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Equine stomach ulcers – a suitable and special case for treatment?

Up to 90% of horses in training are afflicted by some degree of gastric ulceration

The well-publicised disqualification of the Godolphin horse Sky Hunter from the Doonside Cup last year, following the presence of anti-ulcer medication in a post-race sample, has focused attention on the condition of equine gastric ulcers. So what are they, why do they occur, what can we do about them and what stance should the sport's regulatory body be taking in regard to their control?

DR MARK HILLYER, NEH

Dr Mark Hillyer of Newmarket Equine Hospital using the three-metre long gastroscope to examine the inside of a horse's stomach, displayed on the monitor

The problem

In man the development of stomach ulcers is often linked to the presence of a specific bacterium, Heliobacter pylorum, which predisposes the host to the condition. In the horse, no link to a specific bacterial pathogen has been established, but what has been pretty firmly proven is that the conditions which take place when a thoroughbred horse is in routine full training are highly effective in producing gastric ulcers. Several factors are thought to be involved.

1. The horse naturally grazes for 13-14 hours a day when in the wild state. As it grazes it produces copious amounts of saliva which naturally contain the acid-buffer, sodium bicarbonate. So with each mouthful of grass it swallows the horse is, in effect, taking a natural antacid treatment. The saliva production is truly prodigious, with a normal horse producing upwards of 50 litres a day, which is trickled into the stomach along with the ingested food, and then recycled by absorption through the intestines. When we keep horses in stables, and curtail their feeding to several small meals a day, the situation is very different. For long periods of the day the horse will be unable to access forage and therefore will not produce large quantities of saliva. This raises the acidic environment of the stomach.

2. Coupled to this, it is common practice not to feed horses immediately prior to exercise as we know very recent feeding has a performance-limiting effect, and this means that the horse goes out with an empty stomach, full of acid which is then liberally splashed around the walls as the horse exercises.

3. High-intensity exercise seems to be a risk factor in the development of ulcers, and high-intensity exercise is what racehorses do for a living.

4. High grain/low roughage diets don't help but, again, to get the calories into the horse needed to support full training they have to be employed.

Is there a safe withdrawal period?

In common with several other drugs, the BHA has carried out a trial on the period of time in which they can detect omeprazole following its oral administration and published this as a declared detection period.

The normal advice 'on the street' to form a safe withdrawal period is to add a margin of error of half as much again to this detection period. As the BHA's declared detection period is three days, most clinicians have therefore advised their trainers to use a withdrawal period of four and a half days, which is normally rounded up to be five clear days from racing, but there are three problems with this.

First, the BHA trial was carried out at a dose level of only 1mg of omeprazole per kilogram for the horse. This dose level is simply not used in practice. The current recommendation in the modern textbooks such as 'The Racehorse, a Veterinary Manual' (Ramzan), and 'Equine Sports Medicine and Surgery' (Hinchcliffe et al), both published in 2014, is for initial treatment at a level of 4mg per kg followed by maintenance at a level of 2mg per kg.

This is four times, or double the dose, which the BHA chose to use in its detection periods study respectively. The BHA's stated defence is that they used the dose level recommended in the data sheet given out with the drug. Whilst this is true, the data sheet recommendation was based on drug use in experimental horses, when the initial application for product registration was made, and these horses were not undergoing full training with all its consequences.

Subsequent to the release of the drug on

How do we diagnose ulcers?

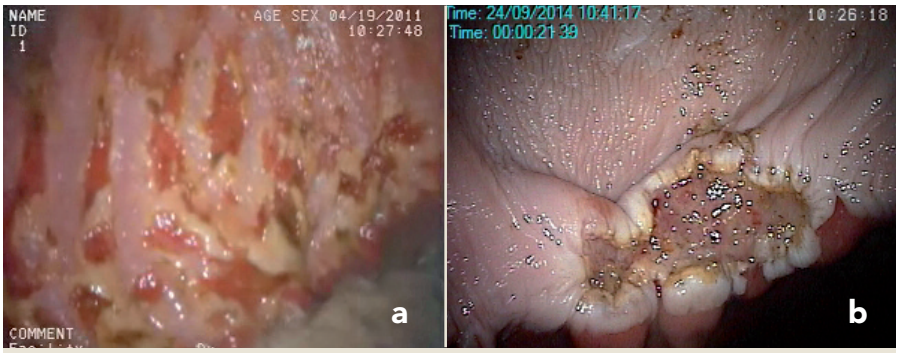
The evolution of a special type of endoscope, the gastroscope (*see facing page*), a tiny camera on the end of a flexible tube long enough to directly examine the lining of the horse's stomach, added to information that we previously had only from post-mortem examinations, established the fact that up to 90% of racehorses in training showed some degree of gastric ulceration. By definition, any feature which is present in 90% of a population could probably be classed as normal.

