Evidence-based Clinical Question

An evidence-based analysis of anabolic steroids as therapeutic agents in horses

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Introduction

Anabolic steroids have been reported anecdotally to be useful in treatment of various conditions of the horse, including anaemia, enhancing muscle recovery after injury and diseases causing cachexia or debilitation, treating orthopaedic conditions, and improving appetite (Beroza 1981; Snow 1993). The evidence for anabolic steroids as performance enhancers in horses has been previously reviewed (Pitts and Davis 2007); such use would be considered nonmedical or production uses. This article reviews the evidence for anabolic steroids for medical (therapeutic) use in horses.

Anabolic steroids and anaemia

No randomised controlled trials of any anabolic steroid in horses for treatment of anaemia were found in a search of the biomedical literature. In man, increases in packed cell volume (PCV) and haemoglobin have been reported in patients on haemodialysis receiving nandrolone decanoate (Barton Pai *et al.* 2002); however, other studies in predialysis patients have shown no changes in PCV after nadrolone administration (Eiam-Ong *et al.* 2007). In human patients with chronic obstructive pulmonary disease, increases in erythropoeitin and haemoglobin have been reported following nandrolone administration (Creutzberg *et al.* 2003). Increased erythropoeisis was also found with the use of nandrolone decanoate in irradiated rats (Gallicchio *et al.* 1984).

Anabolic steroids and muscle recovery and cachexia/debilitation

An anabolic steroid labelled in the US for horses, boldenone undecylenate, has a label claim, "As an aid for treating debilitated horses when an improvement in weight, haircoat or general physical condition is desired" (Anon 2008). The label refers to clinical trials performed for drug approval, but does not present the details of the studies. Another anabolic steroid, stanozolol, labelled for horses in the US includes recommendations, "As an aid for treating debilitated horses when the therapeutic objective is to improve appetite, promote weight gain, improve general physical conditions, and accelerate recovery." No clinical trial data are included on the stanozolol label to evaluate how these claims were validated.

Published data in horses with clinical disease related to muscle recovery are limited. Nandrolone increased the rate of muscle glycogen repletion in treated animals after strenuous exercise (Hyyppa 2001). Whether strenuous exercise correlates well with muscle damage during clinical disease is unclear.

In man, there is some evidence for the efficacy of anabolic steroids in increasing muscle mass in, for example, burn victims, AIDS patients, and renal failure. Less loss of muscle mass after bone fracture (Hedström *et al.* 2002), improvement in the wasting from AIDS (Hengge *et al.* 2003a,b; Anon 2008), improvement in muscle loss due to ageing (Sheffield-Moore *et al.* 2006), improved muscle function and exercise capacity in patients on glucocorticoids (Creutzberg *et al.* 2003) and increased albumen and dry weight in patients on dialysis (Barton Pai *et al.* 2002) have all been reported in man. Extensive burns can result in significant muscle catabolism in man, and anabolic steroid treatment has been demonstrated to reduce that loss (Demling and DeSanti 2001, 2003; Hart *et al.* 2001).

In rats, creatine kinase levels were reduced after an exhaustive bout of weight lifting (Tamaki *et al.* 2001), as well as after muscle contusion (Beiner *et al.* 1999), by treatment with nandrolone, suggesting that muscle damage might be reduced by an anabolic steroid. However, this has not been demonstrated in clinical studies in horses to date.

Conversely, a negative effect of anabolic steroids on muscle mass has also been reported in man. Ventilator-dependent patients treated with oxandrolone spent more time on the ventilator than nontreated patients (Bulger *et al.* 2004). This group attributed the negative effect to the enhancement of collagen deposition and fibrosis by the anabolic steroid. These negative results suggest that 'debilitation' or 'muscle wasting' conditions must be clearly defined and studied in order to appropriately apply the results of clinical data.

