References

1. Dutka AJ. Clinical findings in decompression illness: a proposed terminology. In *Treatment of Decompression Illness: the Forty-fifth Workshop of the Undersea and Hyperbaric Medical Society*. Moon RE and Sheffield PJ. Eds. Kensington, Maryland: Undersea and Hyperbaric Medical Society, 1996
2. *Describing Decompression Illness: The Forty-second Undersea and Hyperbaric Medical Society Workshop*. Francis TJR and Smith DH. Eds. Bethesda, Maryland: Undersea and Hyperbaric Medical Society, 1991
3. Dick AP and Massey EW. Neurologic presentation of decompression sickness and air embolism in sport divers. *Neurology* 1985; 35: 667-671
4. Ball R. Effect of severity, time to recompression with oxygen, and retreatment on outcome in forty-nine cases of spinal cord decompression sickness. *Undersea Hyperbaric Med* 1993; 20 (2): 133-145
5. Gardner M, Forbes C and Mitchell SJ. 100 divers with DCI treated in New Zealand during 1995. *SPUMS J* 1996; 26 (4): 222-226
6. Boussuges A, Thirion P, Molenat F and Sainty J-M. Neurologic decompression illness: a gravity score. *Undersea and Hyperbaric Medicine* 1996; 23 (3): 151-155
7. Kelleher PC, Pethybridge RJ and Francis TJR. Outcome of neurological decompression illness: development of a manifestation based model. *Aviat Space Environ Med* 1996; 67 (7): 654-658

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NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN DECOMPRESSION ILLNESS: A PRELIMINARY REPORT

Mike Bennett

Key Words

Decompression illness, drugs, hyperbaric oxygen, treatment.

Introduction

This brief presentation is a progress report on the multi-centre, randomised controlled trial currently underway into the efficacy of adjunctive tenoxicam (Tilcotil, Roche Pharmaceuticals), a non-steroidal anti-inflammatory drug (NSAID), in the treatment of decompression illness (DCI). The pharmacology of such an agent and the rationale for administration are subjects for another presentation at this meeting and so will not be dealt with in any detail.

At the Prince Henry and Prince of Wales Hospitals in Sydney it has been the practice of some of our clinicians to administer a NSAID as adjunctive therapy for divers (and others) suffering with DCI. Thus, in addition to standard recompression tables and fluid replacement, divers would typically receive piroxicam (Feldene - Roerig Pharmaceuticals) dispersible 20 mg daily for 7 days in the expectation that such treatment may improve the resolution of symptoms both in the short and medium term. This practice was not based on any objective evidence. This study is to elucidate the efficacy or otherwise of this approach. It is in the early stages and no analysis which involves breaking the randomisation code has yet been made.

Rationale of the study

The treatment of DCI has traditionally been limited to recompression, use of 100% oxygen and appropriate decompression schedules. Correction of dehydration and appropriate posturing to prevent any (or further) gas entering the cerebral circulation are accepted as important adjunctive measures.

This regime has proved very effective in treating military and professional divers where recompression facilities are immediately available. However, it has recently become clear that there is a significant rate of incomplete resolution of symptoms and signs in several series of recreational divers with DCI. In Australasia this rate is typically between 20 and 35% of all cases seen.[1-4] This has recently been confirmed in a report from our unit in Sydney.[5] In addition, it is often noted that recreational divers require more treatments to achieve resolution than professionals.

The reasons for these differences are likely to be multifactorial but are assumed to be, at least in part, due to increased times between symptom onset and recompression, although this remains to be clearly demonstrated.[5] A number of adjunctive therapies have been suggested to improve the resolution rate and reduce the number of compressions required. To date no randomised, controlled studies have suggested that any are of practical value. Much of the research that has been done, and is in progress, has focussed on the more dramatic end of the DCI spectrum, including cerebral arterial gas embolism. We do not propose that NSAIDs are likely to significantly alter the course of these profound problems. With regard to the peripheral and less severe forms of the illness, a number of pharmacological modifiers have been suggested, but no formal prospective studies have been reported.

