NITRAZEPAM IN EMOTIONAL DISORDERS OF CHILDHOOD

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SUMMARY

The therapeutic results obtained with Nitrazepam in 30 children with emotional disorders between 4 and 14 years of age are reported, 17 children with habit disorders, 6 with behaviour, 5 with personality and 2 with Neurosis. Employing a flexible dosage schedule, a dose of 1/4 tablet to 1 tablet of 5 mg. Nitrazepam once to thrice daily was effective and safe. 24 of the 30 children (80%) showed recovery or marked improvement with over 50% fall in percentage reduction in total score based on assessing the target symptoms.

Nitrazepam is a benzodiazepine derivative, of which chlordiazepoxide, Diazepam and Lorazepam are well known. By exerting a selective inhibitory effect confined specifically to the nervous structures concerned with the integration of emotional reactions (limbic system), Nitrazepam preserves the balance between the “Wake System” and the Sensory and Autonomic Centres and induces sleep closely resembling physiological sleep in both onset and Course. Chemically, it is 1,3-dihydro-7-nitro-5-phenyl-2H-1,4-benzodiazepine-2-one. The drug has been used mainly as a hypnotic (Le Riche et al., 1966) and considered as quite safe for this purpose. Matthew et al. (1969, 1972) commenting on the safety of Nitrazepam as a hypnotic observed that “the lethal dose in man remains unknown” and thus recommended it as the hypnotic of choice in patients at risk from over dosage. As no authenticated report of death from poisoning could be found even subsequent to his observations, the present study of its possible use in other emotional disorders, was prompted, especially in children, where the safety assumes considerable importance.

MATERIAL AND METHOD

Patients: The study was carried out on 30 patients who were selected from those attending the daily psychiatric Out-patient department of Medical College S.S.G. Hospital, Baroda between April and September 1980. The first 30 patients who satisfied the criteria of selection comprised the material. The patients with known physical or neurological disorder, mental retardation and who were not likely to cooperate to make the trial reliable, were not included in the trial. The children ranged in age from 4 to 14 years with a mean age of 8.4 years and consisted of 21 boys and 9 girls. The duration of emotional disorders varied from 3 days to 9 years (Mean 2.1 years).

Treatment: The tablet provided for use in the trial contained 5 mg. of Nitrazepam. The initial dose was 1/4 or 1/2 tablet depending upon age, once or twice daily which was gradually increased till desired effect was seen. A flexible dosage schedule was employed. The dosage was reduced if the severity of untoward symptoms warranted it. No additional medication was used in any case.

Diagnosis: The emotional disorders were divided into disorders of personality (Tmiti- dity, obstinacy, irritability, sensitiveness, shyness, etc.), behaviour (Truancy, Temper Tantrum, Food Fad, Cruelty, etc.), habit (Stammering, Enuresis, Nail-biting, Thumb-sucking etc.) and Neuroses (anxiety, de-

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pression, obsession, phobia, hysteria). The grouping is for convenience of description, usually a patient had more than one symptom (Table I).

**Table I**—Information about patients (N=30)

| Age Range     | 4—14 Years |
|---------------|------------|
| Mean Age      | 8.4 Years  |
| Diagnosis     |            |
| Habit Disorders| 17         |
| Behaviour Disorders | 6          |
| Personality Disorders | 5          |
| Neurotic Disorders | 2          |
| Total         | 30         |

**Assessment:** In each child the target symptoms of emotional disorder, e.g. Stammering, learning disability etc., were noted and scored on a seven point scale, i.e., 0=absent; 1=Very mild; 2=mild; 3=moderate; 4=moderately severe; 5=Severe; 6=extremely severe. The total score of all symptoms was considered as a parameter of the intensity of emotional disorder.

The treatment was continued for six weeks and the patients were seen at weekly intervals when the target symptoms were scored and computed for percentage reduction in score. In addition global assessment was made taking into account the assessment reported by parents/relatives besides the fall in score. Four arbitrary categories were adopted: Recovered, Markedly improved, Improved and Not improved.

**Assessment of Side Effects:** Side-effects were recorded only if voluntarily complained of by the patients/parents at the weekly interviews. Their intensity was recorded as mild, moderate and severe depending upon whether they were considered unimportant, sufficiently disturbing sometimes requiring reduction in dosage and incapacitating, requiring drastic reduction or discontinuation of the drug respectively.

**Investigations:** One third of the patients were subjected to Laboratory investigations before and after 6 weeks of treatment. They were haemogram, urinanalysis including microscopic examination and determination of S G O T and S G P T.

**RESULTS**

Table II shows the percentage reduction in total score and global evaluations at successive weekly intervals. By either method there was no significant difference statistically (P<0.05), though they appear better by percentage score reduction than by global evaluation. A beneficial effect of the drug was apparent at the end of third or fourth week—24 of the 30 patients (80%) showed a satisfactory response, i.e. recovery to marked improvement.

**Table II**—Response by percentage reduction and global assessment

| Number of Patients | Percentage Reduction in Total Score (P) | Global Assessment (G) | Week 1 | Week 2 | Week 3 | Week 4 | Week 5 | Week 6 |
|--------------------|----------------------------------------|-----------------------|--------|--------|--------|--------|--------|--------|
|                    | P | G | P | G | P | G | P | G | P | G |
| 76 to 100 (Recovered) | 0 | 0 | 1 | 1 | 3 | 5 | 7 | 7 | 10 | 11 | 15 | 14 |
| 51 to 75 (Markedly Improved) | 0 | 1 | 4 | 4 | 5 | 6 | 7 | 7 | 12 | 11 | 9 | 10 |
| 26 to 50 (Improved) | 2 | 1 | 4 | 6 | 7 | 8 | 10 | 11 | 4 | 4 | 2 | 2 |
| 0 to 25 (Not Improved) | 28 | 26 | 21 | 19 | 12 | 11 | 6 | 5 | 4 | 4 | 4 | 4 |
| Total               | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 |
The usual effective dose was \( \frac{1}{2} \) tab. thrice daily for children under the age of 8 and \( \frac{1}{4} \) tab. thrice daily above that age, excepting in some where only one dose was necessary (Enuresis) or a larger dose of 1 tablet thrice daily (Personality disorder with irritability).

Side-Effects: 14 patients complained of drowsiness, 2 severe, 8 moderate and 4 mild, necessitating reduction of dosage in 5. No other side effect was complained of.

DISCUSSION

As it is inappropriate to use a fixed dosage in Clinical Phase I trials of anxiolytic drugs (W.H.O., 1967; Hollister 1970, F.D.A. 1974), a variable dosage regimen was employed in the present study. Moreover in actual clinical practice, drugs are used by individualising their doses.

The recovery that was observed by the use of Nitrazepam in a remarkably high percentage of emotional disorders of childhood, raises the question of the mode in which the drug exerts this effect. It appears that the sedative hypnotic effect, well recognised for the drug cannot by itself explain the benefit derived. It is not unlikely that some other mechanism would explain the therapeutic efficacy, as no attempt was made to modify or influence the environment and no social agencies took part in the treatment. The trial appears to have been successful in determining efficacy, clinical dosage, side-effects and safety.

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