USE OF LEVOMEPROMAZINE IN THE MANAGEMENT OF AGGRESSION IN ADULTS WITH INTELLECTUAL DISABILITY

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Introduction

Behaviour disorders such as aggression is a significant clinical problem in adults with intellectual disability (ID). It is one of the most common reasons for referral to mental health services, admission to hospital and prolonged hospital stay (Felce et al., 2000). If not managed appropriately it significantly impairs quality of life for individuals and may lead to exclusion of individuals from participation in community activities. Aggression especially may lead to significant risks to others and to self.

Behaviour disorder in the absence of mental / physical health and social / environmental problems is best managed with psychological therapies but success rate is variable. Some individuals may therefore end up being treated with antipsychotic medications along with other approaches despite the lack of clear evidence base for drug use in this area (Brylewski and Duggan, 2004), with the exception of Risperidone which, in small doses, has been found to be beneficial for a subgroup of patients with behaviour disorders (Boksanska et al., 2003; Cohen et al., 1998; Horrigan and Barnhill, 1997; McAdam et al., 2002; Zarcone et al., 2001).

Levomepromazine (Methotrimeprazine) is a phenothiazine that was first introduced in 1956. It is structurally similar to Chlorpromazine and Clozapine. The contraindications, cautions and side effects of Levomepromazine listed in the British National Formulary (British National Formulary, 2006) are essentially the same as
those for other typical antipsychotics such as Haloperidol and Chlorpromazine. It is also known to cause hypothermia (van Marum et al., 2003) and postural hypotension in ambulant patients over the age of 50 years. It is licensed for use in the treatment of Schizophrenia and as adjunctive treatment in palliative care including management of pain and associated restlessness, distress, or vomiting (Oliver, 1985; Skinner and Skinner, 1999; O’Neill and Fountain, 1999). Although several studies have shown it to be an effective antipsychotic and anxiolytic (Blin et al., 1996; Lal and Nair, 1992) it is seldom used nowadays in psychiatry. It has also been used as premedication for dental treatment in people with ID (Asan et al., 1986) and also for behaviour disorders in people with ID suffering from epilepsy (Oettinger, 1976). Recently there has been a renewal of interest in its use as it has been found to be of benefit in the treatment of sleep problems associated with posttraumatic stress disorder (PTSD) (Aukst-Margetic et al., 2004) and in the management of agitation in acquired brain injury patients (Maryniak et al., 2001).

In ID services in Leicestershire especially in inpatient population, Levomepromazine has been used to manage severe aggression in some patients. We decided to evaluate its efficacy in this group of patients.

**Method**

The Leicestershire health district has a catchment population of approximately 1 million. The ID services are based at the Leicester Frith hospital, which comprises of a 70-bedded long stay unit (now closed), 10-bedded challenging behaviour unit for adults with Autistic Spectrum Disorders and sever challenging behaviour and 12-bedded assessment and treatment unit for people with ID and mental health problems. All these units are staffed by 24 hour nursing support with access to other professionals (psychologists, speech and language therapists, occupational therapists and physiotherapists) including regular reviews by psychiatrists. Therapeutic interventions whilst in hospital include input from speech and language therapists for development of communications strategies and input from psychologists for behavioural management of problem behaviours. All patients included in this study received input from psychology services. Additional input was accessible from speech and language therapists and physiotherapists. The rest of the service is largely community based and multidisciplinary in nature.

**Aims of the study**

1. To establish the efficacy of Levomepromazine in controlling aggression in adults with ID in inpatient setting.
2. To determine how this medication can be most appropriately prescribed in terms of efficacy, tolerability and safety.

**Objectives of the study**

1. To establish the indications for the use of Levomepromazine in patients with Learning Disability.
2. To establish the characteristics of patients who were prescribed Levomepromazine.
3. To describe the dosage and frequency of use of Levomepromazine in this group.
4. To establish the outcome of the use of Levomepromazine on target symptomatology.
5. To describe the tolerability of Levomepromazine and describe any adverse effects encountered.

The study population included all adults (19+) with ID who had been an inpatient at the Leicester Frith hospital at some point during the 3-month period 1st August 2004 to 1st November 2004. In order to identify the sample, all wards were visited for a list of patients who had been inpatients during this period. The drug charts for all these patients were examined to determine whether they had been prescribed Levomepromazine. The hospital pharmacy department was also contacted to obtain a list of all patients who had been prescribed Levomepromazine according to their records. Following the identification of the patients who had either been prescribed or currently on Levomepromazine during the study period, further information was obtained on those individuals from the hospital case notes, named nurse and consultant psychiatrist.

A data collection tool was used by the researchers and information on age, sex, length of hospital stay, degree of ID, primary cause of ID, psychiatric (axis1) diagnoses, presence or absence of any secondary disabilities such as sensory or motor impairment or epilepsy and current medication were obtained.

Data was collected using the questionnaires and included the following rating scales that were administered retrospectively, to identify the range and degree of behaviour problems before and after commencement of Levomepromazine with information obtained from the case notes and the key workers:

Aberrant Behaviour Checklist (ABC) (Aman et al., 1985) to identify the range and the extent of the behaviour problems.