Douglas[6] reported an excellent response to intramuscular diclofenac sodium in a patient with residual pain. The theoretical basis suggested to explain this improvement was the ability of the NSAID to modify the inflammatory response through the inhibition of prostaglandin synthesis. This effect has not been reported in other clinical cases or series.

In a retrospective review, Kizer[7] found that the administration of corticosteroids to a group of patients suffering delays to treatment greater than 12 hours did result in some benefit, but not in the peripheral manifestations of DCI. Aspirin in anti-platelet doses has been reported on by Bove[8] and by Catron and Flynn[9] but no positive benefit elucidated.

While other adjuvant agents are currently under examination, including intravenous lignocaine and high dose steroids, these are aimed at the more severe forms of the disease and we felt it was reasonable to evaluate the role of NSAIDs more effectively at this time.

Method

Ethics committee approval was granted through the Eastern Sydney Area Health Service for a prospective, randomised, masked and controlled study of the efficacy of tenoxicam for the treatment of DCI. All patients presenting to the department with DCI grades one to five would be eligible, with exclusion only for patient refusal and the presence of known contraindications to NSAID administration (Table 1). The protocol flow diagram is shown in Figure 1 (page 96).

Following fully informed consent, a randomisation schedule is consulted to allocate a trial number and a corresponding course of tablets pre-packaged by the pharmacy department of the hospital. Only the Chief Pharmacist has knowledge of the randomisation code, although this is accessible in an emergency. The patient is

TABLE 1

REASONS FOR EXCLUSION FROM NSAID TRIAL

Refusal to consent.
History of sensitivity or complications secondary to NSAID administration.
History or symptoms suggestive of peptic ulceration, upper GIT bleeding, NSAID sensitive asthma or renal impairment.
Concurrent therapy with analgesic medication, anti-coagulants, frusemide, lithium or methotrexate.

TABLE 2

THE ADMISSION SEVERITY CODING TABLE

Grade	Symptoms and signs	Severity
ONE	Pain Rash Itching	Peripheral Mild
TWO	Muscle/joint pain Numbness/tingling Restlessness Headache	Peripheral and/ or Neurological Mild to moderate
THREE	Tinnitus Severe pain Fatigue Altered reflexes	Peripheral and/ or Neurological Moderate
FOUR	Weakness Nausea/Vomiting Hearing loss Personality change Inco-ordination	Peripheral and/ or Neurological Moderate to severe
FIVE	Visual disturbance Speech disturbance Weakness Paralysis Bladder/bowel dysfunction	Neurological and/ or Peripheral Severe
SIX	Reduced level of consciousness Paralysis Convulsions Cardiac dysrhythmia	Neurological and/ or CAGE Severe early onset

Taken from Bond et al.[10] with some modification.