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Anabolic steroids and orthopaedic or bone conditions

No randomised controlled trials of any anabolic steroid in horses for the treatment of orthopaedic conditions were found in a search of the biomedical literature. Human studies are equivocal: Hedström *et al.* (2006) reviewed the literature on anabolic supplementation and hip fracture recovery and found published studies underpowered or logistically problematic. A Cochrane Database systematic review (Palmer *et al.* 2007) of interventions for preventing bone disease in kidney transplant patients found no data on the effect of anabolic steroids on fracture risk or bone density.

Anabolic steroids and appetite

No randomised controlled trials of any anabolic steroids in horses for treatment of anorexia or inappetance were found in a search of the biomedical literature. Studies in man have also found no effects on appetite (Darnton *et al.* 1999; Carlsson *et al.* 2005).

Conclusion

With the collapse of Eight Belles at the Kentucky Derby in May 2008, the spotlight was on horse racing. Whether or not Belles was treated with anabolic steroids, their use in training and racing horses entered the mainstream media. Prior to the Derby, the Racing Medication and Testing Consortium published the Model Rule, which called for withdrawal times on the use of anabolic steroids. Since then, some racing jurisdictions have implemented withdrawal times or recommended voluntary bans. If an outright ban on anabolic steroids in racing animals were agreed upon among jurisdictions, there is the potential that a useful medical therapy will be removed from use by veterinary medical professionals. At issue, therefore, is whether anabolic steroids are actually medically useful in racing animals. Evidence of the efficacy of anabolic steroids in medical therapy must be reviewed as part of the discussion on the regulation of these drugs, so that if they are effective, they will remain available for therapeutic use.

The best (Level 1) research evidence for efficacy of therapeutics is the randomised controlled trial or a systematic review of randomised controlled trials in the animal species of interest. Level 1 evidence for the efficacy of anabolic steroids in horses for therapeutic uses is not found in the biomedical literature. Evidence in other species exists for the efficacy of anabolic steroids in treating anaemia and increasing muscle mass after illness or injury, but that evidence is not unequivocal, and the applicability to horses has not been demonstrated. There is little evidence in other species for the efficacy of anabolic steroids for increasing appetite.

References

Anon (2008) *Compendium of Veterinary Products,* North American Compendiums, Port Huron.

Barton Pai, A., Chretien, C. and Lau, A.H. (2002) The effects of nandrolone decanoate on nutritional parameters in hemodialysis patients. *Clin. Nephrol.* **58**, 38-46.

Beiner, J.M., Jokl, P., Cholewicki, J. and Panjabi, M.M. (1999) The effect of anabolic steroids and corticosteroids on healing of muscle contusion injury. *Am. J. sports Med.* **27**, 2-9.

Beroza, G.A. (1981) Anabolic steroids in the horse. *J. Am. vet. med. Ass.* **179**, 278-280.

Bulger, E.M., Jurkovich, G.J., Farver, C.L., Klotz, P. and Maier, R.V. (2004) Oxandrolone does not improve outcome of ventilator dependent surgical patients. *Ann. Surg.* **240**, 472-478; discussion 478-480.

Carlsson, P., Tidermark, J., Ponzer, S., Söderqvist, A. and Cederholm, T. (2005) Food habits and appetite of elderly women at the time of a femoral neck fracture and after nutritional and anabolic support. *J. Hum. Nutr. Diet* **18**, 117-120.

Creutzberg, E.C., Wouters, E.F., Mostert, R., Pluymers, R.J. and Schols, A.M. (2003) A role for anabolic steroids in the rehabilitation of patients with COPD? A double-blind, placebo-controlled, randomized trial. *Chest* **124**, 1733-1742.

Darnton, S.J., Zgainski, B., Grenier, I., Allister, K., Hiller, L., McManus, K.G. and Steyn, R.S. (1999) The use of an anabolic steroid (nandrolone decanoate) to improve nutritional status after esophageal resection for carcinoma. *Dis. Esophagus* **12**, 283-288.

