

## Time-blind videotaped evaluation of injectable diazepam, lorazepam and placebo\*

by D.P. BOBON, J. FANIELLE, C. MORMONT,  
M. BREULET and J. BOBON

Department of Psychiatry, University of Liège Medical School  
(director : Jean BOBON)

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### ABSTRACT

*Eighteen inpatients suffering from a severe anxiety received in double-blind and crossover conditions iv and im injections of 10 mg diazepam, 5 mg lorazepam or saline t.i.d. during 5 days. The morning injections was made iv in a CCTV studio. Before injection and 20 mn after it, the patient filled out a 100 mm Visual Analogue Scale; his doctor-in-charge proceeded to a standard interview and to physiological measurements (tremor of hand, patellar reflexes, blood pressure, pulse rate).*

*The videotaped interviews were randomly, i.e. time-blind, rated by two independent observers on 3 scales : the VAS, the Hamilton Anxiety Scale and an ad hoc Verbal and Non-Verbal Anxiety Scale (VNVA). The statistical analysis was completed by a logical analysis according to Lewis Carroll.*

*The results demonstrate the superiority of lorazepam over diazepam on psychic anxiety, somatic anxiety, sleep and blood pressure, the only significant side-effect being drowsiness (Acta psychiat. belg., 1978, 78, 619-634).*

*Key words : anxiety scales, diazepam, lorazepam, placebo, statistics, time-blind measurement of change, video methodology, visual analogue scales.*

### Introduction

The aim of the trial was to demonstrate significant differences, if any, between injectable diazepam (Valium®) and lorazepam (Temesta®) as regards sedation of wakefulness and sedation of psychic v. somatic anxiety.

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## Method

### Medication.

At the time the trial was designed, literature was scanty regarding the dose-effect relationship between both minor tranquillizers or, in our terminology, *psychorelaxants* (\*). It was decided to use 5 mg lorazepam as in a previous open trial, and to compare this dosage to 10 mg diazepam. No other medication was administered throughout the washout period and the trial except for amobarbital at night for ethical and practical reasons.

### Patients.

Eighteen inpatients, aged 24 to 74 years (mean 47 years) — 7 males and 11 females — were selected according to two main criteria :

1° a severe acute or chronic anxiety (of a neurotic type in 15 cases, of a psychotic one in 3 cases) ;

2° reported and/or observed with an intensity and a sensitivity allowing a psychometric evaluation.

The present paper will tentatively summarize the results of the 17 patients who have had a complete psychometric evaluation.

### Procedure.

In order to sort out the respective influence of drug, time and subject, a *crossover* design was decided. It was limited to 7 days due to the severity of patients : 2 days of washout, 2 days on one active drug, 1 « buffer » day on placebo, and 2 days on the other active drug in *double-blind* conditions. Diazepam, lorazepam and saline were administered parenterally t.i.d. (iv at 8 a.m., im at noon and at 8 p.m.). The morning injection was intravenous in order to maximize and speed its clinical effects since the videotaped evaluation was done before and after this injection.

### Psychometric evaluation.

Each morning, the patient was taken to the CCTV studio and told that he would be taperecorded in order to allow the staff to discuss the effectiveness of therapy. Before injection and 20 mn after it (table I), the patient was asked to evaluate his degree of well- or ill-being on a vertical 100 mm *Graphic Rating Scale* or *Visual Analogue*

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\* As one knows, the WHO has recommended to avoid the expressions *minor* and *major* tranquillizers.

Scale labelled « Right now, I am feeling extremely well » at its top v. « extremely bad » at its bottom. Afterwards, the doctor-in-charge proceeded to a *standard interview*; he was asked to avoid temporal references. He then took blood pressure and pulse rate, and evaluated tremor of hands and patellar reflexes on a 4-pt scale.

