CLINICAL EVALUATION OF A NEW MYDRIATIC—MYDRILATE*

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Cyclopentolate hydrochloride was first introduced into Great Britain under the name “Cyclogyl”, but recently a British preparation under the proprietary name “Mydrilate” (Ward, Blenkinsop and Co.) has become freely available, and after the first teething troubles has become a valuable addition to our pharmacological armamentarium. When it was first introduced there was slight difficulty in finding the correct pH, and some of the solutions provided showed instability. Now, at the pH found to be most constant, we have a solution which gives very constant dilatation of practically every type of eye, pathological and normal.

This new drug was submitted to a clinical trial in various types of cases, which may be divided into four groups:

1. Routine diagnostic dilatation of pupils.
2. Dilatation in pathological cases.
3. Pre-operative dilatation.
4. Refraction in children of all ages.

“Mydrilate” is supplied in two strengths, 0.5 and 1 per cent., in a buffer solution giving pH 5, with benzalkonium chloride as a preservative, and the solution is quite stable at room temperature. This drug acts by producing paralysis of the iris sphincter and ciliary muscle by local anticholinergic action. Sympathetic stimulants increase the mydriasis slightly by stimulation of the dilator fibres.

ROUTINE DIAGNOSTIC DILATATION OF THE IRIS SPHINCTER

Ordinarily the 1 per cent. of homatropine and cocaine is used in my outpatients for routine diagnostic dilatation. This was found satisfactory, but the dilatation took a considerable time. The speed and efficiency of “Mydrilate” 1 per cent. were therefore compared with 1 per cent. homatropine and cocaine in over fifty patients. A note was made of the preliminary size of both pupils, measured with a millimetre scale under the full illumination of an ophthalmoscope light with the rheostat at its maximum. The pupil size was measured 10 and 20 minutes after putting “Mydrilate” in the right eye.

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and homatropine and cocaine in the left. The colour of the iris, patients' age and sex, and the condition for which dilatation was required were also noted. Table I shows ten results which are typical of all those recorded in the out-patients' department. Dilatation was quick and efficient with both types of drops, but the 10-minute measurement shows that practically the maximal dilatation was obtained with "Mydrilate", whereas the pupils treated with homatropine and cocaine were still often half as large. At the end of 20 minutes, however, dilatation was about equal with both drugs.

**TABLE I**

**COMPARISON OF PUPILLARY DIAMETERS AFTER MYDRilate IN THE RIGHT EYE, AND HOMATROPINE IN THE LEFT**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Time (min.)</th>
<th>Colour of Iris</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Condition</th>
<th>Pupillary Diameter (mm.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>1</td>
<td>0 10 20</td>
<td>Blue</td>
<td>69</td>
<td>F.</td>
<td>Fundus</td>
<td>2 6 7 F</td>
</tr>
<tr>
<td>2</td>
<td>0 10 20</td>
<td>Blue</td>
<td>41</td>
<td>M.</td>
<td>Fundus</td>
<td>2 6 8 F</td>
</tr>
<tr>
<td>3</td>
<td>0 10 20</td>
<td>Blue</td>
<td>65</td>
<td>M.</td>
<td>Fundus</td>
<td>3 8 10 F</td>
</tr>
<tr>
<td>4</td>
<td>0 10 20</td>
<td>Brown</td>
<td>28</td>
<td>M.</td>
<td>Fundus</td>
<td>2 5 6 F</td>
</tr>
<tr>
<td>5</td>
<td>0 10 20</td>
<td>Brown</td>
<td>61</td>
<td>F.</td>
<td>Fundus</td>
<td>2 8 8 F</td>
</tr>
<tr>
<td>6</td>
<td>0 10 20</td>
<td>Blue</td>
<td>16</td>
<td>F.</td>
<td>Fundus</td>
<td>2 7 8 F</td>
</tr>
<tr>
<td>7</td>
<td>0 10 20</td>
<td>Blue</td>
<td>80</td>
<td>M.</td>
<td>Fundus</td>
<td>3 5 6 F</td>
</tr>
<tr>
<td>8</td>
<td>0 10 20</td>
<td>Brown</td>
<td>47</td>
<td>F.</td>
<td>Fundus</td>
<td>2 7 8 F</td>
</tr>
<tr>
<td>9</td>
<td>0 10 20</td>
<td>Brown</td>
<td>14</td>
<td>M.</td>
<td>Fundus</td>
<td>2 3 4 (A)</td>
</tr>
<tr>
<td>10</td>
<td>0 10 20</td>
<td>Blue</td>
<td>14</td>
<td>M.</td>
<td>Fundus</td>
<td>3 7 8 F</td>
</tr>
</tbody>
</table>

F=Fixed Pupil  A=Active pupil
In each case one drop of the drug was instilled just after the preliminary pupillary measurement, and no further application was used. Throughout all these tests and investigations, the 1 per cent. solution was used because it was felt that the maximum speed and efficiency would result from using the stronger solution.

