

At the coalface

Should a doctor prescribe hormone replacement therapy which has been manufactured from mare's urine?

Dennis Cox *The Spinney Surgery, St Ives, Cambridgeshire*

Abstract

Many clinicians are experiencing consumer resistance to the prescription of equine HRT (that is hormone replacement therapy which has been manufactured from mare's urine). In this paper I consider the ethical implications of prescribing these preparations. I decide that patients should have a right to refuse such treatment but also ask whether a prescribing doctor should choose one preparation over another on moral grounds.

I determine that there is prima facie evidence to suggest that mares may suffer and that prescription of equine HRT (instead of synthetic oestrogen – oestriol) would therefore have to be justified in terms of either offering greater benefits to the women or offering greater value for money to the health service. I find that there is no substantial evidence to suggest that equine HRT offers unique advantages over and above oestriol. I conclude that it would be preferable for a doctor to recommend the synthetic oestrogen to women who want relief from the symptoms of the menopause and protection from osteoporosis and cardiovascular disease.

It is unusual for doctors to come across consumer resistance to a drug on ethical grounds; this form of protest is usually confined to such commodities as cosmetics produced by companies which test their products on animals or petrol produced by companies with suspect environmental credentials. Over the past year, however, some GPs and gynaecologists have recommended hormone replacement therapy (HRT) to their patients, only to be confronted by a refusal to accept those products which are derived from pregnant mare's urine.

Whilst this refusal can be seen as a perfectly proper exercise of a woman's autonomy, the doctor is faced with the moral issue of whether it is right to prescribe HRT derived from mare's urine to any of his or her other patients when there is an alternative available which is derived from plants.

Are the mares harmed?

The first question I propose to ask is whether or not the mares are harmed in the production of equine HRT. If there is any evidence to suggest that they are harmed then I would suggest that there is a *prima facie* case for the manufacturers to answer. In other words: any harm to the mares must be outweighed by the benefits which people get from using equine HRT as opposed to plant-derived HRT.

Animal rights' campaigners have made the following allegations¹

- That over 75,000 mares throughout Canada and the North American state of North Dakota were confined for urine collection in 1993.
- The mares are made to produce up to 20 foals in their lifetime.
- That these foals are taken away at about four months old and sold for their meat as industrial by-products.
- That the pregnant mares are confined to tiny individual stalls for months at a time when they are not allowed any exercise.
- That they rub against the stalls and can get infected sores as a result.
- That the mares are attached to urine bags and that this causes them discomfort.

Wyeth, which manufactures Premarin and Prempak-C (equine HRT), counters these allegations by pointing out that the animals have regular veterinary inspections and that they would suffer more if they were left outside, throughout the North American winter. They also point out that the mares have access to pasture in the summer. In a letter, Wyeth states "that the horses are extremely well looked after according to high and established standards of care. Only the urine is used to produce the oestrogens and this is done without mistreating the horses in any way".²

Few would now doubt that an animal has the capacity to suffer. Marian Dawkins has written about the difficulties in assessing the amount of suffering that an animal experiences. She suggests it might be possible to measure animal suffering by

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using an assessment which would include the construction of a picture of the animal (What does the animal like? What makes it healthy? What are its signs of fear and frustration?).³ It is alleged that many of the horses used for the production of this hormone develop the repetitive movements seen in animals at zoos and fur farms. This is seen as evidence that they are distressed.⁴

I am not qualified to make a detailed assessment as to whether the animals are distressed but my impression is that Wyeth have not provided sufficient evidence to place it beyond any doubt that the animals do suffer to some extent as a part of the production of equine HRT. There can be little doubt that mares have the ability to express a preference, anyone who has tried to catch a wilful horse on a cold morning will vouch for that. Personally I find it inconceivable that a mare would choose to stay confined to a tiny individual stall with a concrete floor for months at a time if it had the choice of leaving the stall and having some exercise or had the choice of moving to a bigger stall.

