Clinical Experience with Elixophyllin in Dyspnea

H. I. SAPOZNIK, M.D., F.C.C.P.
Chicago, Illinois

Dyspnea may be a symptom of pulmonary or cardiac disease or both. In the dyspnea of cardiac origin, digitalis is generally considered specifically indicated. However, in some circumstances digitalis may provide little or no relief of cardiac dyspnea. In early failure when there are no physical signs of congestion, relief of dyspnea is unimpressive and equivocal. In frank failure, digitalis helps in remission of major signs and symptoms, but some exctional dyspnea usually remains.¹

Diuretics sometimes offer additional help in these cases. However, there is need for more effective drug therapy for relief of dyspnea, orthopnea, fatigue, wheezing and coughing which persists in many of these patients. These symptoms tend to make the patient morbid, fearful and so restricted in activity that he may be virtually a "cardiac invalid." In older patients with congestive failure complicating chronic asthma, bronchitis or bronchospastic pulmonary emphysema, the dyspnea may be of combined cardiac and pulmonary origin.

From pharmacologic considerations, theophylline would appear to be an ideal drug for these patients. It increases the pulmonary circulation, especially when the lungs are congested from left ventricular failure. In patients in congestive failure, theophylline shortens abnormally prolonged circulation time and decreases venous pressure.²

Clinically, aminophylline (theophylline ethylenediamine) administered intravenously is usually effective for relieving the paroxysmal dyspnea of congestive failure, acute bronchial asthma, Cheyne-Stokes respiration and pulmonary edema.³

The prophylactic use of aminophylline orally or rectally to prevent dyspnea, especially that of cardiac origin, has been rather unsatisfactory. Occasionally the drug is of benefit, but it is often disappointing.

Theophylline blood-level data indicate that the source of this disappointment lies in the uncertain absorption of aminophylline administered orally or rectally. By mouth, gastric intolerance generally limits oral doses to inadequate amounts. By rectum absorption may be comparatively rapid, it may be delayed for many hours or there may be no detectable theophylline in the blood-stream at any time after administration.⁴

More recently, a hydroalcoholic solution of theophylline (Elixophyllin®) has been reported to be well tolerated, and rapidly and completely absorbed after oral administration. In 15 minutes following oral administration in doses equivalent to 500 mg. of aminophylline, the mean blood level was 8.0 mcg/ml. (higher than the 7.0 mcg/ml following intravenous aminophylline, 300 mg.). Moreover, absorption appeared to be essentially complete and showed less patient variation. The mean peak blood level was reached in one hour. All patients had blood levels over 5.0 mcg/ml. at that time.⁴

⁴Sherman Laboratories, Detroit, Michigan.
During the past two years Elixophyllin has been studied rather extensively in bronchial asthma. Following its administration, 85 of 107 acute asthmatic attacks were terminated in 10 to 30 minutes. Greater relief of chronic bronchial asthma has been reported. More predictable absorption and better maintenance of therapeutic blood levels is responsible for better clinical results.

It appeared that this preparation might be helpful in the dysnea of cardiac origin unrelieved by digitalis; bronchospastic pulmonary emphysema and chronic asthma with or without cardiac involvement. This is a report of the clinical experience gained in such cases.

Method and Material

The study included 10 cases of cardiac asthma, four of bronchial asthma and five of chronic obstructive emphysema. The ages of these patients ranged between 35 and 70 years.

Most of the patients have had other drugs including aminophylline by mouth. Some have had aminophylline per rectum. In these patients dyspnea, orthopnea, fatigue, wheezing and coughing were prominent clinical symptoms.

Patients were started on Elixophyllin, four tablespoonfuls four times a day. This dose was gradually reduced to a maintenance dose of one tablespoonful four times a day. The follow-up on individual patients varied from five to eight months.

Results of the study are summarized in the following table.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of Patients</th>
<th>Duration of Treatment (months)</th>
<th>Results Satisfactory</th>
<th>Unsatisfactory</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Asthma</td>
<td>10</td>
<td>4-6</td>
<td>80%</td>
<td>20%</td>
<td>1 case nausea</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 case nausea and heartburn</td>
</tr>
<tr>
<td>Bronchial Asthma</td>
<td>4</td>
<td>2-3</td>
<td>75%</td>
<td>25%</td>
<td>none</td>
</tr>
<tr>
<td>Emphysema</td>
<td>5</td>
<td>4-6</td>
<td>80%</td>
<td>20%</td>
<td>1 case of nausea</td>
</tr>
</tbody>
</table>

Discussion

Eight of 10 patients with cardiac asthma received good to excellent results from Elixophyllin therapy. One complained of nausea and discontinued its use. Another received limited benefit. One complained of nausea and heartburn in the beginning which was prevented on administration of an antacid. Satisfactory results essentially without side effects were seen in eight cases. The duration of treatment in cases of cardiac asthma was four to six months.