Table I shows that excellent dilatation was obtained in patients whose ages ranged from 60 to 14 years. This was quite sufficient for ordinary diagnostic purposes, and was obtained within 10 minutes, and sometimes much sooner. Very heavily pigmented eyes were, as is common with any mydriatic, rather difficult to dilate, but ordinarily they dilated better with "Mydrilate" than with homatropine. There was only one exception in our whole series, that of a 14-year-old coloured boy with intensely pigmented eyes; the pupil diameter doubled in 20 minutes, that in which "Mydrilate" had been placed being slightly larger than the other.

Many young babies are referred from the paediatric unit, and whereas atropine and the usual mydriatics often have little or no effect, "Mydrilate" in combination with phenylephrine gave better pupillary dilatation, and therefore a better view of the fundus than could be obtained in any other way.

Dilatation of Eyes in Pathological Cases

In pathological cases we have used "Mydrilate" only in eyes with atropine irritation. This was very satisfactory both in inflammatory conditions, and for post-operative use and the dilatation was as satisfactory as that obtained with atropine. The eyes were often previously bound down by synechiae, and obviously in no state to respond very efficiently to any mydriatic, but the dilatation was obtained with no further evidence of sensitivity. One point was that "Mydrilate" had to be instilled into the eyes at frequent intervals, as it acts for only a short time, and has not the long-lasting dilatory effect of atropine. This is a disadvantage, but one which could not in the present state of our knowledge be overcome in any other way as atropine provoked an allergic reaction.

Pre-operative Cases

As it is generally held that the pre-operative preparation of cataract cases should include wide dilatation of pupils, "Mydrilate" was tested for pre-operative use. Two drops were instilled the night before the operation, and then 2-hourly the next morning until the time of the operation. All pupils so tested were excellently dilated when the patient was brought to the operating table, but when the eye was fixed with forceps this stimulation was sufficient to cause pupillary contraction, and when the section was made with the knife, the pupil contracted down very fully. This happened in several cases and the usual pre-operative routine had to be re-instituted (homatropine and cocaine before coming to the theatre, and phenylephrine instilled into the eye on the operating table).
Refraction in Children

In school clinics entailing atropine refraction in a large number of children, there are many complaints about the time taken before the examination in instilling the ointment in the child’s eyes, and of the upset brought about in class when pupils are unable to read for a certain period after the examination, which runs to some weeks in many cases. It was therefore decided to ask the Local Education Authority to cooperate in referring fifty school children who were to be examined under atropine mydriasis and then under “Mydrilate”.

It had been found by previous investigators (Abraham, 1953; Ehrlich, 1953; Stolzar, 1953; Gettes, 1954; Gordon and Ehrenberg, 1954; Mitchell, Linfield, and Francis, 1958) that residual accommodation 20 to 40 minutes after the instillation of “Mydrilate” was as low as that produced by atropine, and that maximal cycloplegia was maintained for about 20 minutes. Mydriasis is produced very rapidly, and an average pupil diameter of 7 mm. is usually reached after 15 to 30 minutes with a drop of 0.5 solution (No. 6). It was decided to adopt four routines in the examination of these children, and on two separate days 25 children were sent for. At the first visit they had their pupils fully dilated with 1 per cent. atropine (dispensed as an ointment in small gelatine containers) put into both eyes three times a day for 3 days before the examination. The refraction was then carried out, and the result noted. The colour of the eyes was also recorded, again to see if there was any difference in the reaction of blue and pigmented eyes. The first 25 children were given postcards, and were asked to let us know when they could read their school books again, and with the help of the Local Authority Health Visitors checked their reading ability. If the postcard was not received, a health visitor called and asked when the reading ability had returned to normal. The first 25 children were then seen 4 weeks after their atropine test, and this time they were each supplied with a plastic dropper bottle containing 1 per cent “Mydrilate”, and asked to use this exactly as they had used the atropine ointment, namely one drop in each eye, three times a day, for 3 days before the test. They were then examined and the refraction noted.

When the second group of 25 children was to be re-examined with “Mydrilate” a suggestion put forward by the Education Authority was adopted, namely, that some children should be asked to instill the drops at hourly intervals for 4 hours before the refraction, and the other half should be asked to put in one drop at bedtime the night before, one drop 2 hours before the refraction, and one drop one hour before. The second scheme was suggested because four drops at hourly intervals would give insufficient time to prepare for a morning refraction clinic. The reason for asking for the drops to be put in so frequently and before coming to the clinic, was that, with the numbers usually seen, nursing or medical staff would not be able to instill
the drops into the children's eyes as they appeared and then to keep them sitting about until dilation and mydriasis had taken place. Also, one cannot be sure that the parent will always get one drop into the child's eyes, and the chances of getting in one drop out of four or five are much greater.

One other question asked after the first batch of children had been seen was the difference noticed by the child and the parents in the ease of application of atropine or "Mydrilate". Some children found "Mydrilate" stung slightly and irritated, but in no case did this prevent further drops being put in, and one or two children insisted that "Mydrilate" was more comfortable to have instilled than atropine.

