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INFLUENCE OF ANABOLIC AGENTS ON MUSCLE PROTEIN TURNOVER IN YOUNG BULLS AS MEASURED BY 3-METHYLHISTIDINE EXCRETION

Introduction

Anabolic agents are known to improve growth in beef cattle, mainly by enhancing muscle protein (MP) accretion. This effect could be ascribed to a stimulation of MP synthesis, a decrease of MP degradation or to a combination of both processes. In studies with rats Vernon and Buttery (1976) suggested that both synthesis and degradation rates are lowered but the latter to a greater extent, resulting eventually in a positive net effect. Harris et al. (1984) observed a decrease in MP degradation in beef steers implanted with Revalor (140 mg trenbolone acetate + 20 mg 17ß-oestradiol) when using 3-methylhistidine (3MH) as a marker of myofibrillar breakdown. There are only a restricted number of studies available on in vivo MP turnover measurements with cattle. Nishizawa et al. (1979) measured fractional synthesis and breakdown rates of myofibrillar proteins in Holstein steers equally using 3MH excretion. Lobley et al (1980) reported synthesis rate measurements on 2 heifers and a cow (Hereford-Friesian) using the irreversible loss rate method with infusions of radioactive amino acids (tyrosine, leucine). Lanka and Broderick (1980) described muscle protein and body protein turnover and synthesis rate measurements based on 3MH-excretion and N-balance studies. Despite some criticisms, mainly from the human biochemistry field, 3MH-excretion continues to be used as an in vivo index of MP turnover in large animals as is illustrated by several recent publications (McCarthy et al, 1983; Gopinath and Kitts, 1984). In a former publication (Van Eenaeme et al., 1983) we reported on the use of 3MH-excretion and nitrogen balance (cfr Lanka and Broderick) to estimate the anabolic effect of trenbolone acetate and 17ß-oestradiol (TBO) implants in young bulls. In the present communication this approach is extended to other anabolic preparations.

Material and methods

Twenty five young bulls of the Belgian blue breed weighing around 375 kg were alotted to 10 treatment groups implanted once or twice respectively on week 8 or 16 and 8 before slaughter with the following implants : trenbolone acetate 200 mg - 17ß-oestradiol 40 mg (TBO 1x and 2x; 4 animals each), trenbolone acetate 200 mg - zeranol 36 mg (TBZ 1x and 2x), testosterone 200 mg - 17ß-oestradiol 20 mg (TEO 1x and 2x), progesterone 200 mg - 17ß-oestradiol 20 mg (PO 1x and 2x) and zeranol (Z 2x). Each of these groups contained 2 animals. The remaining three animals received no implant (control group C). Urinary 3MH-excretion and N-balance were measured during 8 days periods, once before and three times after each implantation. Muscle protein degradation was calculated assuming a 3MH-content in muscle protein of 594 µg/g as reported by Nishizawa et al. (1979) and confirmed by our own analysis. MP accretion (net synthesis) was estimated as N-balance x 6,25 assuming that all retained N was transformed into muscle protein. While this might not be entirely true, it could however represent an upper estimate and serve on a comparative base. MP synthesis was obtained as the sum of degradation and accretion. Before the first implantation all animals were considered as controls, so the first point (week -1) is the mean of 25 animals. Similarly the late implanted bulls served as controls during the initial 8 weeks.

Results and discussion

3MH-excretion patterns were similar for all late implanted groups (except PO1) : after a rather constant excretion during the first 6 weeks a sharp rise occurred at the last 2 weeks of the experimental period. For the PO1 group the 3MH-excretion rised even immediately after implanting. With the bulls implanted twice a more or less pronounced decrease was observed after each implant, followed by a significant increase afterwards. Based on growth performances the anabolic combinations could be classified as follows : highly potent combinations such as TBO; medium effective ones, like TBZ and TEO; and finally almost non effective preparations such as PO and Z. In this respect TBZ and TEO as well as PO and Z were grouped together and compared to TBO - and control groups. Synthesis, degradation and accretion rates are depicted in fig. 1. For the control group these rates increased steadily with time. For the "effective" anabolic combinations accretion rose after each implantation, remained high during

