suppuration distal to the bronchial carcinoma contributes to the observed roentgen shadow, regression may occur simply with antibiotic therapy (albeit temporary) and lead to an inaccurate evaluation. It is for this reason that such an evaluation is best made by focusing attention on the fate of isolated circumscribed lesions in which the inflammatory component is likely minimal or non-existent. In the group treated with colchicine alone, moderate regression in size of such metastatic lesions was noted in one patient for a period of about three months (case 2). Among the group II cases, considerably regression occurred in a similar type density shortly after the use of colchicine and further

### TABLE 4—TOXICITY

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (Colchicine)</th>
<th>Composite Groups 1A and 1B</th>
<th>Group 2 Colchicine and X-ray</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>1A</td>
<td>1B</td>
<td></td>
</tr>
<tr>
<td>Colchicine</td>
<td>5</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>(average dose mg.)</td>
<td>18</td>
<td>32.8</td>
<td>25.4</td>
</tr>
<tr>
<td>Peripheral Blood Ct.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>depression</td>
<td>none</td>
<td>2 (severe)</td>
<td>2 (severe)</td>
</tr>
<tr>
<td>G.I. Toxicity</td>
<td>1 (mild)</td>
<td>1 (severe)</td>
<td>1 (severe)</td>
</tr>
<tr>
<td>Hematuria</td>
<td>none</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>Total Toxicity</td>
<td>1 (mild)</td>
<td>3 (severe)</td>
<td>3 (severe)</td>
</tr>
</tbody>
</table>

**DEFINITION**: Severe reaction — Platelet count below 100,000 and/or leucocyte count below 1500; diarrhea, vomiting or other gastro-intestinal symptoms difficult to control with conventional medication.
significant improvement was maintained for at least six months after x-ray therapy was instituted (case 3). One patient (case 4) showed marked regression of a massive density in the right lung in association with x-ray, colchicine and antibiotic therapy from distant metastases. Another patient in group II revealed definite regression of a large left sided para-mediastinal and hilar density over a period of about two months, but with progression of right sided metastatic lesions. Finally, one patient exhibited moderate roentgen regression of a large right upper lungfield density with similar therapy but progression of a contralateral hilar shadow. The remainder of the six cases in group II revealed no evidence of improvement on the chest x-ray film. In summary, a total of five cases (one in group I and four in group II) showed at one time or another, regressive radiological changes.

(3) Length of Survival: The effect of the palliative therapy on length of survival is visualized in Table 3. In the evaluation made September, 1958, nine patients in group I and eight in group II were dead. The single living patient in group I is alive 15 months from the onset of treatment and the similar data for the two living cases in group II is 15 and 20 months. It should be mentioned that one of the two living patients in group II had a lobectomy for his carcinoma, but was relegated to the palliative regimen when post-operative histologic examination of removed tissue indicated extension of the malignancy. Now, 15 months later, he has symptoms and signs of cerebral metastasis.

(4) Toxicity: Observed toxicity was confined to gastro-intestinal symptomatology and peripheral blood count depression. The platelet and leucocyte counts were affected more adversely than the red blood cells. It is seen that most of the untoward reactions occurred among the patients who received the heaviest assault with colchicine (group 1B).

Case Reports

Case 1 (Group 1B): G.D.E., white man, age 70, was admitted September 11, 1957 with duration of symptoms from the onset to the beginning of colchicine treatment of about 12 months. Gross bronchoscopic findings were negative. Cytological studies of sputum and bronchial secretions were positive for malignant cells. The chest x-ray film of September 12, 1957 (Fig. 1) showed a density in the right hilar region which was localized in the lateral view in the upper lobe; several calcific foci were also noted in the hilum. He was considered inoperable and colchicine was begun on September 16, 1957—2 mg. intravenously three times weekly for four weeks, then 2 mg. twice weekly for four weeks and finally once weekly for four weeks. He received a total of 48 mg. within a period of 12 weeks without clinical or hematological evidence of toxicity. During the course of treatment, he stated he "felt better" and showed a weight gain of six pounds. However, during colchicine therapy and thereafter, progressive enlargement of the roentgen density was noted (Fig. 2). He died February 21, 1958, about 2 months after colchicine was stopped. An autopsy revealed squamous cell carcinoma, infiltration of the right lung with widespread metastases. Although no major clinical improvement occurred, it is noteworthy that he was able to tolerate 48 mg. of colchicine within a 12 week period.

