

## The Use Of Nicergoline In The Reversal Of Behavioural Changes Due To Ageing In Dogs: A Multicentre Clinical Field Trial

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Until recently, it was widely accepted that although specific diseases of the ageing dog such as arthritis could be at least partially treated, the behavioural changes associated with the ageing process were inevitable and irreversible.

Since the launch of FITERGOL<sup>®</sup> last year by Rhone Merieux, the outlook for the older dog has dramatically improved. FITERGOL<sup>®</sup> has been widely used for the treatment of age related changes in the older dog such as increasing lethargy, sleep disorders, loss of exercise tolerance and age-associated incontinence.

It contains the active component nicergoline, an  $\alpha$ -1 and  $\alpha$ -2 antagonist which acts specifically on the vascular system and cells of the brain. Its clinical actions are based on the fact that nicergoline acts to increase oxygen supply to the brain, thereby reversing the chronic hypoxia which is thought to be one of the main factors underlying age-related behavioural disorders. In addition, nicergoline exerts a neuroprotective action on the neural cells which limits damage caused by chronic hypoxia or anoxic attacks (such as during a fit or "stroke"-like episode) and increases the rate of recovery following damage due to hypoxia.

Following the launch of FITERGOL<sup>®</sup>: in the UK, a multi-centre field trial was set up in this country with the primary aim of collecting individual case studies to illustrate the specific types of disorders which are most likely to benefit from treatment with FITERGOL<sup>®</sup> and to aid veterinary surgeons in case selection.

The trial included 109 dogs from 14 veterinary practices in the UK. In each practice the veterinary surgeon was asked to select up to 20 dogs showing behavioural changes associated with ageing. With the owner's consent, each dog was treated with FITERGOL<sup>®</sup> at the recommended dose rate for one month. A full clinical examination was carried out by the veterinary surgeon at the start of the trial, including a questionnaire on all aspects of the behaviour and medical history of the dog to be completed in conjunction with the owner.

Concurrent treatment was permitted for pre-existing diseases as long as the treatment was long term and the condition was stable (e.g. on-going treatment for heart disease).

The owners were asked to administer the FITERGOL<sup>®</sup> tablets orally either "straight-down" or crumbled onto food. At the end of the one month trial, the owner was asked to return the dog for a further full examination and comparison of clinical signs with the previous month.

### Results

Eighty-nine dogs completed the trial. Over 75% of dogs showed significant overall improvement (see table 1). The results of the questionnaire completed at the start of the trial were compared statistically with those at day 30 in order to highlight the types of conditions which had responded to treatment.

Change	Percentage (n=89)
Deteriorated	2.5%
No change	21%
Improved	76.5%

Table 1. Overall improvement as assessed by the veterinary surgeon.

These can be broadly separated into the following categories:

- Loss of activity,
- Sleep disorders,
- Episodes of collapse/fits/"stroke"-like symptoms,
- Loss of house training and incontinence,
- Loss of appetite,
- Decreasing awareness.

### 1. Loss of activity

The results showed that there was a significant increase in activity level and enthusiasm in dogs on the trial (Table 2).

Dogs were often less listless, able to exercise for longer before tiring and more enthusiastic to go for walks. In addition, treatment with FITERGOL® often increased the mobility of individual animals allowing them to walk and run more easily and often to regain the ability to tackle difficult pathways (such as climbing into the boot of the car or up the stairs).

Change	Percentage
Decreased activity	3.5%
No change	29%
Increased activity	67.5%

Table 2. Improvement in activity(p<0.01)

### 2. Sleep disorders

One of the commonest problems of the older dog is that they tend to sleep for a large part of the day but are restless at night, often to the extent of disturbing the owner. Following treatment with FITERGOL®, significantly more dogs slept for less than one third of the day and fewer suffered from disturbed sleep during the night (Table 3).

Time	Percentage (n=81)
Day 0	14%
Day 30	4%

Table 3. Percentage of dogs showing disturbance of sleep at night

### 3. Episodes of collapse/fits/"stroke"-like symptoms

Analysis of the results showed that treatment with FITERGOL® was likely to reduce significantly the incidence of sudden "attacks" including episodes of collapse, occasional fits or

"stroke-like episodes" (Table 4). In many cases, the aetiology of the attack is uncertain but it is widely thought that sudden hypoxia or anoxia of the brain may be involved. In addition to the pharmacological effect of FITERGOL<sup>®</sup> in increasing the oxygen supply to the brain and thereby reducing the likelihood of anoxic "attacks", the neuroprotective action of FITERGOL<sup>®</sup> may help to reduce the damage caused by such attacks and to increase the rate of the recovery. The neuroprotective effect is based on a stabilisation of enzyme systems and of the neural cell membrane during periods of hypoxia and supports the longterm use of FITERGOL<sup>®</sup> in dogs suffering from such disorders.