Table II shows the results of these tests. It is of interest that when the second series of tests was done the result of the first refraction with atropine was not known, so that the results were strictly impartial. The following points were recorded: the refraction of both eyes with each drug, the length

**TABLE II**

TWENTY REPRESENTATIVE CASES AMONGST THE FIFTY SCHOOL CHILDREN

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Refraction</th>
<th>Duration (days)</th>
<th>Colour of Iris</th>
<th>Pupils</th>
<th>Remarks</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Atropine</td>
<td>&quot;Mydrilate&quot;</td>
<td>&quot;Mydrilate&quot;</td>
<td></td>
<td></td>
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<tr>
<td>1</td>
<td>+2</td>
<td>+2</td>
<td>+3</td>
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<td>+8</td>
<td>+6</td>
<td>+7</td>
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</tr>
<tr>
<td>4</td>
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<td>+1.5</td>
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<td>+1</td>
<td>+1.25</td>
<td>+8.25</td>
<td>24</td>
</tr>
<tr>
<td>11</td>
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<td>High Myope</td>
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<td>+0.75</td>
<td>+2.25</td>
<td>19</td>
</tr>
</tbody>
</table>

*1. "Mydrilate" three times a day for 3 days before test.
2. "Mydrilate" once the night before, and twice at hourly intervals before test.
3. "Mydrilate" at hourly intervals for 4 hours before test.
of time each drug took to wear off, the routine adopted in the instillation of
"Mydrilate", the colour of the eyes, the pain or irritation encountered, the
condition of pupils on examination, and any other remarks thought to be
significant. The children who had had "Mydrilate" instilled by the same
routine as with atropine showed in most cases that the pupils were reacting.
The last dose of "Mydrilate" had been instilled the night before, i.e. some 18
hours before examination, the effect had practically worn off, and most
of the children were able to see and read small print. But with either of the
other two routines, "Mydrilate" gave excellent mydriasis and cycloplegia,
and the refraction was exactly the same as with atropine. The effects of
atropine lasted anything from 3 to 24 days (average 14 days), but the effects
of "Mydrilate" had always completely worn off 2 days after being instilled,
and sometimes much sooner. The colour and the amount of pigmentation
had no effect in this test, heavily-pigmented pupils being well dilated and
mydriasis complete.

Discussion

In diagnostic dilatation this drug gives results in half the usual time, and it
helps in cases in which the use of routine drugs is contraindicated.

Dilation in pathological cases is satisfactory, but the frequency with which
the mydriatic has to be instilled militates against its routine use, and atropine
is still of more value in such cases.

Pre-operative cases presented the one disappointment: although the pupils
were well dilated any slight stimulation to the eye was followed by con-trac-tion.

The application of "Mydrilate" is therefore desirable in routine diagnosis
and in the refraction of schoolchildren, in whom the same results may be
obtained with the least disturbance to the child, both in and out of school.

Although some authors state that the onset of cycloplegia follows very
rapidly after the instillation of the drug, the staff of most school clinics do not
want to have to instill the drops after the child has arrived at the clinic, but
prefer the pupils to be already dilated so that the test can be carried out at
once. This would entail the expense of supplying "Mydrilate" in small
individual containers, but in view of the excellent results, especially in the
refraction of school children, with the avoidance of the difficulties attendant
on atropine mydriasis, the use of this new and excellent mydriatic should be
seriously considered as a routine in school refraction work.

At present prices the normal pack contains 225 drops, and each case can be
treated in the clinic for a little over a halfpenny. The manufacturers have
already informed us that "Mydrilate" 1 per cent. could be made up in an
ointment base and could possibly be dispensed in small gelatine containers,
and it is hoped to test these in a further trial.
Summary

A new mydriatic “Mydrilate” has been tested and compared with homatropine and atropine.

In routine diagnostic dilatation the results were excellent, the maximum pupillary dilatation being obtained much more quickly with “Mydrilate”.

In pathological conditions, eyes which were irritated by atropine tolerated “Mydrilate”, but since its action is short-lived its use is not practicable in eyes requiring long-term dilatation.

For pre-operative dilatation “Mydrilate” is not recommended because, although the pupils dilate fully, they contract rapidly at the slightest stimulation.

In school refraction clinics, “Mydrilate” is of very great value as it promotes dilatation very rapidly and the child’s eyes return to normal after at the most 2 days.

We should like to thank Messrs. Ward, Blenkinsop and Co. Ltd., the manufacturers of “Mydrilate”, for a liberal supply of the drug, both on its first introduction, and in the present stable form of solution, and also for the help of their representative in Northern Ireland who did everything to help us in this survey. We are also grateful to Dr. A. L. Walby, and members of the School Medical Service of Belfast, for their interest and cooperation, and the trouble they took both in supplying premises and in sending for the schoolchildren. They also went to great pains to check the duration of action of the drugs, and to ensure that consistent replies were obtained from the children and their parents.

REFERENCES

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