Case 2 (Group 1B): P.M., a white man, age 51, was admitted on April 16, 1957 with symptoms of two months duration. He appeared chronically ill, dyspneic, with enlarged liver and bilateral dependent edema. A chest roentgenogram, just prior to this admission and dated April 5, 1957 (Fig. 3) revealed densities in the left lung field (parenchymal plus pleural components of the primary malignancy), and two discrete rounded shadows (metastases) measuring 1.5 to 2.0 cm. in diameter in the right lung. The first thoracentesis (left) yielded serous fluid from which tubercle bacilli were reported on smear. He was started on appropriate antituberculosis chemotherapy, although bacteriological confirmation was not obtained either from the aspirations subsequently performed or from the sputum. Bronchoscopic examination was grossly negative, but roentgen examination of the sputum and bronchial secretions were positive for malignant cells. During hospitalization, cervical nodes became apparent and biopsy revealed squamous cell carcinoma.
He received 16 intravenous injections of colchicine (total 46 mg.) between April 25, 1957 and October 7, 1957. The administration of colchicine was at times postponed because of severe depression of the total leukocyte count and the platelets. The lowest recorded white blood cell count was 1700 and the platelets 60,000. No bleeding episode occurred. Antibiotics and five blood transfusions were given with improvement in the blood picture. On April 15, 1957, 0.5 mg. of colchicine was instilled into the left pleural cavity following a thoracentesis. There was noted an increase in pleuritic pain and pleural fluid immediately thereafter and another aspiration was performed on April 16, 1957. Subsequently, for about a two month period there appeared to be a retardation in the re-accumulation of fluid.

For a better appraisal of roentgenological changes which might be influenced by colchicine therapy, attention was concentrated particularly on the right sided lesions in the frequent serial films. An x-ray film of May 3, 1957 (Fig. 4) revealed moderate regression of these foci compared to the film of April 5, 1957 and this status was maintained for about two months. The last film of October 25, 1957 (Fig. 5) revealed an increase in size in the right mid-lung lesion and new lesions in the upper lobe were observed. He resumed a progressive downhill course: paralysis of the left recurrent laryngeal and phrenic nerves with increased left sided effusion were noted and he died on November 28, 1957.

Case 3: J. K. (Group 2A), a 56 year-old white man was admitted on December 27, 1956 with symptoms of one year's duration. The first x-ray film on December 27, 1956 (Fig. 6) showed calcified foci and some linear pleural (?) folds on the right with an increased density in the left hilum and a more or less circumscribed dense area overlying in part the fourth left anterior rib. Bronchoscopy was negative, but cytological examination of the sputum and bronchial secretions revealed cancer cells. Gantrisin was started on admission and penicillin on January 29, 1957. Colchicine therapy was begun on January 7, 1957 in the dosage of 2 mg. once weekly for three consecutive weeks. X-ray therapy was initiated February 8, 1957 and completed March 11, 1957 with 2800 r delivered over three ports. A second similar course of colchicine was begun on April 1, 1957. No clinical or hematological evidence of toxicity were observed during this regimen. He stated he felt much better, cough decreased, dyspnoea improved with a weight gain of 12 pounds from the onset of therapy to the time of his discharge three months later. Significant radiological regression is seen on the film of January 22, 1957 (Fig. 7) during colchicine administration and before irradiation was started. Further slight regression was observed on the plate of March 14, 1957 (Fig. 8). He was followed in the out-patient clinic. The film of July 19, 1957 (Fig. 9) (six months later) revealed a marked increase in the original hilar density, although the smaller satellite density (probably metastatic) was only faintly visible. For the past nine months, he has resided in another state. Recent communication with his private physician disclosed that he has shown slow, but progressive clinical deterioration.