TABLE I

Rating scales filled out before and 20 min. after injection. By two time-blind video raters: Hamilton Anxiety Scale (HAMA), ad hoc Verbal and Non-Verbal Anxiety Scale (VNVA) including items covering the twenty-four-hour period (1-11) and others covering the twenty-minutes period (12-43), plus items not directly related to anxiety and excluded from the total score (A-D). By both time-blind observers and subjects: a global evaluation of well-being on a Visual Analogue Scale or Graphic Rating Scale (GRS)

	Before	After
HAMA . . . . .	+	—
VNVA 1-11 . . . . .	+	—
VNVA 12-43 . . . . .	+	+
VNVA A-D . . . . .	+	+
GRS-O . . . . .	+	+
GRS-S . . . . .	+	+

The main methodological problem lied in the choice of an anxiety scale adapted to the goals of the trial. In our eyes, an adequate scale has to :

- a) have a face validity as regards psychic and somatic anxiety ;
- b) include non-verbal items, possibly more sensitive to diazepam/lorazepam differences than verbal ones ;
- c) exclude items on trait anxiety (lowering sensitivity to change) and on depression (lowering the scale's validity as regards anxiety) ;
- d) be validated in French.

Since no such scale was available, it was decided to develop an ad hoc instrument, that was named the *Verbal and Non-Verbal Anxiety (VNVA) Scale*. The VNVA Scale is in its present stage 43-items strong. The first 11 items can be explored at 24 h intervals or longer ; the other ones can be explored at very short intervals and comprise psychic items (such as apprehension, feeling of impending danger or dramatization), somatic items (as usual) and non-verbal items (such as rate of speech, and facial expression). Four items, named A to D, were included to the scale but left out of the anxiety score : drowsiness, agitation, hostility and euphoria. The scaling was made the same one

as for the Hamilton Anxiety Scale, namely, from 0 (absent) to 4 (extreme). A standard interview was designed for the VNVA Scale.

The videotaped interviews were played back to two independent and trained raters in a randomized, *time-blind sequence*. Besides the VNVA Scale, these two observers filled out the *Hamilton Anxiety Scale* (HAMA) and a Graphic Rating Scale identical to the patient's one : table I.

#### Statistical analysis.

After the normality of our data had been checked with help of the skewness and kurtosis coefficients, the Student t-test was applied. This statistical analysis was completed by a *logical analysis* of significant differences according to Lewis Carroll.<sup>4</sup>

#### Presentation of the results.

The understanding of the results is complicated by the intrication of the crossover design and of carry-over effects : for example, day 4 is a drug day — either diazepam or lorazepam — but the scores obtained before the iv injection are possibly if not probably influenced by the drug administered on the preceding evening, in our example placebo. With the hope of facilitating understanding,

- the group of patients who started on diazepam will be called Diazepam-Placebo-Lorazepam or DPL group ( $n = 9$ ) ; the group started on lorazepam will be called LPD group ( $n = 8$ ) ;
- in the graphical representation of pre- v. post-injection scores, pre-injection values will be designated in relation to the drug given the night before in agreement with the carry-over hypothesis ;
- the graphical representation of pre- v. pre-injection scores, i.e. at 24 h. intervals, will be quite different and will exclusively refer to the day when the injection was made.

### Results and discussion

Table II indicates that randomization was successful as regards age and sex, but not as regards initial anxiety level : the patients who started on diazepam were significantly more anxious than the patients who started on lorazepam. Nevertheless, on day 4, i.e. after the placebo day, both groups became homogeneous according to their total anxiety scores.

TABLE II

Main characteristics (age, sex and initial scores) of the patients belonging to the diazepam-placebo-lorazepam sequence (DPL, n = 9) or to the lorazepam-placebo-diazepam one (LPD, n = 8). Significance level *p* according to the t-test for unpaired samples

	DPL	LPD	<i>p</i>
HAMA . . . . .	23.8	15.6	.04
VNVA 1-11 . . . . .	15.4	10.6	.001
VNVA 12-43 . . . . .	39.2	22.4	.02
GRS-O . . . . .	79.8	70.3	ns
GRS-S . . . . .	78.4	63.4	ns
Mean age . . . . .	46.4	48.1	ns
Sex : M . . . . .	3*	4	ns
F . . . . .	6	4	ns