The moral status of animals

Having decided that it is possible that some animal suffering occurs in the production of equine HRT, I now need to ask whether animal suffering is a moral issue. Are the interests of non-person animals of less moral importance than those of person animals? St Thomas Aquinas held that animals were put on earth under man's dominion, and that it followed that humans could do what they pleased to animals as long as they were not the property of another.⁵ This is an extreme view which I think most people instinctively feel is self-evidently wrong. I feel that the other extreme, that there are no circumstances when it is right to cause suffering to an animal is equally untenable.

The recognition that animal suffering is a moral issue and that there is a need for balance is reflected in legal systems. English law requires a scientist to obtain a licence from the Home Office before he or she is allowed to conduct experiments on living vertebrates. This gives the scientists protection against prosecution under the Protection of Animals Act 1911. In Sweden, experiments are allowed or disallowed by local committees on which lay, animal welfare, animal care (veterinary) and scientific interests are represented.⁶ In other words, it would seem that parliaments have decided that animal suffering is sometimes justifiable if it is outweighed by the good done to person animals.

Jeremy Bentham, one of the founders of utilitarianism, points out the *capacity of suffering* as the vital characteristic which marks an animal out for special consideration.⁷ He put this viewpoint forward at a time when there was widespread disregard for the suffering of people, including black

slaves in Britain's colonies, let alone animals. He concluded that if a being suffers then there can be no moral justification for not taking that suffering into consideration. He then went on to point out that inflicting suffering may well be the right course of action if the utilities work out, that is if the happiness caused by the action outweighs the suffering.

Peter Singer, a contemporary utilitarian, concedes that the interests of people should have priority over non-person animals but thinks there would have to be very strong justification for inflicting avoidable suffering on animals and that no methods should involve the infliction of pain.⁸

Is there any benefit arising out of using equine HRT which might outweigh any suffering to mares?

There seems to be little doubt that women benefit from HRT. They benefit from the reduction or elimination of unpleasant menopausal symptoms such as hot flushes and night sweats. They benefit from the reduced cardiovascular risks resulting from favourable changes in their serum lipids.⁹ They also benefit from the prevention of osteoporotic bone loss and their reduced risk of bone fractures as they get older. But all these benefits can also be obtained from HRT derived from plants and from processes that do not require any animal suffering.

In order to justify the use of equine HRT, I would have to be able to show that it offered considerable advantages over plant-derived HRT. Conversely if I was able to demonstrate that both forms of HRT were equally effective in each of the three areas above, I would be able to conclude that there is no difference which could outweigh any animal suffering.

Oestriol valerate is produced from soya beans. Once taken, it is degraded in the walls of the gut to release free oestradiol, this is the hormone which it is meant to replace. In this regard, oestriol is a very natural substance. Conjugated equine oestrogens are a mixture of many oestrogens of uncertain origins. The major constituents are oestrone sulphate and equilin.¹⁰ The latter has a very long half life.

Effects on menopausal symptoms

I have only the observations of my own practice to go on but I have found that my patients have been just as satisfied with the reduction of their menopausal symptoms when using plant-based oestrogen as they have been with equine oestrogen when I have switched them over. I appreciate that this exercise was in no way a double blind randomised control trial – but clearly the plant-based product has satisfied the licensing authorities that it is suitable for prescription as hormone replacement therapy.

Effects on the cardiovascular system

There seems to be little doubt that HRT is associated with a decreased risk of cardiovascular disease in post-menopausal women. This seems to be because of a beneficial effects on serum lipids.¹⁰ It is considered that all HRT preparations have cardio-protective effects but to date there have been no large-scale studies comparing the incidence of cardiovascular disease in populations using different HRT preparations. It has been shown however that oestriol (that is plant-derived HRT) significantly changes the serum lipids in post-menopausal women in a beneficial way (by decreasing the LDL/HDL ratio).^{12 13}

Bone metabolism

There is some doubt as to whether the minimum dose of conjugated equine oestrogen (0.625 mg) is equivalent to the minimum dose of oestriol in preventing osteoporosis.¹⁴ It is thought, however, that the higher 2 mg dose of oestriol is suitable for the long term prevention of osteoporosis. Two studies have shown that oestriol is effective at stopping the demineralisation of bone.^{15 16} In the second study (Holland *et al*) the author commented in the discussion that the percentage increases in bone density with oestriol are greater than those with conjugated oestrogen 0.625 mg.