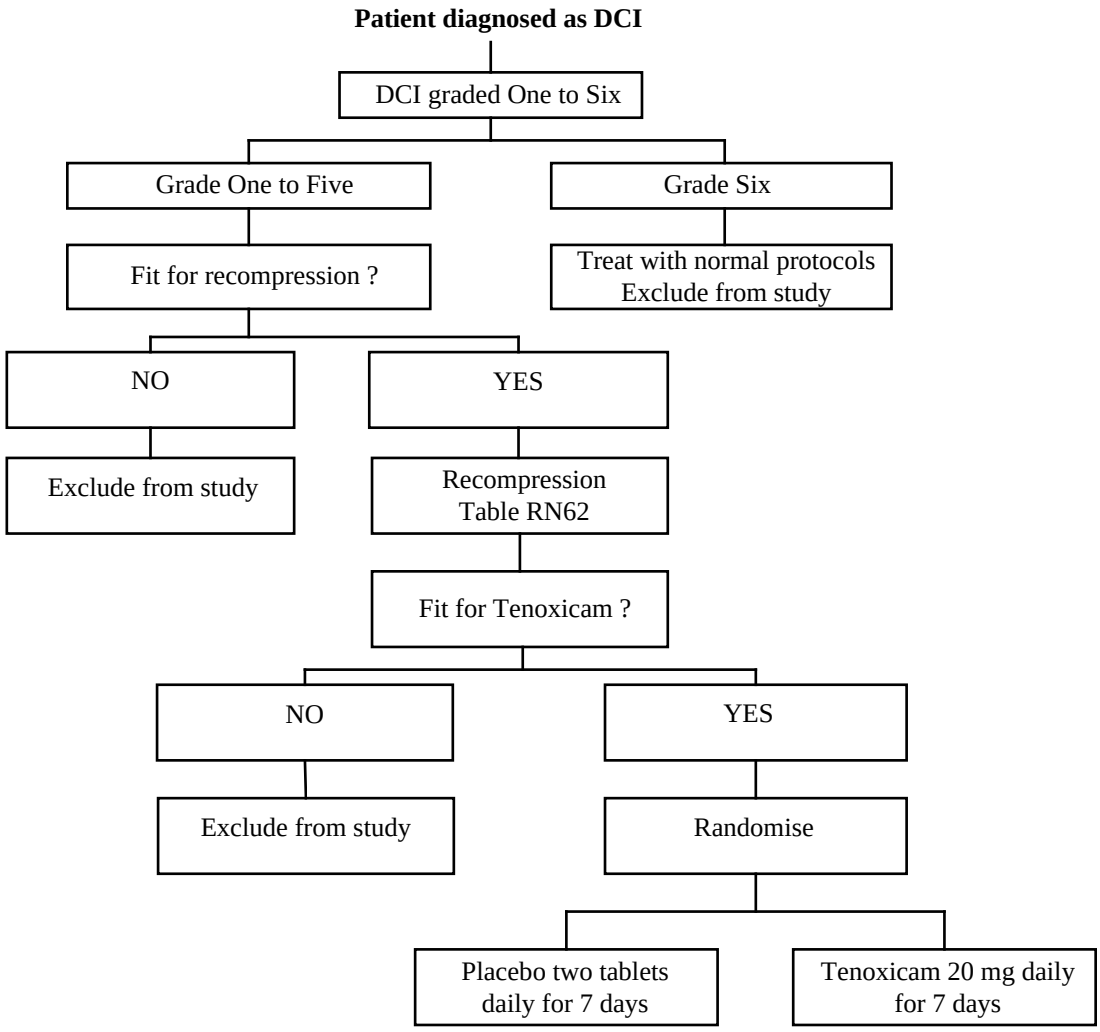

Figure 1. Protocol Flow Diagram.

graded for severity of DCI (Table 2). Grades do not imply bubble load or predict outcome but are generated for inter-unit comparative research. The patient is then recompressed using a standard RN 62 treatment table. At the first air break the patient's condition is reassessed and the first dose of Tenoxicam or placebo administered. Recompression is continued as clinically indicated by symptom resolution or attainment of a recovery plateau and the trial drug administered for seven days. The active treatment group receive 20 mg of Tenoxicam daily over this time. Following completion of the recompression phase of treatment, the patient's health status is assessed and recorded. Further assessments are made at 4 to 6 weeks and 6 months following discharge.

Discharge status is graded, on the scale shown in Table 3 , following clinical assessment at the relevant time. The main distinction sought is any significant difference between level one and levels two to five. Routine neuropsychiatric assessment was not included in this status score as this would be difficult to standardise over geographically separate institutions. All effort was made to make these assessments in the Hyperbaric Unit, however data was accepted from telephone consultations if mandated by practical considerations.

It is not considered, given the present state of our knowledge, that there were any ethical dilemmas involved in the withholding of NSAIDs from the placebo group. The

TABLE 3

DISCHARGE STATUS AT SIX WEEK REVIEW

Level one	Well. No symptoms or signs
Level two	Minor symptoms or signs
Level three	Moderate impairment of function or quality of life.
Level four	Major incapacity.
Level five	Dead

risks associated with short courses of Tenoxicam are well known and unlikely to prove a problem during the remainder of this trial. There have been no attributable side-effects to March 1997.