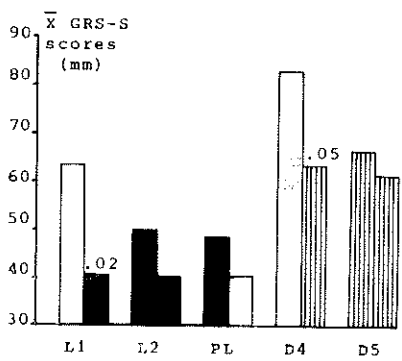
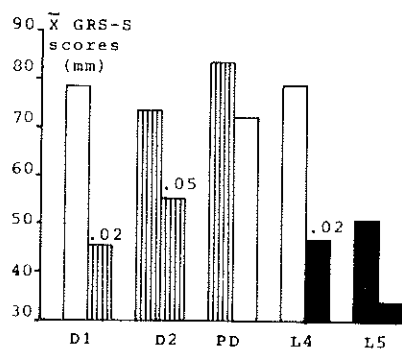


FIG. 1. — Mean pre- vs. postinjection scores of the self-evaluated Graphic Rating Scale (GRS-S). Significance level of the differences according to the t-test for paired samples. D1 = first day, diazepam ; D2 = second day, diazepam ; PD = post-diazepam placebo day ; PL = post-lorazepam placebo day ; L4 = fourth day, lorazepam ; L5 = fifth day, lorazepam. Columns : white = placebo ; striped = diazepam ; black = lorazepam ; pre-injection columns refer to the medication of the previous day.

Figure 1 illustrates the effect of the iv injections on global self-evaluation. Above, the pre- v. post-injections scores of the DPL group ; below, of the LPD group. According to patients' selfreports on the Graphic Rating Scale, diazepam injections induce a significant psycho-relaxing effect in 3 out of 4 occasions, lorazepam in 2 out of 4 occasions.

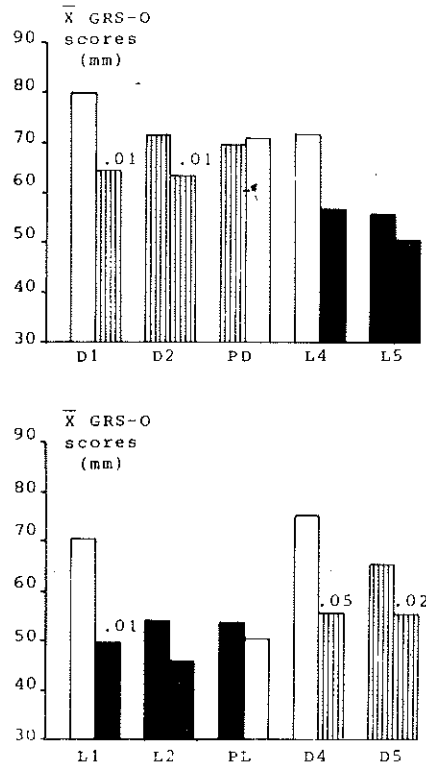


FIG. 2. — Mean pre- vs. postinjection scores of the Graphic Rating Scale filled out by the time-blind observers (GRS-O). For more details, see figure 1.

Observers' scores on the GRS (fig. 2) and on the VNVA Scale (fig. 3) point to a similar difference : significant improvement after diazepam in all 4 occasions ; after lorazepam, in 1 occasion according to the GRS scores, in 3 occasions according to VNVA ones.

Nevertheless, a careful analysis of data brings to light the fact that pre-injection scores are always the lowest ones on the morning following a lorazepam night, be it the GRS self- and observer-scores (fig. 4) or the VNVA scores (fig. 5). It might therefore be hypothesized that the

