The Role of Chlorpromazine in the Treatment of Bronchial Asthma and Chronic Pulmonary Emphysema*

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It is often difficult to achieve adequate sedation without concomitant respiratory depression in patients with bronchial asthma and chronic pulmonary emphysema. The deleterious and occasionally fatal effects of morphine in these disease states are well known.1-4 This agent is a primary and continuous depressant of respiration even with doses too small to produce sleep or disturb consciousness.5 These doses diminish the normal respiratory response to the inhalation of low concentrations of carbon dioxide. The harmful effect of morphine has been attributed in part to an increase in bronchomotor tone.2,3 Herschfus et al4 considered meperidine to be a useful and safe drug in the treatment of acute asthma or of status asthmaticus. Pulmonary function improved in most of their cases. However, these authors warned against the use of repeated and increasing doses which might result in respiratory depression. Rasor and Crecraft6 stressed the frequency of meperidine addiction acquired in the treatment of bronchial asthma. Barbiturates in small doses as well as morphine have been demonstrated to depress the effective alveolar ventilation and produce respiratory acidosis in patients with chronic pulmonary emphysema.7

Recent reports relevant to the use of chlorpromazine (Thorazine) in bronchial asthma have been favorable.5,11 It was therefore decided to investigate the role of this agent in the treatment of bronchial asthma and pulmonary emphysema.

Methods

Ten patients with uncomplicated bronchial asthma, six with bronchial asthma and chronic pulmonary emphysema, and 19 with primary chronic diffuse obstructive pulmonary emphysema, were studied clinically. Chlorpromazine was given as a single intramuscular dose of 25 to 50 mg. in some instances. In others it was administered orally or intramuscularly in similar quantities in combination with therapy designed to improve pulmonary ventilation and arterial blood gas content. These measures included IPPB (intermittent positive pressure breathing with a nebulized bronchodilator and detergent**) with oxygen, antibiotics, expectorants, aminophyllin, mechanical elimination of bronchial secretions and, in some instances, adrenocotical steroids and Diamox.

*From the Medical Service, Veterans Administration Hospital.
**Aerolone compound and zephran hydrochloride (1:1000 aqueous).
The clinical status of each subject was evaluated by at least two observers. Patients whose respiratory distress was felt to be wholly or in part related to other entities than bronchial asthma or chronic pulmonary emphysema were excluded from this study.

Twenty-one patients with chronic diffuse obstructive pulmonary emphysema were also studied in the laboratory under basal conditions. Minute volume of respiration was collected in a Douglas Bag and measured in a dry gas meter.* Arterial blood was collected anaerobically with an indwelling needle. pH was determined with a Cambridge Model R pH meter. Arterial blood carbon dioxide and oxygen content and oxygen capacity were measured on the van Slyke apparatus. Arterial blood carbon dioxide tension was estimated with a nomogram based on the Henderson-Hasselbach equation. These measurements were performed immediately prior to and one hour after the intramuscular administration of 25 to 50 mg. chlorpromazine. Blood pressures were checked repeatedly with a sphygmomanometer.

Results

The effects of the drug in the 10 patients with uncomplicated bronchial asthma were as follows: Single 25 mg. intramuscular doses were followed by marked diminution of wheezing and restlessness within 15 to 30 minutes in five instances. One of these patients maintained a satisfactory course when the oral preparation was combined with a bronchodilator and expectorant for the following six days. No change occurred in two subjects within one hour after injection. Chlorpromazine was combined with other therapy in three cases. Drug-induced vomiting (aminophyllin) was alleviated in one and subsidence of wheezing with relaxation occurred in the other two patients.

Of the six patients with bronchial asthma and chronic pulmonary emphysema distinct lessening of dyspnea and wheezing was noted after a single intramuscular dose in one subject. Similar benefits occurred in two patients when the drug was combined with conventional bronchodilator therapy. Drug-induced emesis (aminophyllin) was alleviated in one instance. Drowsiness without amelioration of dyspnea ensued in one subject. No effect was achieved in one patient. These two severely ill patients did not respond to conventional measures. Adrenocorticotropic hormone was followed by remission in each.

Of the 19 patients with primary chronic diffuse obstructive pulmonary emphysema relief of marked respiratory embarrassment with wheezing and cyanosis was achieved in one instance when the agent was given as a single intramuscular dose. Aminophyllin-induced vomiting was controlled when it was administered orally to the same subject over a period of eight days. Eight patients exhibited a favorable hospital course, with relaxation and control of restlessness and irritability on "combined" therapy. An additional subject received four different courses of Thorazine, in combination with intensive therapy, for a total of 164 days. Adequate relaxation

*American Meter Company, Albany, N. Y.
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SD: ±1.18

md—mean difference

*Technical difficulty

**Too drowsy to cooperate

***Patient uncooperative
and control of the mental symptoms of carbon dioxide intoxication were achieved during three of these courses. Temporary clinical improvement with sedation occurred during the fourth course, before the eventual fatal outcome.

Despite adequate relaxation, clinical improvement was not attained by intensive therapy in nine subjects. Five of these died after receiving chlorpromazine from three to 33 days. In view of the severity of the disease in this group, it is difficult to ascribe any untoward effect of the drug.

