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Promethazine-Chlorpromazine Combination in the Treatment of Unmanageable Psychotic Patients

Armando R. Favazza, M.D.*

Administering a combination of promethazine and chlorpromazine to patients with a “galloping psychosis” has an antipsychotic and tranquilizing effect which calms them down to a more manageable and less aggressive state. The drugs are chemically similar; promethazine's actions are strongly potentiated in the combination, so large doses must be given under careful supervision. Case histories demonstrate successful short term management of acutely psychotic, aggressive patients who were a danger to themselves and others.

Acute, intense psychotic episodes can pose difficult problems for both the patient and those who care for him. Use of trifluoperazine may aggravate such patients, while thioridazine and haloperidol cannot be given parenterally. Most commonly used drug in treating such patients is chlorpromazine; because of its great ability to calm patients, its relative safety in large doses, its availability in both oral and parenteral forms, and also because most physicians are familiar with it.

While most patients can be brought under rapid control with chlorpromazine alone, there are some who seem to resist this treatment. It is not un-common in the author's experience for some patients to receive massive doses (up to 3 grams a day) and yet remain psychotic and unmanageable. During these episodes of “galloping psychosis” patients may be abusive to themselves and others, unable to follow orders, to eat or rest, and frightening to other patients. In the past such patients who were obviously out of control were placed in seclusion rooms and/or given electroshock. In many institutions, however, electroshock is not frequently resorted to, and seclusion rooms have been abandoned in favor of a combination of a better trained and more abundant staff, a well conceived milieu, and modern drugs. But when the usual drugs and milieu fail, even the best trained staff may have difficulty handling patients in whom a psychotic process rages unabated. For such patients the author has found ef-
effective a combination of promethazine (Phenergan) and chlorpromazine.

The chlorpromazine is used for its anti-psychotic and tranquilizing effects. Whether chlorpromazine affects symptoms alone or has a direct effect on some psychotic processes, it appears to be beneficial in causing these chaotic episodes to abate. The physician certainly would be remiss to withhold the drug or another like it.

Promethazine, marketed primarily as an anti-histaminic, is used because of its ability to slow down the patient rapidly so that he can be cared for. The manufacturer's package insert notes that promethazine "relieves apprehension and produces a light sleep from which a patient can be easily aroused" (the manufacturer specifically notes this is conjunction with nighttime surgical or obstetrical sedation).

Promethazine is a phenothiazine derivative and is chemically similar to chlorpromazine. (See below.)

Laborit, the French surgeon, attracted great attention to the drug in the early 1950's with his papers on its use in artificial hibernation. The drug has also been widely used in sleep therapy. For psychiatric use promethazine has not been found to be as effective as the other phenothiazines despite some early enthusiasm. In 1958 Shea et al wrote: "The data suggests that promethazine unlike other phenothiazine derivatives when administered intravenously in relatively large concentrations may induce a depression of both cortical and subcortical centers. In view of this action the drug would seem to have considerable therapeutic value in the management of those patients with increased psychomotor activity not clinically controlled by either promazine or chlorpromazine."

Promethazine's actions are strongly potentiated when administered with chlorpromazine. In moderate doses it makes a patient feel fatigued or sleepy and greatly slows him down. In large doses it can put a patient to sleep. It is possible to regulate the medication so that a patient achieves a light sleep from which he can be awakened easily to eat, drink, void, breathe deeply and take short walks. The state of sleep can be so regulated that the patient will respond to questions so that the progression or diminution of the psychotic episode can be roughly gauged. One or two doses of promethazine can be withheld if the patient is sleeping so deeply as to make evaluation of his mental state impossible. Barbiturates, because of their depressing effect on medullary centers and their tendency to induce deep sleep, are not satisfactory substitutes for promethazine.
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Case Reports

The following cases demonstrate the combined use of promethazine and chlorpromazine.

