

*Present day practice**

Premedication with lorazepam before bone marrow biopsy

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SUMMARY Fifty patients were randomised in a double blind placebo controlled study to examine the influence of lorazepam (4 mg orally) before bone marrow aspiration and trephine biopsy. Assessment was made by a visual analogue linear pain scale compiled after the procedure and again 24 hours later. There was no difference in the pain recalled immediately after the procedure between the two groups, but the next day the patients who had received lorazepam showed amnesia with a 60% ($p < 0.01$) reduction in the pain scale; 36% of the patients in this group had no recall of the procedure at all. There was no amnesic effect in the group taking placebo. Side effects were few, and it is concluded that lorazepam is a useful premedication agent before bone marrow biopsy.

Bone marrow aspiration has been in common use for the investigation of haematological disorders for many years. In adults it is often carried out from the sternum under local anaesthetic. It is rapid to perform, and if the periosteum is well infiltrated, is only associated with transient pain during the period of suction. Since the 1970s haematologists have appreciated the advantage of a bone marrow biopsy undertaken at the same time as aspiration. Although initially used only in those patients in whom bone marrow smears were inadequate, bone marrow biopsy is now commonly carried out on all patients. Usually Jamshidi or Islam biopsy needles are used. These are considerably larger than the standard aspiration needles and the biopsy is usually taken from the posterior or anterior iliac spine. Cores of 20×2 mm are removed.

The addition of marrow biopsy has considerably increased the discomfort of the procedure and we felt that local anaesthetic infiltration alone was inadequate. Although in this area bone marrow biopsy in

children is always undertaken under general anaesthetic, this would be impractical and probably unjustified in adults. We decided to test the effect of the addition of lorazepam, an anxiolytic and amnesic agent, to see if it made the investigation more tolerable and recollection less unpleasant.

Patients and methods

All patients aged 15-75 years who required bone marrow biopsy but who had never had one were eligible. They were randomised to receive either oral lorazepam 4 mg or an identical placebo 90-120 minutes before the bone marrow biopsy. The randomisation code was held by the pharmacy. Patients with renal or hepatic impairment were excluded. To qualify patients had to be able to understand the nature of the study and give informed consent. Local ethical committee approval was obtained.

Twenty three women and 27 men were entered (mean age 53 years, range 15-75). After normal skin preparation and five minutes after instillation of 5 ml 2% lignocaine to the skin and deeper tissues bone marrow aspiration and biopsy from the posterior iliac spine was carried out by one of the two authors experienced in the technique. Two millilitres of bone marrow were aspirated using a standard needle and a bone marrow core of 10-20 mm was removed using a 100×2.1 mm Islam biopsy needle (Downs Surgical

*Occasionally articles are received which are appropriate to the generic *Present Day Practice*. The heading has been used by the Journal in the past, and the Editors are pleased to receive short papers written with this section in mind. Manuscripts should be brief (less than 1000 words) and have a minimum of tables, figures, and references.

Ltd, Mitcham, Surrey). Fifteen minutes after the test patients were asked to complete a visual analogue pain score^{1 2} by making a vertical line on the point which best represented the pain felt.

I did not have any _____ 10 cm _____ The pain could not have been worse

Twenty four hours later they were asked to recall the pain felt during the test and to score an identical pain scale so that an estimate of the amnesic effect of the drug could be gauged. The pain score was estimated in millimetres (range 0–100). The results within each group were analysed by the Wilcoxon sign rank sum test and between the groups by the Mann-Whitney U test.

Results

Of the 50 patients entered, we were unable to examine data on four. One patient receiving lorazepam became dysphoric and agitated and a successful biopsy was not possible. Two further patients (one treated with placebo, one with lorazepam) were unable to comprehend the pain scale and a further patient (given placebo) died shortly after the marrow test, of an unrelated cause. Data were thus analysed from 46 patients (24 treated with placebo and 22 with lorazepam). The mean age for each group was 53 and 51 years, respectively (figure). In the group treated with placebo there was no noticeable amnesic effect 24 hours after the test; but in the group receiving lorazepam the main pain score on recall 24 hours later was 60% less than 15 minutes after the procedure (95% confidence interval 40–80%, $p < 0.01$). In addition, the mean scored recall of pain the next day was only 14.7 in the group treated with lorazepam compared with 41.5 in the group given placebo ($p = 0.0004$). The discomfort experienced and recalled immediately after the test was similar in both groups, suggesting that lorazepam had no noticeable analgesic effect.

With the exception of the one patient who became dysphoric no patient complained of adverse side effects. Sedation normally persisted for several hours but patients did not find this unpleasant.

Discussion

Lorazepam has been used widely in other fields as premedication. It is an effective anxiolytic and amnesic before surgery³ and bronchoscopy.⁴ Because of its powerful amnesic properties, it has also been used to reduce unpleasant recall and anticipatory vomiting after treatment with cisplatin.⁵

We chose to give it orally for a variety of reasons. Intravenously it is quite slow to act,⁶ which does not

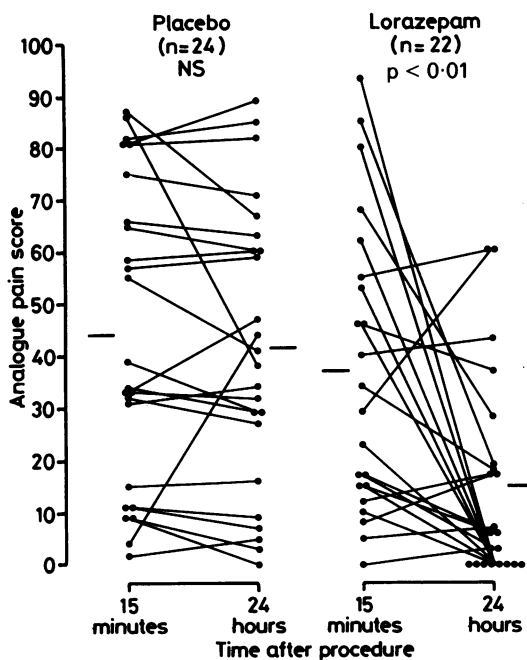


Figure Analogue pain scores of 15 minutes and recall 24 hours after bone marrow biopsy in both groups. Horizontal bars represent mean values.

allow the test to be carried out immediately, and in common with all benzodiazepines is poorly soluble in water and can be painful to inject. Oral absorption is reliable, with an effective concentration after 60 minutes,⁷ and avoids the additional trauma of a venepuncture. In common with other workers, we found that the incidence of unpleasant side effects was low. Most patients receiving the drug were sedated but were able to cooperate, understand, and complete the pain scale. None of the patients receiving lorazepam complained of distress due to the amnesia and most were relieved to have limited recall of the procedure. The use of sedation in outpatients clearly poses problems and we only used it in those who had private or hospital transport arranged.

Despite the fact that the addition of lorazepam conferred no advantage of analgesia its amnesic properties were impressive. Eight of 22 (36%) of the patients receiving the drug had complete lack of recall of the procedure. In patients in whom bone marrow aspiration and biopsy is likely to be repeated often, (such as patients with leukaemia and lymphoma), amnesia for this procedure is clearly a desirable aim.

It seems to us that had bone marrow biopsy been introduced as a distinct procedure and not added to the already established technique of marrow aspiration better methods of sedation and analgesia

would have been more commonly used. We have found lorazepam to be an effective agent in this context and hope its use will be more widely adopted.

We thank Wyeth (UK) Ltd for supplying lorazepam placebo tablets, and physicians at the General Infirmary, Leeds, for their cooperation.

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