Case 4: W. H. (Group 2B), a 51 year-old white man was admitted March 4, 1957 with symptoms dating back for a 10 month period. Fatigability, weight loss, dyspnoea and wheezing were the dominant symptoms. On admission, he was poorly nourished. There was marked dullness with diminished breath sounds over the greater portion of the right lung. The first chest film taken March 6, 1957 (Fig. 10) showed an extensive density involving approximately the upper two-thirds of the right lung. Bronchoscopy revealed the carina to be irregular, thickened and distorted. However, bronchial and scalene node biopsies were negative for malignancy. Cancer cells were found in study of the sputum. X-ray therapy was started April 1, 1957 and completed May
3, 1957 with 2600 r given over each of three ports. Colchicine therapy was started April 15, 1957 in the dosage of 4 mg. intravenously given once weekly for three consecutive weeks. He received a total of 12 mg. with no clinical or laboratory sign of toxicity. He noticed decreased exertional dyspnea, cough and wheezing. This improvement, which lasted for about two months, became apparent soon after irradiation was begun. His clinical status thereafter declined; the liver became considerably enlarged with the development of ascites and jaundice. He died on August 30, 1957. Of interest is the fact that there was marked roentgen regression (Fig. 11) of the original density (which may have been due largely to stelectasis) as late as on the last film taken July 15, 1957. This improvement might be attributed mostly to x-ray therapy, although he also received colchicine, antibiotics and steroids.

![Image](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21342/)

**FIGURE 10**

**FIGURE 11**

**Comment**

It has been amply demonstrated that colchicine arrests cellular division in the stage of metaphase.5,29 Colchicine is one of a number of agents (physical and chemical) which may interfere with mitosis. Both normal and malignant cells are similarly affected, but cells with the greatest rate of division and metabolism are hit earliest by colchicine.11 The optimum duration of a given dose of colchicine varies with the species of animal studied. Levine and Silver2 concluded from their observations that the greatest arrest of nuclear division in the metaphase occurred between 16 to 24 hours, in human cancer cells.

The effect of colchicine on the normal polarized "spindle" is to convert it into an amorphous mass with distortion of its fibrillar structure and disruption of the movements of the chromosomes. Recently, Laster and Blair have indicated that colchicine inhibits the enzyme uric acid riboside phosphorylase.30 However, further investigation is necessary to identify the chemical locus of action of colchicine.

It has been demonstrated in experimental animals that colchicine also induces temporary regression of tumor growth by damage to its vascular supply, thereby inducing hemorrhage and necrosis. The endothelial cells of newly formed capillaries are particularly sensitive to mitotic poisons.13,28

X-ray irradiation, like colchicine, disrupts nuclear division and damages newly forming capillaries; however, a true synergistic action between irradiation and colchicine, although postulated, has not been conclusively demonstrated.13 Lette,14 in conducting experiments in fibroblast cultures, discovered many agents which increased the mitotic inhibitory activity of colchicine, although themselves having no such mitotic action. Among these synergists are the steroid hormones. For a comprehensive review and evaluation of the many experimental studies with colchicine on cellular physiology, the interested reader should refer to the excellent monograph by Elgä and Dustin.35

Recent interest in the clinical efficacy of colchicine as a chemotherapeutic agent in human malignancy has been stimulated by Isach-Wall,8 and Grollman, et al.7 The latter administered the drug in the dosage of 3 mg. intravenously every third day for variable periods to 10 patients with Hodgkin's disease, some of whom were resistant to X-ray therapy and nitrogen mustard. Potent antipyretic and analgesic effects, with marked subjective improvement were obtained. Temporary reduction of enlarged nodes was evident in some cases. The drug was well tolerated.

Despite its equivocal efficacy from our present study, we are continuing to employ colchicine as another tool in the chemotherapeutic attack on inoperable bronchogenic
cancer. The dosage currently used is 2 mg. for patients 130 pounds or under, and 4 mg. for patients above that weight. This is an empirical decision based on our clinical experience to date. The drug appears well tolerated in this dosage and can be given one to three times weekly, depending on whether it is used singly or in combination with other modalities. Weekly blood counts, including platelet counts, are essential for proper guidance as to possible bone marrow inhibition, which may require reducing the dose, postponing, or terminating therapy. The availability now of a safe and acceptable intravenous preparation of colchicine warrants, in our opinion, further trial of its use, preferably in conjunction with other modalities, in palliative therapy.