Case Number 1

The patient was a 17-year-old girl who first became psychotic while visiting a foreign country as an exchange student. She was immediately flown back home and admitted directly to University Hospital. After appearing to restitute, for no discernible reason, she became progressively and severely psychotic. For 36 hours she did not sit down or eat. She was unable to follow orders. She talked loudly about natural and supernatural spirits, the purity of her blood, and the secrets of the universe which she alone understood. She carried a hairbrush and hit anyone near her. She rushed into the nursing station several times attempting to rip the phone out of the wall. The other patients became frightened and relayed their anxiety to the staff. As fairly standard procedure the patient received 50 mgs of intramuscular chlorpromazine for three doses, 30 minutes apart. This had no effect except that she finally agreed to take oral medication rather than be held down for an injection. She then received hourly doses of medication, but seemed unaffected by the high dose of 2500 mgs in 24 hours. Her blood pressure and physical state were closely monitored. Her psychosis appeared to worsen. The addition of 20 mgs of trifluoperazine only seemed to heighten her agitation. Finally, after 500 mgs of a barbiturate was given intramuscularly, the patient fell asleep.

In six hours, she awoke, and if anything, she was more unmanageable. All attempts by staff to handle her failed. Finally she was started on a regimen of 50 mgs promethazine orally every four hours and 300 mgs chlorpromazine orally every four hours. The doses were so administered that she received one medication or the other every two hours. Before each dose her physical and mental status were evaluated. She also received eight mgs of trihexyphenidyl (Artane) daily. Within several hours the patient went into a light sleep. She could be aroused easily. She was able to eat and to void. With help she could walk to the bathroom and even brush her teeth. A nursing chart was set up and faithfully maintained.

In six hours, she awoke, and if anything, she was more unmanageable. All attempts by staff to handle her failed. Finally she was started on a regimen of 50 mgs promethazine orally every four hours and 300 mgs chlorpromazine orally every four hours. The doses were so administered that she received one medication or the other every two hours. Before each dose her physical and mental status were evaluated. She also received eight mgs of trihexyphenidyl (Artane) daily. Within several hours the patient went into a light sleep. She could be aroused easily. She was able to eat and to void. With help she could walk to the bathroom and even brush her teeth. A nursing chart was set up and faithfully maintained.

A typical six-hour period is charted:

<table>
<thead>
<tr>
<th>HOURS</th>
<th>Blood Pressure</th>
<th>Chlorpromazine</th>
<th>Promethazine</th>
<th>Trihexyphenidyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 A. M.</td>
<td>110/80</td>
<td>300 mg</td>
<td>50 mg</td>
<td>4 mg</td>
</tr>
<tr>
<td>10 A. M.</td>
<td>100/70</td>
<td>400 mg</td>
<td>50 mg</td>
<td></td>
</tr>
<tr>
<td>11 A. M.</td>
<td>100/70</td>
<td>300 mg</td>
<td>50 mg</td>
<td></td>
</tr>
<tr>
<td>12 Noon</td>
<td>100/70</td>
<td>200 mg</td>
<td>50 mg</td>
<td></td>
</tr>
<tr>
<td>1 P. M.</td>
<td>100/70</td>
<td>100 mg</td>
<td>50 mg</td>
<td></td>
</tr>
<tr>
<td>2 P. M.</td>
<td>100/70</td>
<td>0</td>
<td>50 mg</td>
<td></td>
</tr>
</tbody>
</table>

- Awake
- & Agitated
- & Walking
- & Dizzy
- Dazed
- & Unresponsive
- & Halted
- & Aroused

The patient was maintained in this state for 10 days. On several occasions she refused to take her medications orally and they were then given intramuscularly. Her room door was kept open at all times and, while other patients could look in, they were not allowed to visit. Her treatment was discussed at the patient-staff conference. A nurse, aide or physician checked the patient every 30 minutes, and her mental status was roughly evaluated by the physician several times daily. Even while she was under the influence of all these medications, it was possible to determine easily at the end of 10 days that her psychosis was lessening. Her medication was reduced by one-half for a four-day period, then by one-half again for four more days. Finally the promethazine and trihexyphenidyl were eliminated and the patient continued on low doses of chlorpromazine.