So are we treating a disease of the endoscope rather than of the horse? Most clinicians feel that this is not the case, and they do so simply as a result of the spectacular improvement in condition, demeanour and trainability of horses which have been treated for gastric ulcers following the diagnosis of the more severe grades. So it's likely that this condition does affect at least some of the horses which carry it and does impact directly on their facility to show their true level of ability.

What are the clinical signs?

The first thing to say is that most horses that carry ulcers show no sign at all of them being present – as we've already said, up to 90% of racehorses have them.

When horses do seem to be affected by them, they show a variety of symptoms, none of which is totally specific to ulceration of the stomach. These include lack of appetite, poor weight gain, a dull staring coat, mild bouts of colic, often around feeding time, and a general change in demeanour where the horse appears to be 'sour' and slightly 'dull' at exercise. These signs often increase in tandem with increasing amounts of galloping exercise. Unfortunately, over-training will produce a very similar set of symptoms and it's often hard to distinguish between the two.



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Two very different cases of what would both be considered Grade 4 ulceration, and likely to cause trouble: a) extensive diffuse lesions in the upper part of the stomach and b) a solitary, isolated but very deep lesion, just near the margin between the keratinised upper stomach and the lower, glandular section

> *"In reality significant management change is often simply not practical for a large number of horses"*

Whilst a correlation between clinical signs and what we find on examining the stomach lining with the gastroscope is not good, most clinicians would be happy to consider the more extensive lesions in the range (ulcers are often graded 1 to 4 and grades 3 and 4 – see images above – are often regarded as significant) to be important in the face of a horse showing these clinical signs.

What can we do about it?

Whilst most in racing would pay lip-service to the fact that altering the management of the horse is the key to controlling stomach ulcers, in reality significant management change is often simply not practical for a large number of horses.

The changes usually suggested are pasture turn-out for as much of the day as possible, the provision of a low-starch, high-fibre diet, reduction of stress and almost ad-lib access to >>

the market, clinicians found that this low dose rate was not enough to prevent the recurrence of ulcers in the racehorse, hence the universally advised and adopted dose at 2mg per kg for control.

This obviously presents a problem, in that the detection periods study now offers no useful information to the true detection periods at the dose rate most commonly employed. Not for the first time, the BHA has carried out an administration study and issued a detection period based on the dose level of a drug which nobody in practice is using. A small amount of prior consultation with the stakeholders in the industry could have established what dose rates veterinary surgeons and trainers are actually using, and the study then be based on this. This would have given much safer advice on the period required for the drug to clear the system.

The second problem is that for many years there was only one product available to treat gastric ulcers, Gastrogard. This came in a syringe size which was very easy to use because the normal treatment rate was a full syringe per day and the maintenance rate was half a syringe per day. In recent years two new products have been released containing omeprazole, by other manufacturers. Because these products are aimed to include larger horses, the syringe size contains enough drug for a 700kg rather than a 550kg horse, as was the case with Gastrogard.

If stable staff continue to use the regime of a full syringe for treatment and half a syringe for maintenance, then they are slightly overdosing the horse, ending up with a drug level approaching three times that which was used in the BHA detection periods study. More drug means a longer detection period, and means that the guidance issued by the BHA based on the low level of 1mg per kg becomes totally unsafe.

The third problem is that gastric ulcers develop relatively quickly once omeprazole medication is withdrawn. Even with the current advice based on a dose level which nobody is using, ulcers will have begun to reform by six days following the end of treatment. If an even longer withdrawal period has to be used going forward, this will pretty much totally negate any effect omeprazole has had by the time the horse races. Just when the horse needs to be at its peak of condition, it may start to 'back out' of its food manger because of pain from the development of further stomach ulcers.