It seems that in these important areas, plant-derived HRT seems to be at least as effective as equine HRT. Wyeth itself admits in a personal communication that "Studies on the pharmacodynamics of piperazine oestrone sulphate, micronised oestradiol and conjugated oestrogens indicate equivalent effects on hormonal systems at appropriate doses. Effects on suppression of menopausal symptoms and on prophylaxis of osteoporosis are likely to be equivalent".² The letter then goes on to point out that conjugated oestrogens have been around longer than plant-derived oestrogens and so there is not equivalent long term data on cardiovascular risks.

It seems then that the only area in which there may be a claim for equine oestrogen to have superior efficacy is in cardiovascular effects. This is because the plant-derived HRT has not been around for long enough. There seems no reason to doubt that in the long term it is very unlikely that the cardiovascular results of using equine HRT will be found to be any better than those of using plant-derived HRT.

Cost

If there were a significant cost-saving in prescribing equine HRT instead of oestriol then this might weigh in favour of using it despite there being some animal suffering involved. This is because those savings could be used elsewhere in the health service to decrease other forms of human suffering.

Comparing the costs of the various preparations is complicated by the fact that whilst low dose oestriol is sometimes adequate to control hot flushes and night sweats, the higher dose is recommended for the prevention of osteoporosis. The manufacturer of oestriol in the form of Progynova seems to have recognised this by charging the same for the 1 mg tabs as the 2 mg tabs. This contrasts with the equine oestrogen Premarin, which costs more if the higher dose is prescribed.

If I confine myself to basic preparations of HRT – (more costly forms of HRT exist for both types of hormone):

- One month's supply of equine oestrogen in the form of Premarin 0.625 mg costs £2.23 according to the British National Formulary.¹⁷ This dose is thought to be sufficient to prevent osteoporosis.
- One month's supply of equine oestrogen in the form of Premarin 1.25 mg costs £3.03 according to the British National Formulary.¹⁷
- One month's supply of plant-derived oestriol in the form of Progynova 1 mg costs £2.34.
- One month's supply of plant-derived oestriol in the form of Progynova 2 mg (the minimum recommended dose to prevent osteoporosis) costs £2.34.

If we look at the minimum doses needed to prevent osteoporosis then the equine oestrogen costs 11p a month less. If, however, the higher dose of Premarin has to be prescribed to relieve the woman's menopausal symptoms then the cost rises to 69p a month more. In view of this, I do not think that cost can be regarded as a significant factor in my calculations.

Utilitarian calculations

It is well known that there are problems with making utilitarian calculations such as deciding which "good" should be maximised (for instance, if we are to maximise welfare, should we only talk about the welfare of people?) There is also the difficulty of making objective calculations about what are often subjective assessments, for example, the amount of suffering that an animal undergoes. Having said this, I do not think there is a strong case to be made for prescribing equine HRT because of the specific benefits it gives women over and above plant-derived HRT. Plant-derived HRT is an effective alternative and although it seems that the higher dose must be given to ensure that the woman gains protection from osteoporosis, it has not been suggested that this higher level is harmful in anyway.

Since it is at least possible that some degree of animal suffering takes place in the production of equine HRT, then the onus is on the manufacturers to prove that some extra benefit to menopausal women or a wider population can be derived from the use of equine HRT. I believe that I have established that the plant-derived alternative is of equal

efficacy to equine HRT and is of comparable cost. My conclusion is that a utilitarian analysis would guide a doctor away from recommending equine HRT to his or her patients.

Other moral considerations

A utilitarian analysis has appeal to a pragmatic working doctor such as myself. I accept, however, that it is not the only way in which people may look at the moral issues concerning the use of equine HRT. From the perspective of enhancing a patient's autonomy (which also appeals to me greatly) it could be argued that the patient who is prescribed equine HRT without having the issues explained to her is being denied a chance to exercise her full autonomy. If we look at the same thing from the standpoint of informed consent, I could ask whether a woman's consent to take HRT is free and informed if she is not told about its mode of production. There are some women who arrive in our consulting rooms having already decided that they would not accept equine HRT, because of what they have read. There may be many more women who would take a similar stand if they were told more about it by their doctor.