SUMMARY

The marked rise in the incidence of cancer of the lung accentuates the importance for its early detection. Unfortunately, since most instances of this type of malignancy seen today are inoperable, the burden of management rests on a medical palliative regimen. A vigorous search for chemotherapeutic agents is being maintained.

There have been extensive experimental studies with colchicine. It exerts: (1) a cytotoxic effect by inhibiting spindle formation and arresting cell division in the metaphase stage and (2) an anti-tumor effect by destroying the endothelial cells of newly formed capillaries thereby inducing hemorrhage and necrosis.

Colchicine has received comparatively little attention in its application to human cancer chemotherapy. The availability of an intravenous preparation prompted the present clinical study. Ten patients with advanced bronchogenic carcinoma were treated with colchicine and an equal number with colchicine combined with the conventional type of irradiation and associated medication. It is noteworthy that large amounts of colchicine administered intravenously were well tolerated by most of the patients. The subjective and objective manifestations of improvement in both groups are recorded. The colchicine - x-ray treated group seemingly fared better but this could possibly be due to the effects of radiotherapy per se.

It is necessary to continue to explore many modalities. Colchicine may merit further application as another tool in conjunction with other currently used measures in the palliative regimen.

RESUMEN

Se han hecho amplios estudios experimentales de la colchicina en el cáncer del pulmón. Ella ejerce: (1) un efecto citotóxico al inhibir la formación fusiforme de acromatina y detención de la división celular en el estado de metafase, y (2) un efecto antitumoral destruyendo las células endoteliales de los capilares neoformados, lo que conduce a hemorragia y necrosis.

La colchicina ha recibido comparativamente poca atención en su aplicación al hombre en quimioterapia del cáncer.

La posibilidad de contar con un preparado para uso intravenoso, condujo a hacer este estudio. Diez enfermos con cáncer avanzado bronquigénico, se trataron con colchicina en combinación con los métodos habituales de irradiación y tratamiento médico. Es de notarse que grandes cantidades de colchicina administradas intravenosamente, se toleraron mejor por la mayoría de las enfermos. Se relatan las manifestaciones subjetivas y objetivas de mejoría en ambos grupos.

Al parecer los tratados con colchicina y rayos X, evolucionaron mejor, pero esto puede deberse a la radiación por sí sola.

Es necesario continuar explorando muchas modalidades. La colchicina puede merecer aplicaciones más adelante como un instrumento más, agregado a las medidas paliativas actuales.

RESUME

Des études expérimentales de la colchicine dans le cancer du poumon ont été faites sur une large échelle. Il en ressort: 1° qu'il existe un effet cytotoxique par inhibition de la formation des fuseaux et arrêt de la division cellulaire dans le stade métaphasique; 2° un effet antitumoral par destruction des cellules endothéliales des capillaires nouvellement formés ainsi l'hémorragie et la nécrose.

La colchicine a peu attiré l'attention dans l'ensemble de la chimiothérapie anticancéreuse chez l'homme. La mise à la disposition des auteurs d'une préparation intraveineuse accélère la possibilité de cette étude clinique. Dix malades atteints de cancer bronchique ont été traités par la colchicine et un nombre égal de malades avec la colchicine associée au type habituel d'irradiation et à la médication associée. Il faut noter que des doses importantes de colchicine furent administrées par voie intraveineuse et bien tolérées par la plupart des malades. Des manifestations subjectives et objectives d'amélioration dans les deux groupes ont été constatées. Le groupe de malades traités par la colchicine et les rayons X sembla se porter mieux mais ceci pourrait peut-être être dû aux effets de la radiothérapie seule.

Il est nécessaire de continuer à explorer toutes les modalités. La colchicine peut justifier des applications ultérieures comme un moyen supplémentaire susceptible d'être associé à ceux qui sont couramment utilisés dans le traitement palliatif du cancer.
ZUSAMMENFASSUNG


Colchicin hat vergleichsweise geringe Aufmerksamkeit erfahren hinsichtlich seiner Anwendung in der menschlichen Krebstherapie. Die zur Verfü hungstellungen eines intravenösen Präparates veranlaßte die vorliegende klinische Untersuchungsreihe.


REFERENCES

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