Modified Overt Aggression Scale (MOAS) (Yudofsky et al., 1986) for identification of the characteristics of aggressive behaviour including severity.

To assess the response to treatment, Clinical Global Impression (CGI) (Guy, 1976) scale was used pre and post treatment with Levomepromazine.

The ID service in Leicester has long been using behaviour monitoring forms to record any incident related to problem behaviours. This form has a number of sections including, any antecedents noted, severity of behaviours, interventions and outcomes. The information is held electronically within the Trust database and was accessed for the purpose of this study along with information from medical and nursing notes.

The retrospective nature of data gathering for ABC was hence possible.

Results

The total number of patients who were on Levomepromazine during the 3-month study period was 14 (100%). The indication for prescribing Levomepromazine was presence of severe aggression in 14 (100%) individuals. Mean age of the sample was 49 years and the age range was 34 years to 67 years. All other characteristics of patients on Levomepromazine are outlined in TABLE 1.

None of them experienced any specific adverse side effects with use of Levomepromazine. However, 4 patients (29%) had abnormal investigation results, which included low haemoglobin (14%), low red blood cell count (7%), low haematocrit (7%), hyponatraemia (14%) (due to concurrent Carbamazepine use in 1 patient), low platelet count (7%) (present prior to initia-
tion of Levomepromazine), low serum ferritin (7%), raised random blood sugar (7%) (however glycated haemoglobin (HbA1c) was within normal range).

The average duration that a patient was on Levomepromazine was 66 weeks (range 4 weeks to 260 weeks) and the average dose was 525mg (range 150mg to 900mg).

So far as efficacy is concerned, 9 out of 14 patients showed improvement following treatment with Levomepromazine. This was supported by pre and post scores of ABC and MOAS (TABLE II). The CGI scores prior to and post treatment showed similar results.

As highlighted in the TABLE II, statistically significant difference was noted in the MOAS and ABC scores before and after Levomepromazine use but no perceptible difference in PRN drug use.

TABLE I
Characteristics of patients on Levomepromazine

<table>
<thead>
<tr>
<th>Gender</th>
<th>Males 12 (86%)</th>
<th>Females 2 (14%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Place of stay</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHS long stay ward</td>
<td>12 (85%)</td>
<td></td>
</tr>
<tr>
<td>Acute inpatient assessment unit</td>
<td>1 (7.5%)</td>
<td></td>
</tr>
<tr>
<td>NHS group home</td>
<td>1 (7.5%)</td>
<td></td>
</tr>
<tr>
<td>Ethnic origin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White Caucasian</td>
<td>13 (93%)</td>
<td></td>
</tr>
<tr>
<td>Afro-Caribbean</td>
<td>1 (7%)</td>
<td></td>
</tr>
<tr>
<td>Cause of ID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autistic spectrum disorders</td>
<td>5 (36%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>9 (64%)</td>
<td></td>
</tr>
<tr>
<td>Degree of ID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>5 (36%)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>3 (21%)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>6 (43%)</td>
<td></td>
</tr>
<tr>
<td>Presence of Axis 1 psychiatric diagnosis</td>
<td>7 (50%)</td>
<td></td>
</tr>
<tr>
<td>Target symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical aggression</td>
<td>14 (100%)</td>
<td></td>
</tr>
<tr>
<td>Damage to property</td>
<td>6 (43%)</td>
<td></td>
</tr>
<tr>
<td>Self injury</td>
<td>4 (28%)</td>
<td></td>
</tr>
<tr>
<td>Faecal smearing</td>
<td>1 (7%)</td>
<td></td>
</tr>
<tr>
<td>Screaming/shouting</td>
<td>5 (36%)</td>
<td></td>
</tr>
<tr>
<td>Wandering/absconsion</td>
<td>2 (14%)</td>
<td></td>
</tr>
<tr>
<td>Physical overactivity</td>
<td>6 (43%)</td>
<td></td>
</tr>
<tr>
<td>Sexual behaviour</td>
<td>3 (21%)</td>
<td></td>
</tr>
<tr>
<td>Other behaviours</td>
<td>2 (14%)</td>
<td></td>
</tr>
<tr>
<td>Epilepsy</td>
<td>2 (14%)</td>
<td></td>
</tr>
<tr>
<td>Motor and sensory impairments</td>
<td>1 (7%)</td>
<td></td>
</tr>
</tbody>
</table>
Discussion

This study has its limitations in that it was conducted only in inpatient setting and did not include those who were tried on Levomepromazine before the study period but are currently not maintained on it due to side effects, intolerability or lack of efficacy. However the study highlighted that for a small number of patients with severe aggression due to underlying behaviour disorder, Levomepromazine is an useful adjunct drug which may be considered for use provided other approaches have been tried with little benefit and there is no accompanying significant contraindications to the use of this medication. One of the difficulties of using this product lies with the fact that the tablets come only in 25mg strengths and hence some patients may end up taking huge amount of tablets, the maximum dose being 1000mg a day. There is also the issue of side effects that are encountered with the use of traditional antipsychotic drugs including that of postural hypotension, extra pyramidal side effects (EPSE) and drowsiness. Monitoring arrangements for the use of this drug should therefore include regular monitoring of blood pressure (lying and standing) and also close observation for EPSE or unacceptable levels of drowsiness. Care should be taken not to co-prescribe other antipsychotic drugs at the same time and also in relation to monitoring of epileptic seizures in those who are actively epileptic. The researchers feel that this product should only be used in inpatient setting where such close monitoring is possible.