Based on an expected rate of complete resolution of 75% in the placebo group and an assessment that an improvement to 88% would be clinically significant in the active drug group, it is anticipated that about 180 patients will be needed to have a 90% chance of detecting such a difference with 95% confidence. In order to complete such a study within a reasonable time, other centres have been invited to contribute their patients. In March 1997 the Prince of Wales Hospital and HMAS PENGUIN were actively involved. Two other established Australian centres are to join shortly.

Progress

By March 1997 we had enrolled 26 individuals in the trial. There have been five other cases who did not enter the trial. Three chose to decline the opportunity while one was not asked and in one there was a contraindication to NSAID administration. The randomisation codes have not been broken for this report.

The majority (18 cases) fell into grade two on the admission scale, while the other four groups have contributed 2 cases each. The average number of treatments before discharge is 2.6 at this early stage.

Three cases have not yet had their 6 week follow-up. At this appointment 18 cases had complete resolution of symptoms while some symptoms persisted in 5. This represents a rate of less than complete resolution (discharge level >1) of 21.7%. Lying between the previously published rate for this unit (27%) and the proposed rate for a demonstration of clinically significant efficacy (12%), this result looks promising.

References

1 Weinmann M, Tuxen D, Sheinkestel C and Millar I. Decompression illnesses. 18 months experience at the Alfred Hospital Hyperbaric Unit. *SPUMS J* 1992; 22 (1): 228-231

2 Brew SK, Kenny CT, Webb RK and Gorman DF. A factorial analysis of 125 diving accidents treated at HMNZS Philomel. *SPUMS J* 1990; 20 (4): 226-230

3 Walker R. Fifty divers with dysbaric illness seen at Townsville General Hospital during 1990. *SPUMS J* 1992; 22 (2): 66-71

4 Unsworth IP. Analysis of 100 cases of decompression sickness among Australian sports divers. In: *Proceedings of the Tenth International Congress on Hyperbaric Medicine. Amsterdam* 1990: 65-70

5 Bennett MH. The retrieval of diving injuries in NSW. *SPUMS J* 1995; 25 (3): 142-147

6 Douglas JD. Intramuscular diclofenac sodium as adjuvant therapy to Type I decompression sickness. *Undersea Biomed Res* 1986; 13 (4): 457-460

7 Kizer KW. Corticosteroids in the treatment of serious decompression sickness. *Annals of Emergency Medicine* 1981; 10: 485-488

8 Bove AA. The basis for drug therapy in decompression sickness. *Undersea Biomed Res* 1982; 9: 91-112

9 Catron PW and Flynn ET. Adjuvant drug therapy for decompression sickness: a review. *Undersea Biomed Res* 1982; 14: 101-111

10 Bond JG, Moon RE and Morris DC. Initial table treatment of decompression sickness and arterial gas embolism. *Aviation Space Environ Med* 1990; 61 (8): 738-743

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LIGNOCAINE AND NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AS ADJUVANT THERAPY IN TREATING DECOMPRESSION ILLNESS.

David Cosh

Key Words
Decompression illness, drugs, treatment.

Lignocaine

Simon Mitchell has reviewed the evidence supporting the use of lignocaine, an aminoethylamide local anaesthetic with class 1B anti-arrhythmic properties, as adjuvant therapy to the accepted modalities of compression and hyperbaric oxygen (HBO) in the treatment of decompression illness (DCI).[1] It is well known that tissue damage secondary to the presence of intravascular and extravascular bubbles can be caused by ischaemia, mechanical effects and inflammation. Nellgård et al. have demonstrated a potent anti-inflammatory effect of lignocaine in a rat model of bowel obstruction where jejunal fluid loss was converted into net fluid absorption by the administration of intravenous lignocaine in conventional doses (2 mg/kg). Lignocaine applied topically to the serosa proximal to the ligation was also effective.[2,3]