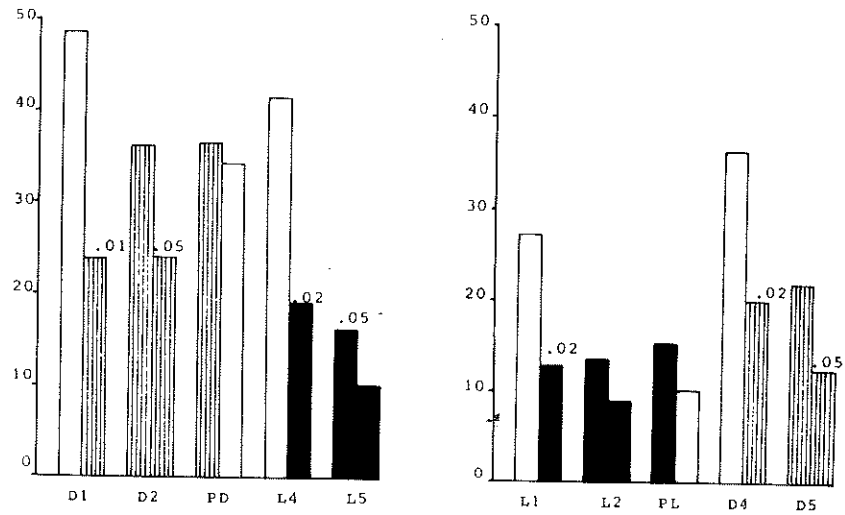


FIG. 3. — Mean pre- vs. postinjection scores of the Verbal and Non-Verbal Anxiety Scale (VNVA). For more details, see figure 1.

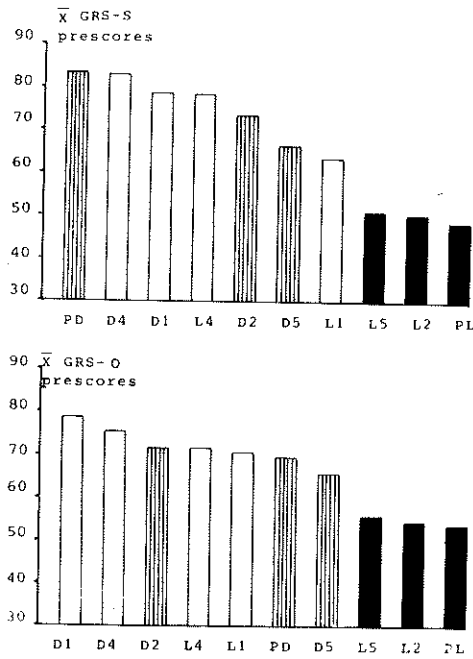


FIG. 4. — Pre-injection scores of the subjects' and observers' Graphic Rating Scale (GRS-S, GRS-O) in rank order. For more details, see figure 1.



second lorazepam injection is less active than the first one because of lower baseline levels of anxiety. On the other hand, pre-injection score differences are not significant.

Item score differences are significant for 18 items after diazepam on day 1, against 6 items after lorazepam, but it must be recalled that DPL patients were initially much more anxious than LPD ones. On

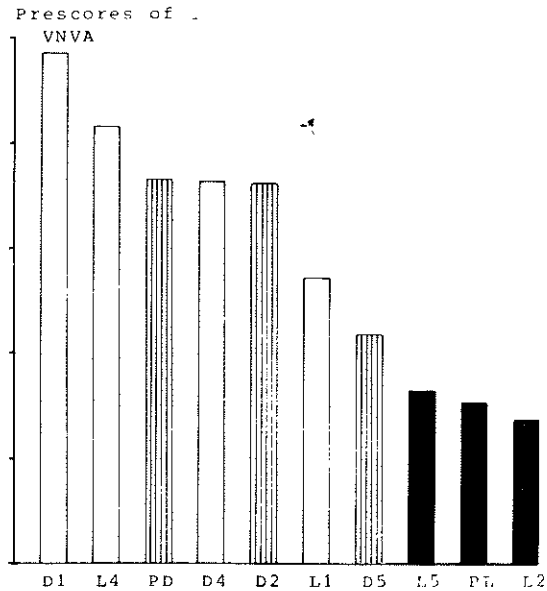


FIG. 5. — Pre-injection scores of the Verbal and Non-Verbal Anxiety Scale (VNVA) in rank order. For more details, see figure 1.

day 4, after baseline scores have become similar in both groups, the reverse effect is observed : 16 items significantly improve after lorazepam, against 5 after diazepam.

The logical analysis of significant improvements demonstrates that some items are sensitive to both drugs (such as fearful anticipation, perplexity, constrictions and sweating), but that very few of them are either drug-related, i.e. improved after one drug only but in one group only, or drug-specific, i.e. improved after one drug only and in both groups (table III). No anxiety item is specific for lorazepam, while 4 items are probably related or specific for diazepam : *dramatization, stomach complaints, cardiac sensations and dry mouth.*



TABLE III

Items of the HAMA and VNVA scales significantly improved after one drug only but on one occasion only (without asterisk) vs. after one drug only and on both occasions (with asterisk). Significance level .05 according to the t-test for paired samples for pre- vs. postinjection scores + logical analysis according to Lewis Carroll for drug-specific changes.

