CONTROLLED CLINICAL STUDY OF THE EFFECTIVENESS AND ADVERSE EFFECTS OF IMIPRAMINE AND AMOXAPINE FOR TREATMENT OF RETROGRADE EJACULATION

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Objective

• Retrograde ejaculation (RE) is an ejaculation disorder that can cause male infertility.

• RE is defined as a pathological condition in which some or all semen is not emitted despite orgasm.
• The main cause of RE is believed to be decreased function of the bladder neck due to conditions such as diabetes, pelvic surgery, and drug resistance.

• Currently imipramine is the drug of choice for treatment of RE, but side effects such as drowsiness sometimes develop.

• In this controlled clinical study we evaluated the effectiveness and adverse effects of imipramine and amoxapine for treatment of RE.
Objective

Number 17 cases
Age 30 - 52 y.o. (Ave. 41y.o.)
Disease duration 3m - 5y (Ave. 1.6 y)

- All patient have no emission completely before the treatment.
- Male infertility was the reason for consultation in 13 cases.
- ED was observed in three patients, but erection hardness was greater than EHS3 after use of PDE5I.
Cause of RE

- Diabetes 8 cases
- Surgery for rectal cancer 2 cases
- RLND for testicular cancer 1 case
- Cerebral infarction 1 case
- Spina bifida 1 case
- Unknown 4 cases
Method

• We check the sperm appearance in patient urine after orgasm.

• The men were provided with a 2.5-cc syringe for self-measurement of semen volume during ejaculation.

• All procedures in the present study were approved by the Toho University Medical Center Omori Hospital Ethics Review Committee, and informed written consent was received from all participants.
Schedule for medication

Group A

Amoxapine 50mg/Day → Wash-out → Imipramine 50mg/Day

Group B

Imipramine 50mg/Day → Wash-out → Amoxapine 50mg/Day

14days 14days 7days

Self-measurement of semen volume

Self-measurement of semen volume
Examination Results

- FSH: 2.0-18.6 mIU/ml (Ave. 6 mIU/ml)
- LH: 3-11.2 mIU/ml (Ave. 5.01 mIU/ml)
- PRL: 3.0-24.5 ng/ml (Ave. 12.68 ng/ml)
- E2: 20.0-43.9 pg/ml (Ave. 25.84 pg/ml)
- Total T: 1.95-6.16 ng/ml (Ave. 4.256 ng/ml)

- In nine cases, we can see sperm in their urine after orgasm.
## Result

<table>
<thead>
<tr>
<th></th>
<th>First medication</th>
<th>Second medication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group A</strong></td>
<td>Amoxapine</td>
<td>Imipramine</td>
</tr>
<tr>
<td>Emission</td>
<td>6/8 cases (75%)</td>
<td>6/8 cases (75%)</td>
</tr>
<tr>
<td>Semen Volume</td>
<td>0.5-1.5 cc (Ave. 1.05 cc)</td>
<td>0.3-0.5 cc (Ave. 0.26 cc)</td>
</tr>
<tr>
<td>Side effect</td>
<td>drowsiness 2 cases</td>
<td>drowsiness 2 cases</td>
</tr>
<tr>
<td><strong>Group B</strong></td>
<td>Imipramine</td>
<td>Amoxapine</td>
</tr>
<tr>
<td>Emission</td>
<td>6/9 cases (77.8%)</td>
<td>8/9 cases (88.9%)</td>
</tr>
<tr>
<td>Semen Volume</td>
<td>0.5-1.5 cc (Ave. 1.05 cc)</td>
<td>0.1-1.5 cc (Ave. 0.79 cc)</td>
</tr>
</tbody>
</table>
| Side effect    | drowsiness 2 cases (One case gave up.) | drowsiness 2 cases
|                |                  | constipation 1 cases |
Result

Semen appearance rate: sperm (+) VS sperm (-) in urine before medication

<table>
<thead>
<tr>
<th></th>
<th>Sperm (+)</th>
<th>Sperm (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>amoxapine</td>
<td>9 /9 cases (100%)</td>
<td>5 /8 cases (62.5%)</td>
</tr>
<tr>
<td>imipramine</td>
<td>8 /9 cases (88.9%)</td>
<td>4 /8 cases (50%)</td>
</tr>
</tbody>
</table>

p<0.01

p<0.08

p<0.15
## Result (Total)

<table>
<thead>
<tr>
<th></th>
<th>Amoxiapine</th>
<th>Imipramine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Emission</strong></td>
<td>14/18 cases (77.8%)</td>
<td>11/18 cases (61.1%)</td>
</tr>
<tr>
<td><strong>Semen Volume</strong></td>
<td>0.1-1.5cc (Ave. 0.9cc)</td>
<td>0.3-1.5cc (Ave. 0.57cc)</td>
</tr>
<tr>
<td><strong>Adverse effects</strong></td>
<td>Drowsiness: 4 Constipation: 1</td>
<td>Drowsiness: 4</td>
</tr>
</tbody>
</table>

* p<0.01
Result 1

• Semen volume was significantly greater with amoxapine than with imipramine ($p < 0.01$).

• All men who reported semen emission with imipramine were also able to ejaculate while receiving amoxapine.

• The incidence of adverse effects was similar for amoxapine and imipramine. Amoxapine was effective for all men who had positive results with imipramine.
Result 2

- Advertise effect is almost equal between amoxapine and imipramine, but one patient got strong drowsiness with imipramine, and he couldn’t complete his medication.

- After this study, 13 patients chose amoxapine in 14 cases who reported semen emission.
Discussion

• In this study, 100% patient who had spermaturia and over 60% patient who didn’t have spermaturia get emission with amoxapine.

• Advertise effect of amoxapine is almost equal to imipramine and much more mild.

• Good medical compliance can be expected.

• On-demand treatment and treatment for refractory RE are subjects for future analysis.
Conclusion

• We evaluated the effectiveness and adverse effects of imipramine and amoxapine for treatment of RE in this controlled clinical study.