Fig 1

about 4 weeks and finally declined. This increase was more important at the first anabolisation. The highest and longest sustained increase was observed with TBO. For the TBO1 group this increase in deposition rate resulted entirely from a higher synthesis rate, while for TBO2 and TBZ1 + TEO1 it was obtained from both increased synthesis and slightly decreased degradation rates. For TBZ2 + TEO2 a decrease in degradation rate was accompanied by a decrease in synthesis rate. Analysis of RNA-content in longissimus dorsi samples obtained after 3-rib cut dissection revealed higher muscle RNA concentrations in anabolized animals, e.g. 6 to 8 mg/g Prot. vs 4 mg/g in control animals. So, apparently synthesis rates are stimulated by anabolic agents.

From the present observations the following working hypothesis about the action of anabolic agents could be proposed. For the slower growing animals treated with less potent combinations such as TBZ or TEO apparently increased accretion can be obtained by a decrease of both synthesis and degradation rates as proposed by Vernon and Buttery (1976). For the more "potent" combinations (TBO) immediately after implantation both a rise in MP synthesis and a fall in degradation are observed. After about 2 weeks both rise in a parallel way resulting in a steady state of maximal MP accretion. Finally after 5-6 weeks MP synthesis levels off while MP degradation continues to rise, resulting in a fall in accretion rate. Apparently, in fast growing animals both synthesis and degradadion rates are high.

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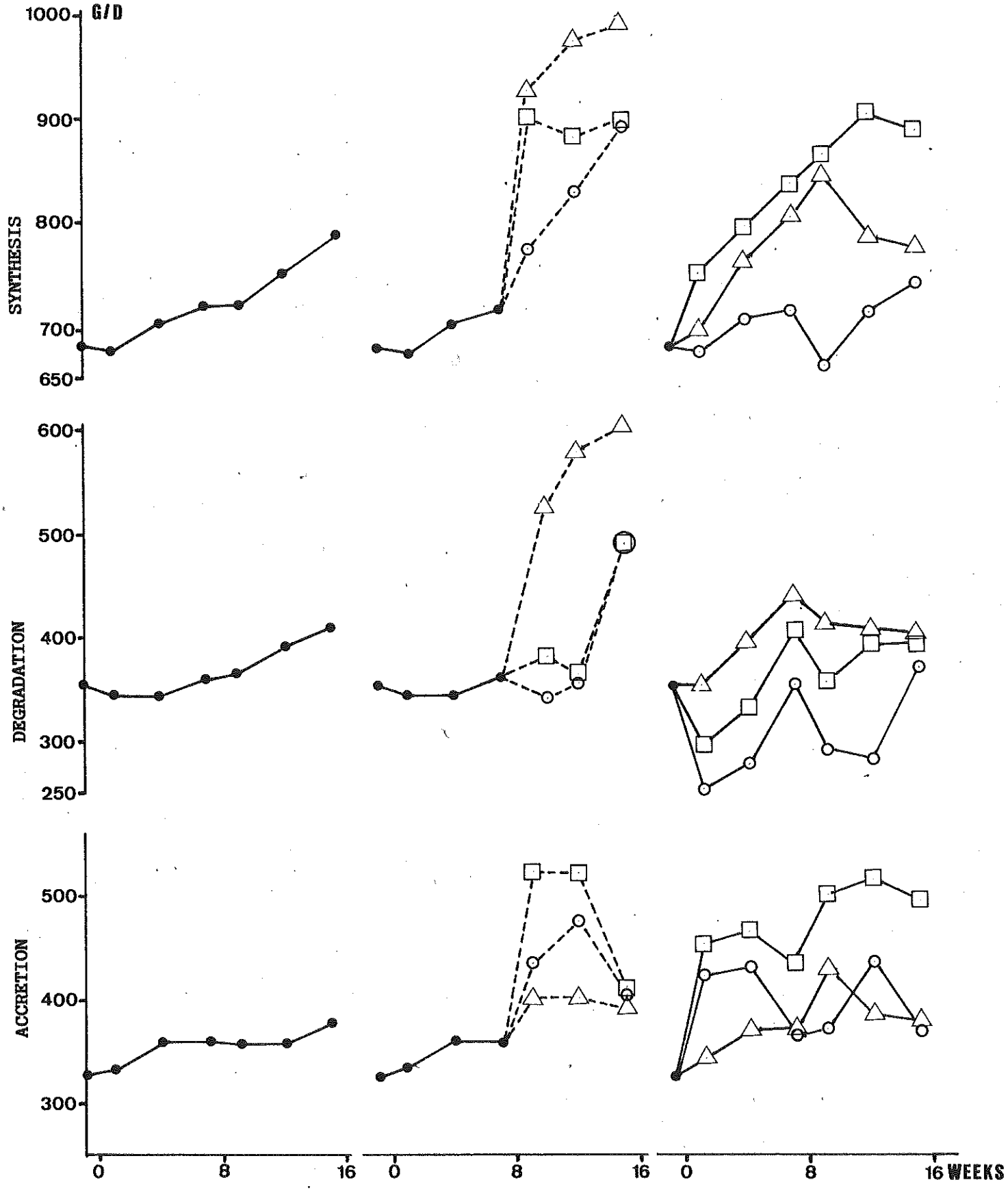
Fig. 1.- Muscle protein synthesis degradation and accretion rates for control (●) and for TBO (□), TBZ + TEO (○) and PO or PO + Z (△), either implanted once (- - - - -) or twice (———).