		DIAZEPAM	LORAZEPAM
HAMA		0	Tension* Cardiovasc. sympt. Behavior*
	before inj.	0	Inner tension Ruminations Musc. tension* Inner restless. Motor restless. Dizziness Rate of speech
VNVA		0	
<hr/>			
HAMA		0	0
	after inj.	Dramatization* Stomac* Cardiac* Dry mouth	Drowsiness*
VNVA			

*Drowsiness* worsens after lorazepam only, at the .05 level of significance. Tremor of hands, pulse rate and patellar reflexes significantly improve after both psychorelaxants and to the same extent. *Systolic blood pressure* significantly drops after both drugs on the first day, but this drop persists on the second day on diazepam only. A significant drop in *diastolic blood pressure* is specific for both diazepam second days (D2 and D5).

Let us now come to the analysis of day-to-day pre-injection scores (fig. 6). A double line refers to a lorazepam day, a single line to a

diazepam day, and a dotted line to a placebo one. The global evaluation by the patients and by the time-blind raters give very similar profiles, especially for the LPD group. The only significant 24 h improvements occur after lorazepam, the only significant worsening after placebo.

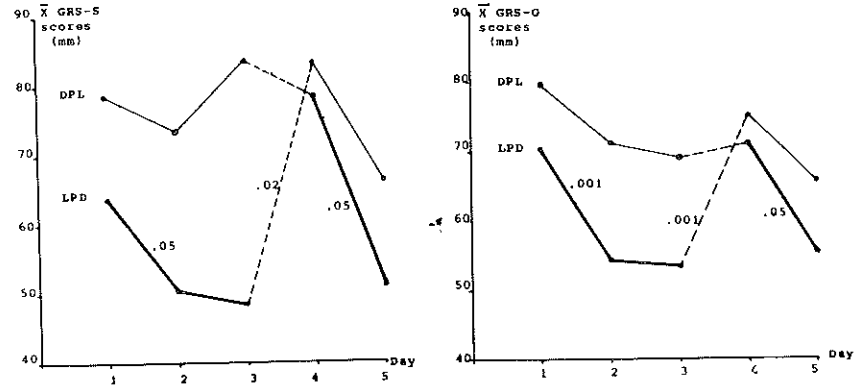


FIG. 6. — Pre-injection scores of the subjects' and observers' Graphic Rating Scale (GRS-S, GRS-O) for the diazepam-placebo-lorazepam patients ( $n = 9$ ) and for the lorazepam-placebo-diazepam ones ( $n = 8$ ). Significant level of the differences according to the t-test for paired samples. Lines: single = diazepam day; double = lorazepam day; dotted = placebo day.

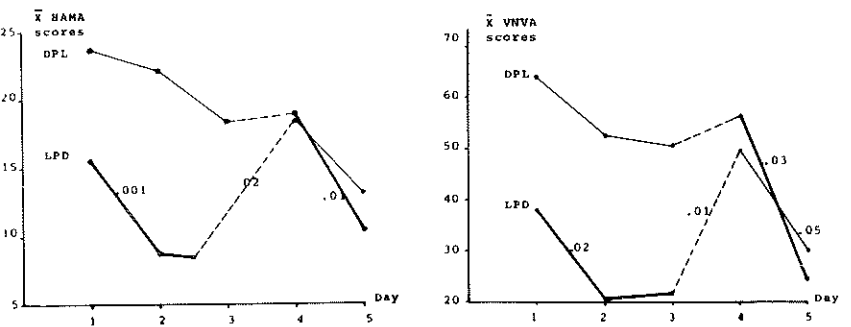


FIG. 7. — Pre-injection scores of the Hamilton Anxiety Scale (HAMA) and of the Verbal and Non-Verbal Anxiety Scale (VNVA) rated by the time-blind observers. For more details, see figure 6.

HAMA and VNVA total scores (fig. 7) stress the same profile. On both scales, the first lorazepam day is characterized by a significant improvement in both groups, whereas diazepam is responsible for a significant improvement in one group only and on one scale only, namely, the VNVA.