>> feed and hay. In practice, it's very difficult to maintain horses in peak fitness if allowing all of these management changes to take place.

For affected horses there are obviously some common sense minor modifications which can be carried out. For instance, the short-feed component of the ration could be divided into four to six portions and this delivered into the feed manger throughout the day and night. Fillies can be given pasture access, if available, in small play pens, but the mass turn-out of an entire yard of horses in training, including colts, is clearly a completely impractical approach in the environment in which most racehorses live. Management changes being only partially effective, this throws us back on medication, so what drugs are available and how are they used?

Ulcer medication

Whilst there are several drugs available to treat ulcers in the horse, only one presents a realistic opportunity, and that is omeprazole. Other drugs which were used in the past, such as ranitidine, have such a variable and long excretion period after cessation of treatment (up to three weeks) that it makes their use during the training season itself impractical under present BHA drug rules.

Omeprazole was originally developed for treating gastric ulcers in man and is a highly effective inhibitor of acid secretion in the stomach, allowing rapid healing of ulcerated areas. It is easily administered by mouth using oral dosing syringes. Although most of the administered product is destroyed in the stomach because of the high acidity, enough survives to reach the small intestine, where it is absorbed and circulates in the bloodstream, eventually acting back on the stomach.

This is an important distinction, as local action within the stomach is irrelevant, and what is needed for the drug to be effective is a blood level. It is this blood level of drug that leads to problems with the current BHA stance in racing, in that they have zero tolerance of the presence of omeprazole in the blood on raceday and this is where the problems lie (*see panel: 'Is there a safe withdrawal period?'*).

The National Trainers' Federation has for some time been proposing that omeprazole be removed from the list of prohibited substances and treated as a special case, just as happened in the past with antibiotics and wormers, which are now allowed to be used, but previously would result in disqualification of the horse if present on raceday. The argument goes that, as stated in the BHA press release issued at the time of the publication of a detection period, omeprazole had no direct effect on performance in the racehorse.

As it is treating a disease which is an occupational hazard of being in training, and as the disease is widespread, many believe that medication with omeprazole should be encouraged rather than punished, on welfare grounds. This has already happened in other countries which are perceived to have drug-free racing (*see panel above*). It is hoped that the BHA will think again about this important disease, and take on board the concerns of trainers and owners in their future regulation of the use of drugs to control gastric ulcers in the racehorse.

Use of medication internationally

Other jurisdictions which do not, in principle, allow the use of medication have taken a different stance to the BHA.

The Fédération Equestre Internationale (FEI) allows the use of omeprazole up to the day of competition. Although the FEI does not govern horseracing, it is not alone in allowing the use of omeprazole up to the day of competition, even within racing jurisdictions.

In Australia, all anti-ulcer medications, including ranitidine, are permitted to be administered right up to (but not including) raceday. These drugs have simply been removed from the 'prohibited substances' list altogether. This decision was taken on welfare grounds and there is no evidence that these drugs alter performance, other than allowing the horse to express its true level of ability because of lack of disease.

Similarly, in Hong Kong the administration of omeprazole is permitted up to two clear days prior to a race. Again, this advised withdrawal period was presumably agreed on the basis that the Hong Kong Jockey Club did not wish to have their horses affected with stomach ulceration by the time they ran. Dr Terence Wan, head of the HKJC Racing Laboratory, comments: "Based on our experience in Hong Kong, the detection time for repeated use of oral omeprazole, in accordance with the recently-adopted IFHA International Screening Limit (ISL) for the parent drug only, is well within two clear days (not less than 60 hours since we seldom race before noon) of the last treatment.

"However, we do not know yet which other countries are or will be signatories to this new ISL. If anyone chooses to detect the omeprazole metabolite instead of the parent drug in urine, the detection time would be much longer. Furthermore, while monitoring the omeprazole metabolite can result in a long detection time, in our experience a prolonged detection time can also be due to stable or feed bin contamination with this drug, even when only the parent drug is monitored."

It remains to be seen whether or not the BHA will adopt this more pragmatic approach, shown by the regulators in other 'drug-free' racing jurisdictions, such as Hong Kong and Australia, going forward.