G/D
1000
900
800
700
650
SYNTHESIS
600
500
400
300
250
DEGRADATION
500
400
300
ACCRETION
0
8
16
0
8
16
0
8
16 WEEKS

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Anabolic agents are known to improve growth, hence to enhance muscle protein (MP) accretion. This effect can be ascribed to a stimulation of MP synthesis or to a decrease of MP degradation or to a combined action of both processes. In this experiment the influence of anabolic agents on in vivo MP turnover in young bulls has been estimated by urinary 3-methylhistidine excretion.

Twenty five young bulls of the Belgian Blue breed (350-400 kg) were alotted to 10 treatment groups implanted once or twice (16 and 18 weeks before slaughter) with the following implants : Trenbolone acetate - 17ß-oestradiol (TBO 1x and 2x), Trenbolone acetate - Zeranol (TBZ 1x and 2x), Testosterone - 17ß-oestradiol (TEO 1x and 2x), Progesterone - 17ß-oestradiol (PO 1x and 2x) and Zeranol (Z 2x). 3-methylhistidine excretion and N-balance were measured in 8 days periods, once before and three times after implantation.

Muscle protein turnover rised steadily from about 350 to 400 g per day for the control group. The animals treated only during the last 8 weeks exhibited a similar 3-methylhistidine excretion pattern during the first 8 weeks of the experiment. Directly after the implantation MP turnover remained fairly constant or decreased slightly while N-balance increased for most of the treatment groups. However, during the last 3 weeks of each treatment period the degradation rate increased sharply (from 400 to 550-600 g/day). Immediately after the second implantation MP degradation decreased but it rose again after 2 to 3 weeks. The highest degradation rates were observed with the PO1 and Z groups (500-600 g/day). Growth performances were also lowest with these treatments. Based on these results the following working hypothesis concerning the action of anabolic agents could be proposed : MP turnover may drop slightly immediately after implantation while MP synthesis rises sharply, as based on N-retention data. After about two weeks a steady state between synthesis and degradation results in a fairly constant N-retention during the next 2 to 3 weeks. Finally, 5 to 6 weeks after implanting MP degradation rises sharply provoking a decrease in N-retention. This final increase in degradation rate could explain the lowering of N-retention and hence of growth rate frequently observed with anabolic agents at the end of the treatment period.

Roxtoek 1984

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