Of course medical practice is not a simple matter of giving out information so that the patient can make an informed decision; I would argue that a doctor has a duty to point out which of the options he or she would recommend. For example, I have seen patients thrown into a state of panic and confusion because they were given the task of deciding whether or not to have their ovaries taken out as part of a planned hysterectomy. In such cases even though the patients' autonomy was enhanced, their welfare was diminished by having choice imposed upon them without any accompanying medical advice.

It is a view endorsed by the English courts that a doctor has a duty to act in a patient's best interest.¹⁸ I would argue that this duty is not absolute. Even if the doctor were to decide that equine HRT gave his patient a slight advantage over plant-derived HRT, I do not think that it necessarily follows that he has a duty to prescribe it. Modern doctors in the NHS are required daily to balance the welfare of an individual patient against the welfare of the population the doctors serve. An example of this might be a doctor deciding that cheap aluminium hydroxide should be prescribed for indigestion rather than expensive omeprazole in the first instance, in order to preserve his drug budget for the good of the whole practice population, even though it is likely that the omeprazole might give a faster resolution of the symptoms. It is not unknown for a doctor to take a moral stance which looks at factors outside the interests of his practice population. An example which comes to mind would be a decision not to prescribe inhalers to patients which contained ozone-damaging CFCs. In a similar way, I think that it would be reasonable for

a doctor to include the suffering of non-person animals – specifically mares in this context – in the wider consideration of his or her duties.

Summary

I have gone through the moral arguments surrounding the production of HRT as I see them. I am convinced by the integrity of the manufacturers of equine HRT and am sure that they have genuine grounds for believing they are not responsible for animal suffering. The benefits of HRT are well established and I think that they would have a good case for saying that the benefits of HRT outweigh any suffering conceivably caused to the animals if there was no viable alternative. Unfortunately for them, this is not the case. There is an effective economical and acceptable alternative to equine HRT and as a result of this I conclude that it would be preferable to recommend the plant-derived alternative to women who want relief from the symptoms of the menopause and protection from osteoporosis and cardiovascular disease.

Dennis Cox, MA MRCP, is a General Practitioner and Assistant Director of Studies in General Practice, Cambridge University Clinical School.

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News and notes

Ethical review of Clinical Research

A training conference for ethics committee members, entitled Ethical Review of Clinical Research, will be held at Robinson College, Cambridge from the 29th of September to the 1st of October this year.

The conference aims to provide practical training for ethics committee members, to bring together those with mutual areas of interest and experience in ethical review, and to provide a forum for discussion of current issues in ethical review.

The conference, organised jointly by the Association for Independent Clinical Research Contractors (AICRC)

and the Centre for Philosophy and Health Care, University of Wales, will be of interest to members and chairs of ethics committees, and to those involved in the planning and ethical approval of clinical research. Among the plenary lecture topics will be an update from the Department of Health on arrangements for ethical review of multi-centre trials, and a presentation by Dr Frank Wells of the Association of the British Pharmaceutical Industry on future directions of ethical review.

For further details contact: Mrs Jill Williams: phone/fax: 01222 626651.

News and notes

BMA call for evidence – ethics and human genetics

The British Medical Association has recently established a multi-professional steering group to examine the ethical implications of new genetic technology and to provide practical guidance for health professionals who are not specialists in genetics but who are increasingly asked to advise on the implications of this technology.

The steering group is anxious to gather as much information as possible on current practice and the

practical ethical problems which arise, from health professionals, counsellors, social workers and lawyers. The group would welcome evidence of good practice and unresolved issues from any of these sources or from others who have experience of these issues.

Correspondence should be sent to the Medical Ethics Department, British Medical Association, BMA House, Tavistock Square, London WC1H 9JP.