Time	Percentage (n=84)
Day 0	20%
Day 30	8%

Table 4. Percentage of dogs showing collapse/"stroke-like" episodes.

#### 4. Loss of house training

This is one of the most distressing problems of ageing both for the dog and in particular for the owner who may be subjected to severe inconvenience as the problem becomes worse. The incontinence may take the form of urinary incontinence or occasional faecal incontinence or a combination of both. The trial results showed that there was a distinct tendency for FITERGOL<sup>®</sup> to help in these situations and often to lead to full recovery of house-training (Table 5). It must be stressed that FITERGOL<sup>®</sup> will not help in all cases of incontinence but is most likely to be of use in dogs in which the incontinence has a gradual onset associated with ageing.

Time	Percentage (n=84)
Day 0	19%
Day 30	11%

Table 5. Percentage of dogs showing incontinence.

#### 5. Reduced appetite

Many older dogs, especially of the smaller breeds, tend to become very "picky" with food and lose their appetite as they get older. Following treatment with FITERGOL<sup>®</sup>, dogs showed a significant improvement in appetite and were generally more enthusiastic at meal times (Table 6).

Time	Percentage (n=84)
Day 0	15%
Day 30	2%

Table 6. Percentage of dogs showing reduced appetite.

#### 6. Decreased awareness

A gradual loss of hearing and sight is a common finding in dogs as ageing occurs. The trial results showed a significant improvement in the reaction to sight or sound in dogs with

these problems. This suggests that FITERGOL<sup>®</sup> may help to reduce the effects of age-related chronic hypoxia on the processing of information relating to sight and sound at a central level. Alternatively, the increased reaction to sight and sound may be the result of an increased level of alertness in the dogs treated with FITERGOL<sup>®</sup> (figure 7).

In those dogs showing signs of confusion or senility (e.g. "barking at the moon") treatment with FITERGOL<sup>®</sup> often led to a distinct improvement or disappearance of the clinical signs although there were insufficient numbers for statistical analysis.

Time	Percentage (n=83)
Day 0	14%
Day 30	8%

Table 7. Percentage of dogs showing decreased awareness.

### 3 Case Studies

Included are four case studies from individual dogs on the trial. They are intended to illustrate the types of age-related behavioural problems which were shown to respond to treatment with FITERGOL<sup>®</sup>.

#### Case 1

A 12-year-old male neutered German Shepherd Dog presenting due to "a general slowing down and loss of interest" associated with ageing. FITERGOL<sup>®</sup> was prescribed and administered by crumbling onto food.

At the end of the trial he was much more lively and active. He tired much less quickly on walks and was generally more enthusiastic and welcoming to his owner.

Overall conclusion: improved.

#### Case 2

A 16-year-old male neutered Yorkshire Terrier, presenting with signs of ageing including sleeping for a large part of the day, loss of enthusiasm lethargy and jumping at shadows". FITERGOL<sup>®</sup> was prescribed and administered by crumbling onto food.

After 30 days treatment, he was much improved. He was more enthusiastic to go for walks, able to walk for longer and more normally and slept less during the day. In addition, the strange episodes of "jumping at shadows" completely disappeared.

Owners comment: "I didn't think he would make it when we first took him to the vets but he's now full of life - he's even able to get up and down the stairs again."

Overall conclusion: improved.

#### Case3

A 12-year-old male cross bred, presenting with age associated urinary incontinence which occurred especially at night and general signs of ageing including decreased appetite. FITERGOL<sup>®</sup> was prescribed and administered by crumbling onto food.

By the end of the trial the incontinence had disappeared. In addition, his general demeanour had significantly improved, he was much more active and willing to go for walks and his appetite was more normal.

Overall conclusion: improved.

#### Case 4

A 13-year-old female neutered Labrador Retriever presenting due to a recent "slowing down", increased lassitude and loss of enthusiasm. She was also showing increasing deafness as she became older and occasional "messaging in the house". FITERGOL<sup>®</sup> was prescribed and administered by crumbling onto food.

At the end of the one-month trial, she appeared a generally happier dog ('jumping up more and wagging her tail!'). She tired less easily and was more active and willing to exercise. Her appetite was improved and the occasional episodes of incontinence had disappeared. Her reaction to sight and sound was also improved.

Overall conclusion: improved.

As can be seen from the results given above and the case studies, FITERGOL<sup>®</sup> may help in a variety of situations to improve the quality of life of the older dog and consequently the owner. Individual responses may vary according to the underlying pathology, but the effects of FITERGOL<sup>®</sup> in increasing the supply of oxygen to the brain and in neuroprotection of cerebral tissue make it a useful tool in many of the age-related behavioural problems occurring in older dogs.

This trial was by no means exhaustive and it is certain that future studies and widespread use will increase the range of age-related behavioural changes known to respond to treatment with FITERGOL<sup>®</sup>.