Neither Hamilton factor score — psychic score or somatic score — is significantly improved after any diazepam day, while both factors reach significantly lower values after the first and the fourth lorazepam days (at the .02 and .01 level for the psychic score, at the .05 level on both days for the somatic score).

HAMA item score significant differences indicate that

- a) more items improve after either drug on the first day than on the second day ;
- b) more items improve after lorazepam than after diazepam ;
- c) the only worsenings happen after the placebo day only, and in the LPD group only.

The logical analysis of HAMA item score differences (table III) demonstrates that no item specifically improves after a diazepam day, whereas 3 items are related to or specific for lorazepam : *tension*, *cardiovascular symptoms* and *behavior at interview*.

The statistical analysis of VNVA item scores give the same results as for the HAMA item scores : more items improve on the first day of either drug, more items improve after lorazepam than after diazepam. The logical analysis of these significant differences restricts to the following items the ones possibly related to or specific for lorazepam : *inner tension*, *ruminations*, *muscular tension*, *inner restlessness*, *motor restlessness*, *dizziness* and *rate of speech*. No single item remains related to or specific for diazepam.

Drowsiness is near to nil each morning. As regards the HAMA item on insomnia and the 3 VNVA items on sleep (difficulties in falling asleep, startled awakenings and nightmares), the relevance of the few significant differences is impaired by rebound phenomena, that cannot be further analyzed due to the rapid drug shifts in our trial. Nevertheless, if one ranks the averaged means for L2+L5 pre-injection item scores (corresponding to lorazepam nights), D2+D5 means (corresponding to diazepam), L4+D4 (corresponding to placebo) and L1+D1 (corresponding to washout), it becomes apparent that patients on lorazepam, as compared to diazepam and placebo, fall faster asleep, recall less awakenings and less nightmares but are slightly drowier in the morning.

All physiological measurements that significantly improve or worsen after the iv injections (tremor of hand, patellar reflexes, blood pressure and pulse rate) are not significantly modified by either drug at 24 h intervals.

## Conclusions

### Regarding the method.

1. The *video* methodology represents a major asset in clinical psychiatric research since it allows, among others, a time-blind evaluation and multirater evaluations. On the other hand, the artificiality of the CCTV setting as compared to the ward setting may be responsible for a loss of clinically relevant information. For example, in the present trial, patients, nurses and doctors-in-charge reported on lorazepam a mood-elevating effect that was not perceived in the standardized studio situation.

2. Despite its high variance, the *Graphic Rating Scale* seems to give valid information, since its scores were very similar for patients and observers.

3. *Hamilton* and *VNVA* total scores parallel global evaluation, but the *VNVA* Scale demonstrates a significant improvement once more than the *Hamilton* Scale. In day-to-day differences, 46 % of *HAMA* items are significantly modified, against 53 % of *VNVA* items, despite similar training. The *VNVA* interview requires on an average 6 mn for all 43 items, 4 mn for the strictly situational 32 items.

4. The *simultaneous evaluation of verbal and non-verbal information* was biased by the pre-eminence of the former one. This aspect will be discussed at length on a later occasion.

5. The combination of a *crossover design* and of the *Lewis Carroll logical analysis* allowed to go far beyond the mere statistical analysis of significant differences by sorting out drug, sequence and group. Without these two methods, drug-specific items could have not been demonstrated.

6. The usefulness of all second days on the same drug was limited by the improvement consequent to the first day or, in some cases, by rebound phenomena. It appears that such a second day is too much or not enough.

### Regarding the drugs.

1. Both diazepam and lorazepam at 10 v. 5 mg induce a significant psychorelaxation, contrary to placebo in our sample.

2. *The effect of the iv injection* itself may be summarized as follows :

a) according to *GRS-S*, *GRS-O* and *VNVA* total scores, 10 mg diazepam are superior to 5 mg lorazepam, but these results may have



been altered by two facts : on all scales, all pre-injection scores subsequent to a lorazepam night are the lowest ones, which reduces the chance of a significant improvement after injection, and — for the same latency of action of about 5 mn — the pharmacokinetics of both psycho-relaxants is dissimilar : diazepam reaches its peak faster than lorazepam and decreases faster ; in other words, the 20 mn lapse between both interviews was probably favoring diazepam ;

b) according to item scores on day 4, when total scores are homogeneous, 16 items are significantly improved after lorazepam against 5 items after diazepam.