Demling, R.H. and DeSanti, L. (2001) The rate of restoration of body weight after burn injury, using the anabolic agent oxandrolone, is not age dependent. *Burns* **27**, 46-51.

Demling, R.H. and DeSanti, L. (2003) Oxandrolone induced lean mass gain during recovery from severe burns is maintained after discontinuation of the anabolic steroid. *Burns* **29**, 793-797.

Eiam-Ong, S., Buranaosot, S., Eiam-Ong, S., Wathanavaha, A. and Pansin, P. (2007) Nutritional effect of nandrolone decanoate in predialysis patients with chronic kidney disease. *J. Ren. Nutr.* **17**, 173-178.

Gallicchio, V.S., Chen, M.G. and Watts, T.D. (1984) The enhancement of committed hematopoietic stem cell colony formation by nandrolone decanoate after sublethal whole body irradiation. *Int. J. Cell Cloning* **2**, 383-393.

Hart, D.W., Wolf, S.E., Ramzy, P.I., Chinkes, D.L., Beauford, R.B., Ferrando, A.A., Wolfe, R.R. and Herndon, D.N. (2001) Anabolic effects of oxandrolone after severe burn. *Ann. Surg.* **233**, 556-564.

Hedström, M., Ljungqvist, O. and Cederholm, T. (2006) Metabolism and catabolism in hip fracture patients: nutritional and anabolic intervention - a review. *Acta orthop.* **77**, 741-747.

Hedström, M., Sjöberg, K., Brosjö, E., Aström, K., Sjöberg, H. and Dalén, N. (2002) Positive effects of anabolic steroids, vitamin D and calcium on muscle mass, bone mineral density and clinical function after a hip fracture. A randomised study of 63 women. *J. Bone Joint Surg.* **84**, 497-503.

Hengge, U.R., Stocks, K., Faulkner, S., Wiehler, H., Lorenz, C., Jentzen, W., Hengge, D. and Ringham, G. (2003a) Oxymetholone for the treatment of HIV-wasting: a double-blind, randomized, placebo-controlled phase III trial in eugonadal men and women. *HIV Clin. Trials* **4**, 150-163.

Hengge, U.R., Stocks, K., Wiehler, H., Faulkner, S., Esser, S., Lorenz, C., Jentzen, W., Hengge, D., Goos, M., Dudley, R.E. and Ringham, G. (2003b) Double-blind, randomized, placebo-controlled phase III trial of oxymetholone for the treatment of HIV wasting. *AIDS* **17**, 699-710.

Hyyppa, S. (2001) Effects of nandrolone treatment on recovery in horses after strenuous physical exercise. *J. vet. med. A. Physiol. Pathol. Clin. Med.* **48**, 343-352.

Palmer, S.C., McGregor, D.O. and Strippoli, G.F. (2007) Interventions for preventing bone disease in kidney transplant recipients. *Cochrane database of systematic reviews (Online)* **3**, CD005015.

Pitts, S. and Davis, M. (2007) An evidence-based analysis of anabolic steroids as performance enhancers in horses. *Equine vet. Educ.* **19**, 388-391.

Sheffield-Moore, M., Paddon-Jones, D., Casperson, S.L., Gilkison, C., Volpi, E., Wolf, S.E., Jiang, J., Rosenblatt, J.I. and Urban, R.J. (2006) Androgen therapy induces muscle protein anabolism in older women. *J. Clin. Endocrinol. Metabol.* **91**, 3844-3849.

Snow, D. (1993) Anabolic steroids. *Vet. Clin. N. Am.: Equine Pract.* **9**, 563-576.

Tamaki, T., Uchiyama, S., Uchiyama, Y., Akatsuka, A., Roy, R.R. and Edgerton, V.R. (2001) Anabolic steroids increase exercise tolerance. *Am. J. Physiol. Endocrinol. Metab.* **280**, E973-981.