Three of four bronchial asthmatic patients showed excellent response. The clinical response in one case was equivocal. No side effect was present in these patients. The duration of treatment was two to three months.

Five emphysema patients were treated for four to six months. One complained of slight nausea but he continued the medication with good clinical results. Another did not receive satisfactory results. Good to excellent results were seen in four of five patients.

In the three groups of patients, satisfactory results were obtained in 15 of 19 cases. Results in two were equivocal. One complained of nausea and heartburn and two of nausea. No other side effect was present.

The one who had previously received aminophylline by mouth or by rectum provided a basis for comparison with Elixophyllin. Faster, greater and more consistent relief was obtained with Elixophyllin. The patient-acceptability of Elixophyllin was excellent except for a few complaints of nausea and heartburn after initial administration of Elixophyllin. This was prevented by use of antacids.
Discussion of two representative case histories will be of interest.

A woman, 45 years of age, had hypertensive heart disease and mitral regurgitation for nine years. Her major symptoms were dyspnea, orthopnea and fatigue on the slightest exertion and marked wheezing and coughing. The x-ray examination showed an enlargement of her heart both to the left and to the right. There was some pulmonary congestion involving both lung fields. Other general findings were essentially negative. Complete blood count was normal. Urinalysis was normal. ECG showed left ventricular preponderance. She was on digitalis and diuretics for a number of years. In addition, she had been on various xanthine combinations, namely aminophylline, theominal, theocalcin and tedral. All these drugs had helped her to be more comfortable, but until she was put on Elixophyllin she did not walk as far or walk as much and feel as well. She has been on this drug now for six months. The dose of Elixophyllin required to achieve this effect is one tablespoonful four times a day. In the beginning, she started on four tablespoonfuls four times a day and gradually reduced where she is now maintained on one tablespoonful four times a day.

A man, 55 years old, had been known to have mitral regurgitation with stenosis for the last six years. He entered the hospital with cyanosis, orthopnea, dyspnea and pulmonary edema. His general condition was poor and he was critically ill. His condition continually worsened in spite of oxygen, aminophylline intravenously, digitoxin and diuretics, namely 2 cc. of Thimerin, three times a week. His ECG showed coronary changes. His chest x-ray films revealed left ventricular preponderance with pulmonary edema. After 10 days on chlorothiazine 1 gram daily, he started to improve. Pulmonary congestion was relieved by the diuretics, but symptoms of coughing and wheezing continued unabated. He was unable to retain aminophylline suppositories. Meticorten 5 mg. q.i.d. for two weeks was administered. Steroid therapy provided some relief, but eventually in spite of the diuretics given, it produced salt retention and was discontinued. After two days, he was put on Elixophyllin, four tablespoonfuls four times daily. There was immediate marked improvement of dyspnea, orthopnea and wheezing. This man was kept on a regimen of one tablespoonful four times a day for two months. He responded favorably. Wheezing stopped and coughing subsided. He continued to take Elixophyllin p.r.m. for dyspnea and orthopnea.

**SUMMARY**

A new oral preparation of theophylline (containing 80 mg. of free theophylline and 3 cc. of ethyl alcohol per 15 cc.) provides faster, more complete and more dependable absorption than other oral theophylline preparations hitherto available. In some cardiac patients, dyspnea, orthopnea, fatigue, wheezing and coughing often persist despite full digitalization. Good to excellent relief of these symptoms was secured with Elixophyllin in eight of 10 such cardiac patients; in three of four patients with chronic bronchial asthma and in four of five with pulmonary emphysema.

**RESUMEN**

Una preparación nueva de teofilina oral (conteniendo 80 mg. de teofilina libre y tres cc. de alcohol etílico por 15 cc.) proporciona una absorción más rápida y segura que otras preparaciones hasta ahora obtenibles. En algunos enfermos cardíacos, la disnea, ortopnea, fatiga, síntomas y tos, persisten a menudo a pesar de la digitalización. Se obtiene buen alivio o excelente en estos síntomas con la Elixofilina en 8 de 10 de tales casos de cardíacos; en tres de cuatro enfermos con asma bronquial crónica y en cuatro de cinco con enfisema pulmonar.

**RESUMÉ**

Une nouvelle préparation buccale de théophylline (contenant 80 mg. de théophylline libre et 3 cc. d'alcool éthylique pour 15 cc.) permet une absorption plus rapide, plus complète et plus efficace que les autres préparations buccales de théophylline dont on a disposé jusqu'à présent. Chez quelques malades cardiaques, la dyspnée, l'orthopnée, la fatigue, le "wheezing" et la toux persistent souvent malgré une digitalisation complète. Chez de tels cardiaques, un bon soulagement allant jusqu'à un soulagement parfait de ces symptômes fut obtenu avec l'"Elixophylline"; le même résultat fut obtenu pour trois sur quatre malades atteints d'asthme bronchique chronique, et pour quatre sur cinq malades atteints d'emphysème pulmonaire.

**ZUSAMMENFASSUNG**

REFERENCES