3. The *effect of the 24 h parenteral treatment* is, according to all psychometric approaches, superior with lorazepam :

a) GRS-S, GRS-O and HAMA total scores significantly improve after lorazepam days only in both patient groups ; VNVA total score demonstrates a significant improvement after 2 lorazepam days, against 1 diazepam day ;

b) HAMA factor scores significantly improve in no diazepam occasion but in both lorazepam ones ;

c) more HAMA and VNVA item scores significantly improve after lorazepam days than after diazepam days.

4. Within the limits of our procedure, the *qualitative differences* between both psychorelaxants may be summarized as follows :

a) no drug-specificity could be demonstrated as regards a preferential effect on psychic or on somatic anxiety ; 5 mg lorazepam appear superior to 10 mg diazepam on both types of anxiety ;

b) 20 mn after an iv injections, 3 items are improved to a significant level after diazepam only and in both patient groups : dramatization, stomach complaints and cardiac sensations ;

c) on a 24 h basis, reported inner tension and muscular tension are specifically improved by lorazepam, without a significant modification of patellar reflexes or tremor of hands ; though not significant, there is a trend for lorazepam to be superior to diazepam as regards difficulty in falling asleep, awakenings and nightmares ;

d) as regard side-effects, systolic and diastolic hypotension are specific for diazepam, drowsiness specific for lorazepam.

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## RESUME

*Evaluation vidéo en temps aveugle d'injections de diazepam, de lorazepam et de placebo.*

Dix-huit patients hospitalisés et souffrant d'une anxiété grave ont reçu durant cinq jours, à double insu et en administration croisée, des injections iv et im de 10 mg de diazepam, de 5 mg de lorazepam ou de sérum physiologique à raison de trois injections quotidiennes. L'injection matinale était iv; elle était faite dans un studio de TVCF. Avant l'injection et vingt minutes plus tard, les patients remplissaient la ligne analogique de 10 cm, tandis que leur thérapeute procédait à un entretien standardisé et à des mesures biologiques (tremblement des mains, réflexes patellaires, pression artérielle, pouls).

Les enregistrements vidéo furent cotés dans une séquence aléatoire, i.e. en temps aveugle, par deux observateurs indépendants qui remplirent trois échelles: la ligne analogique (VAS), l'échelle d'anxiété de Hamilton et une nouvelle échelle d'anxiété verbale et non verbale (VNVA). L'analyse statistique fut complétée par une analyse logique d'après Lewis Carroll.

Les résultats montrent la supériorité du lorazepam sur le diazepam sur les paramètres d'anxiété psychique, d'anxiété somatique, de sommeil et de pression artérielle, le seul effet indésirable significatif du lorazepam étant la somnolence.

## SAMENVATTING

*De video en « time-blind » benadering van de gevolgen van het toedienen van Diazepam, Lorazepam en placebo inspuitingen.*

Gedurende vijf dagen werden achttien gehospitaliseerde, zeer angstige patiënten, dubbel blind en met gekruiste toediening, driemaal daags iv en im ingespoten met 10 mg Diazepam, 5 mg Lorazepam of fysiologisch serum. De morgen inspuiting werd toegediend in een TVCF-studio. Vóór de inspuiting en 20 minuten erna werd de patiënten gevraagd de 10 cm lange « analogie » lijn in te vullen terwijl een therapeut hen een gestandaardiseerde vragenlijst voorlegde en biologische metingen deed (handbeven, kniepeesreflexen, pols en bloeddruk).

De video opnamen werden gecodeerd, in wisselende delen en in « time-blind », door twee afzonderlijke medewerkers die drie verschillende schalen gebruiken: de « analogie » lijn (VAS), de angstschaal van Hamilton en een nieuwe, verbale en niet verbale angstschaal (NNVA). De statistische ontleding werd gevolgd door een logische analyse naar Lewis Carroll.

Lorazepam had een betere invloed dan Diazepam op de psychische en de lichamelijke angstuïtingen, de slaap en de bloeddruk, maar gaf ook als enige ongewenste bijwerking meer slaperigheid.