Case Number 2

The patient was a 43-year-old male with a long history of mental illness. He had received ECT 20 years ago and insulin shock therapy six years ago. Eight months previously he was diagnosed as a manic-depressive at a state mental hospital and was treated with massive doses of chlorpromazine (2500 mg a day) for his "mania." At this time he was quite paranoid and was threatening people with an axe. He presented a serious management problem for three months until he appeared to "set-
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tle down." Three months after discharge he
was admitted to the Ann Arbor Veterans
Hospital where he was diagnosed as having
a schizo-affective disorder. He was admitted
by court order after two psychiatrists found
him to be dangerous to himself and others.
In the hospital he talked confusedly about
religion and about wanting to be the presi-
dent of the United States. His son had been
killed in Vietnam two weeks previously.
The patient felt that machines were in-
fuencing his mind and that he had to kill
"some people." He refused to take any medi-
cation. He carried a pool cue and hit sev-
eral patients who tried to talk with him.

He was forcibly given 100 mg of intra-
muscular chlorpromazine. Four hours later,
still severely agitated and hostile, he was
given another 100 mg intramuscularly.
There was little change in symptoms. He
raged through most of the night except for
a few brief naps.

The next morning he was as hostile as
ever and struck several patients. He finally
agreed to take oral medication when told
he would be given more intramuscular
medication by force. He was started on
Q.I.D. oral doses of 200 mg chlorproma-
zine and 75 mg promethazine. After two
doses he felt somewhat drowsy, and still
refused to cooperate but did not strike any-
one. That night he was more responsive to
verbal orders and, while still hostile, was
more easily approachable. He developed
mild extra-pyramidal signs and was given
benztrozone (Cogentin) 2 mg orally B.I.D.
With each passing day he became easier
to approach. Two days later he agreed to
attend group therapy. Within a week he
was much calmer, cooperative and not very
aggressive. His medication was reduced to
chlorpromazine 50 mg and promethazine 50
mg, both Q.I.D. Four weeks after admis-
sion he was given a two-week leave of ab-
sence on the medication. When he was dis-
charged from the hospital, he continued
with both drugs. He is being followed in
the outpatient clinic every two weeks and
his medication has been continued. There
has been no evidence of neurological side
effects. Liver function and other chemical
tests have been normal.

Comment

It must be emphasized that in the
first case, the medication was not
given simply to make it easier for the
staff. She received very close staff con-
siderations after being placed on the
medication. The medication made it
possible for the staff to care for the
patient better and for the patient her-
self to weather her psychosis better.

Because other patients on the ward
became apprehensive, and some had
fantasies about being punished should
they begin to "act up" keeping the
doors open to the patient's room and
discussing the treatment at the patient-
staff conference served to allay their
anxiety.

In the second case the addition of
promethazine appeared to decrease the
patient's ability to act upon his hostile
feelings. He felt sleepy, groggy and
weak at times but was able to stay
awake and eventually engage in sociali-
ization. It should be mentioned that
(perhaps because of its military associ-
ations) the V. A. hospital milieu gen-
erally serves to decrease aggressive be-
avior in rapid fashion. The patient
described is well remembered by the
staff as being an especially difficult pa-
tient in whom chemical restraint was
a necessity.

Although combination of prometha-
zine and chlorpromazine has been
mentioned in the psychiatric literature
rather infrequently, the author
discovered that the combination has
been used, and is currently being used,
by psychiatrists at the Ypsilanti State
Hospital and the Ann Arbor Veterans
Hospital. In personal communications
from psychiatrists in those two hos-
pitals, the author was informed that
the combination is being used for ag-
gressive, difficult to manage psychotc
patients when chlorpromazine (2000
mg orally or its equivalent) alone was
not effective. These psychiatrists re-
ported using the combination also in
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hospitals in Kansas, Iowa and Europe. A check of 10 patient histories, in which the combination was mentioned, showed that nine patients were rendered more manageable and less aggressive. The usual oral doses of medication were 200 mgs chlorpromazine Q.I.D. and 25 mgs promethazine Q.I.D. An anti-parkinsonian drug was usually needed. In no patients did liver function or other chemical tests become abnormal.

The doses of both drugs greatly exceed the doses recommended in the manufacturers' direction circulars. They must be administered with care. The promethazine - chlorpromazine combination is evidently in fairly common use and would appear to be helpful in the short term management of the acutely psychotic, aggressive patient.

REFERENCES


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