Wherever practicable, the head-low position was employed with the intramuscular administration of Thorazine. An additional patient sat up after 15 mg. were injected and was noted to be pulseless and cyanotic 30 minutes later. This subject was desperately ill, with pyloric obstruction and electrolyte disturbance, complicating his disease, and eventually succumbed.

There was no instance of jaundice or leukopenia in this series of 35 patients.

Table I is the summation of the physiologic measurements obtained before and one hour after administration of 25-50 mg. chlorpromazine intramuscularly. Drowsiness or sleep occurred in 19 of the 21 emphysematous subjects. There was no significant change in the mean values for minute volume of respiration, and the arterial oxygen saturation carbon dioxide tension (PaCO₂), and pH. The clinical status of one patient became alarming within one hour after drug administration. There was increased respiratory embarrassment and a state of semi-stupor. This patient responded to IPPB with oxygen therapy. It is emphasized that the clinical status of this individual was precarious prior to study, with marked hypoxia and hypercapnia. Only two subjects exhibited falls in diastolic pressure over 20 mm. Hg. The head-low position was maintained whenever possible.

Discussion

The pharmacologic properties of chlorpromazine have been reported by others. This agent depresses central and autonomic nervous systems. There is an anti-emetic effect. It is also anticholinergic, adrenolytic, antihistaminic, and antispasmodic. It has been claimed that the drug produces little or no respiratory depression, although Dobkin et al reported decreased tidal volume with some increase in the oxygen consumption in 14 patients.

Some authors have reported relief of bronchospasm in severe asthmatic crises with Thorazine. The experiences reported in this paper indicate that the drug is safe and effective when used singly or combined with conventional bronchodilator therapy in uncomplicated bronchial asthma and in some cases complicated by pulmonary emphysema.

When the irreversible changes of chronic diffuse obstructive pulmonary emphysema are present, this effect is less apt to occur. In this group, chlorpromazine was employed primarily for its relaxant qualities. As stated in the introduction, the problem of adequate and safe sedation in this disease is often vexing.
Any agent which induces relaxation quickly with little respiratory depression should facilitate the administration of intensive therapy, including the various mechanical measures employed in the treatment of severe pulmonary emphysema.

From the evaluation of the emphysematous subjects on chlorpromazine combined with intensive therapy described previously, it may be concluded that chlorpromazine appears to satisfy this requirement. The physiologic data obtained incident to single intramuscular dose administration offer no evidence for respiratory depression in the 21 patients studied.

SUMMARY

Clinical experiences with the use of Thorazine in 35 patients with bronchial asthma and/or chronic pulmonary emphysema are reported. The effect on minute volume of respiration and arterial blood gases and pH, was determined in 21 patients with chronic diffuse obstructive pulmonary emphysema.

It is concluded that the drug may be safely and effectively administered, either singly or in combination with known bronchodilator agents, in the therapy of paroxysms of bronchial asthma. In chronic pulmonary emphysema, chlorpromazine appears to be a useful adjunct, in combination with intensive therapy designed to correct pulmonary ventilation.

RESUMEN

La experiencia clínica en el uso de la Toracina en 35 enfermos de asma y/o enfisema pulmonar crónico se relatan.

Los efectos sobre el volumen minuto de la respiración y los gases arteriales y pH, fue determinado en 21 enfermos con enfisema crónico obstructivo.

Se concluye que la droga puede ser administrada con seguridad y eficacia ya sea sola o en combinación con los agentes broncodilatadores en el tratamiento del paroxismo de asma. En el enfisema crónico pulmonar la chlorpromazina parece ser un adyuvante útil en combinación con la terapia adecuada para corregir la ventilación pulmonar.

RESUME

Les auteurs rapportent leur expérience clinique de la “Thorazine” chez 35 malades, atteints d'asthme bronchique associé ou non à l'emplysème pulmonaire chronique. L'effet sur le volume respiratoire minute, sur les gaz du sang artériel et le pH, fut déterminé chez 21 malades atteints d'emphysème pulmonaire obstructif chronique et étendu.

Les auteurs arrivent à la conclusion que la médication peut être administrée efficacement et sans danger, soit seule, soit en association avec des agents bronchodilatateurs connus, dans le traitement des atteintes aiguës d'asthme bronchique. Dans l'emphysème pulmonaire chronique, la chlorpromazine semble être un appoint utile, en association avec un traitement énergique destiné à améliorer la ventilation pulmonaire.
ROLE OF CHLORPROMAZINE

ZUSAMMENFASSUNG

Bericht über klinische Erfahrungen beim Gebrauch von Thorazin bei 35 Patienten mit Bronchial-Asthma und/oder chronischem Lungenemphysem. Es wurde die Wirkung auf das Atem-Minuten-Volumen und die arteriellen Blutgase sowie pH bestimmt bei 21 Kranken mit chronischem diffusen obstruktivem Lungenemphysem.

Es wird der Schluss gezogen, dass das Mittel mit Sicherheit und guter Wirksamkeit angewandt werden kann, sei es allein, oder in Verbindung mit bekannten bronchodilatatorischen Stoffen zur Therapie von Anfällen von Bronchial-Asthma. Beim chronischen Lungenemphysem dürfte das Chlorpromazin ein nützliches Hilfsmittel sein in Kombination mit einer intensiven auf Besserung der pulmonalen Ventilation gerichteten Therapie.

REFERENCES

15 Communication from Manufacturer.