#### ZUSAMMENFASSUNG

*Zeitblinde Video-Auswertung von Diazepam, Lorazepam und Placebo Injektionen.*

Achtzehn schwer ängstliche stationäre Patienten erhielten 3 mal täglich iv bzw. im. Injektionen von 10 mg Diazepam, 5 mg Lorazepam oder NaCl, während 5 Tagen und nach einem Doppelblind-Crossover Protokoll. Die morgendliche Verabreichung war intravenös und fand im Fernsehstudio der Klinik statt. Vor der Injektion und 20 mn danach wurde von dem Therapeuten ein standardisiertes Interview vorgenommen ebenso wie biologische Messungen (Hand-Tremor, Patellarreflexe, Blutdruck, Puls); die Patienten kreuzten ihr Befinden auf der 10 cm-Analogskala an.

Die Video-Aufnahmen wurden in einer randomisierten Reihenfolge — d.h. nach dem Zeitblind-Verfahren — von zwei unabhängigen Beobachtern ausgewertet, die drei Skalen ausfüllten: die Analogskala (VAS), die Hamilton Angst-Skala und eine eigene « verbale und nichtverbale Angst-Skala » (VNVA). Die übliche statistische Analyse wurde vervollständigt durch die sog. logische Analyse nach Lewis Carroll.

Die Ergebnisse zeigen die Überlegenheit von Lorazepam über Diazepam für die Parameter der psychischen Angst, der somatischen Angst, der Schlafstörungen und des Blutdruckes. Die einzige signifikante und spezifische Nebenwirkung von Lorazepam war die Schläfrigkeit der Patienten.

#### RIASSUNTO

*Valutazione video in « time-blind » di somministrazione iniettiva di diazepam, lorazepam e placebo.*

Diciotto pazienti ricoverati e colpiti da ansia grave hanno ricevuto durante cinque giorni in doppio cieco ed in somministrazione incrociata del diazepam 10 mg, del lorazepam 5 mg e soluzione fisiologica, iv e im tre volte il giorno. L'iniezione mattutina, endovenosa, avveniva in uno studio di TVCF. Prima della somministrazione e 20 minuti dopo il paziente completava la linea analogica di 10 cm, mentre il terapeuta procedeva in un colloquio standardizzato e a delle misurazioni biologiche (tremore delle mani, riflessi patellari, pressione sistemica, polso).

Le registrazioni video furono quantificate in una sequenza aleatoria, i.e. in « time-blind », da parte di due osservatori indipendenti che riempirono tre scale: la linea analogica (VAS), la scala per l'ansia di Hamilton ed una nuova scala d'ansietà verbale e non verbale (VNVA).

L'analisi statistica venne completata da un'analisi logica secondo Lewis Carroll. I risultati evidenziano la superiorità del lorazepam sul diazepam nei parametri dell'ansia psichica, dell'ansia somatica, del sonno e pressione sistemica, col solo effetto secondario della sonnolenza.



## RESUMEN

*Evaluación en « time-blind » de inyecciones de diazepam, de lorazepam y de placebo.*

Diez y ocho pacientes hospitalizados han recibido durante 5 días, en « double-blind » y en administración cruzada, inyecciones iv e im de 10 mg de diazepam, de 5 mg de lorazepam o de suero fisiológico a razón de tres inyecciones cotidianas. La inyección matinal era iv; era hecha en un estudio TVCF. Antes de la inyección y 20 mn después, los pacientes rellenaban la línea analógica de 10 cm; durante este tiempo su terapeuta procedía a una entrevista uniformada y a medidas biológicas (temblor de las manos, reflejos patelares, presión arterial, pulso).

Las secuencias pasadas in video fueran anotadas en « time-blind » por 2 observadores independientes que rellenaron 3 escalas: la línea analógica (VAS), la escala de ansiedad de Hamilton y una escala nueva de ansiedad verbal y no verbal (VNVA). El análisis estadístico fue completado por un análisis lógico (Lewis Carroll).

En lo que se refiere a su acción sobre las ansiedades psíquicas y somáticas, el sueño y la presión arterial, el lorazepam se revela superior, su solo efecto indeseable es la somnolencia.

Daniel P. BOBON, M.D.  
Department of Psychiatry  
Rue Saint-Laurent 58  
B-4000 Liège (Belgium, EEC)