Additional issues such as capacity to consent to treatment, application of best interest principles, multidisciplinary input

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**TABLE II**

Scores on MOAS and ABC, pre and post Levomepromazine use

<table>
<thead>
<tr>
<th>Scales</th>
<th>Before LMP use</th>
<th>After LMP use</th>
<th>Mean difference</th>
<th>Significance</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOAS</td>
<td>5.871</td>
<td>4.0714</td>
<td>1.78571</td>
<td>.008</td>
<td>0.562</td>
<td>3.009</td>
</tr>
<tr>
<td>‘As required’ drug use</td>
<td>15.0000</td>
<td>15.5000</td>
<td>-5.0000</td>
<td>.500</td>
<td>-6.853</td>
<td>5.853</td>
</tr>
<tr>
<td>ABC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irritability</td>
<td>19.14</td>
<td>12.86</td>
<td>6.286</td>
<td>.000</td>
<td>4.132</td>
<td>8.439</td>
</tr>
<tr>
<td>Lethargy</td>
<td>9.00</td>
<td>7.71</td>
<td>1.286</td>
<td>.042</td>
<td>.057</td>
<td>2.514</td>
</tr>
<tr>
<td>Stereotypy</td>
<td>3.86</td>
<td>3.14</td>
<td>.714</td>
<td>.012</td>
<td>.187</td>
<td>1.242</td>
</tr>
<tr>
<td>Hyperactivity</td>
<td>18.36</td>
<td>12.50</td>
<td>5.857</td>
<td>.000</td>
<td>3.367</td>
<td>8.347</td>
</tr>
<tr>
<td>Speech</td>
<td>2.21</td>
<td>1.71</td>
<td>.500</td>
<td>.314</td>
<td>-.532</td>
<td>1.532</td>
</tr>
</tbody>
</table>

LMP - Levomepromazine; MOAS - Modified Overt Aggression Scale; ABC - Aberrant Behaviour Checklist

**TABLE III**

Change in CGI and Target symptoms pre & post Levomepromazine use

<table>
<thead>
<tr>
<th>CGI</th>
<th>Global improvement following LMP</th>
<th>Improved</th>
<th>No change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall change in target symptoms</td>
<td>9 (64%)</td>
<td>5 (36%)</td>
<td></td>
</tr>
</tbody>
</table>

CGI - Clinical Global Improvement; LMP - Levomepromazine
in decision making, user and carer involve-
ment etc should be addressed in the same
way as for any psychotropic medication
use in behaviour disorder in this popula-
tion.

The results highlight the improve-
ment especially in aggression and other
symptoms including those of lethargy,
stereotypy, irritability and hyperactivity.
Therefore before initiation of prescribing
Levomepromazine, clinicians should care-
fully look at the target symptoms and de-
cide accordingly. It is acknowledged that
the number of audited patients is small and
therefore it is impossible to draw a mean-
ingful conclusion from this study. How-
ever the study confirms the fact that this
product may be useful in the same way, as
it has been with brain injury patients for
management of agitation.

Conclusions

Use of Levomepromazine may be
considered for inpatients with serious ag-
gressive behaviour in the absence of any
underlying mental health / physical health
problems, pain, communication and envi-
ronmental issues, provided other therapeu-
tic approaches such as psychological and
behavioural approaches have been tried
and have failed to bring on any significant
improvement. Care must be taken during
drug prescribing and dose titration should
be done gradually on a weekly basis. Dur-
ing the titration phase, nursing staff on a
daily basis should monitor blood pressure,
pulse rate and emerging EPSE. Unaccept-
able drowsiness if noted should be report-
ed to medical staff. Blood pressure and
pulse rate should be monitored on weekly
basis during the maintenance phase. Care
should be taken in its use in the presence
of active epilepsy and the product should
not be prescribed for anyone with hypoten-
sion. During the use of Levomepromazine,
no other antipsychotic drug should be pre-
scribed with the exception of PRN use, pro-
vided, the total combination dose does not
exceed the maximum BNF limit.

Summary

This study reviewed the efficacy of
Levomepromazine in managing aggres-
sion in adults with ID in a small number
of in-patient population and also aimed to
identify the issues in relation to tolerability
and safety. The study findings indicate that
Levomepromazine may be useful in a small
number of patients with severe aggression
especially in in-patient setting where oth-
er approaches have failed. The study has
highlighted that this drug appears to be
efficacious not only in controlling aggres-
sion but also lethargy, stereotypy, irritabil-
ity and hyperactivity symptoms. However
this drug is not without its side effects and
care should be taken to monitor patients’
blood pressure, pulse rate and blood pa-
rameters during titration and maintenance
phase of treatment with this drug.

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