

## RINGKASAN

### **Pengaruh Pemberian Asam Mefenamat Terhadap Pertumbuhan Memanjang Pada Tulang Femur Tikus Putih Jantan Muda**

*(Rattus norvegicus)*

Muhamad Hasan

Obat golongan *non steroidal anti inflammatory drugs* (NSAIDs) merupakan obat yang sering digunakan dalam sediaan farmakologi. Mengganggu proses pembentukan prostaglandin melalui penghambatannya terhadap enzim siklooksigenase. Sedang prostaglandin (PG) mempunyai peran mengatur proliferasi, deferensiasi dan sintesa matrik dari sel-sel kondrosit pada lempeng pertumbuhan (*growth plate*) melalui aktifitas protein kinase C (PKC).

Rancangan penelitian yang digunakan adalah The Separate pretest, *Posttest Only Control Group Design*. Penelitian dilakukan terhadap 40 ekor tikus putih jantan (*Rattus norvegicus*) jenis wistar berumur 4 minggu yang dibagi secara acak menjadi 4 kelompok. Kelompok tersebut terdiri dari 1 kelompok kontrol pre dan 1 kelompok kontrol post, 2 kelompok perlakuan. Kelompok kontrol pre langsung diukur BB dan panjang femurnya. Kelompok kontrol post mendapat 2 ml aquades / 200gr BB / hari (K1). Kelompok perlakuan mendapat larutan asam mefenamat sebanyak 2 ml / hari dengan perincian dosis sebagai berikut : untuk kelompok perlakuan 1 dengan dosis 27 mg asam mefenamat / 200 gr BB / hari (K2), kelompok perlakuan 2 mendapat 54 mg asam mefenamat / 200 gr BB / hari (K3) semuanya diberikan peroral. Setelah 4 minggu perlakuan, panjang femur diukur dengan menggunakan jangka sorong, sedang panjang lempeng pertumbuhan (*growthplate*) dan jumlah sel diukur dan dihitung menggunakan mikroskop sinar dengan bantuan kamera digital dan program komputer.

Hasil penelitian menunjukkan rerata panjang femur bagi kelompok kontrol pre adalah sebesar  $24,010 \pm 1,003$  mm, sedang rerata panjang lempeng pertumbuhan (GP) dan jumlah sel yang tersusun memanjang dari lempeng pertumbuhan masing-masing  $144,2650 \pm 69,5197$  mikron dan  $17,3670 \pm 7,1430$ . Sedang, pada kelompok kontrol post

rerata panjang femur adalah  $30,410 \pm 0,711$  mm , sedang rerata panjang lempeng pertumbuhan (GP) dan jumlah sel yang tersusun memanjang dari lempeng pertumbuhan masing-masing  $89,9120 \pm 23,6441$  mikron dan  $11,2230 \pm 2,7285$  . Pada kelompok perlakuan mefenamat 27 menghasilkan rerata panjang femur adalah  $29,230 \pm 0,835$  mm , sedang rerata panjang lempeng pertumbuhan (GP) dan jumlah sel yang tersusun memanjang dari lempeng pertumbuhan masing-masing  $64,5930 \pm 13,8842$  mikron dan  $7,9340 \pm 1,3312$ . Pada kelompok perlakuan mefenamat 54 menghasilkan rerata panjang femur adalah  $29,388 \pm 1,146$  mm sedang rerata panjang lempeng pertumbuhan ( GP ) dan jumlah sel yang tersusun memanjang dari lempeng pertumbuhan masing-masing  $41,2012 \pm 6,7291$  mikron dan  $5,0000 \pm 0,5036$ .

Dari uji beda pengaruh secara individu melalui *Pairwise comparisons* ternyata terdapat perbedaan yang bermakna dari masing-masing kelompok, kecuali pada perlakuan mefenamat 27 dan mefenamat 54, dimana pada variabel panjang femur nilai signifikannya 0,722, variabel panjang lempeng pertumbuhan / GP nilainya 0,210 dan jumlah sel GP nilainya 0,131 ( $>0,05$  )

Dari analisis regresi didapatkan p untuk semua variabel diatas  $< 0,05$ . hal ini berarti bahwa pemberian asam mefenamat berpengaruh secara bermakna terhadap penurunan panjang femur, penurunan panjang lempeng pertumbuhan serta penurunan jumlah sel pada susunan memanjang dari lempeng pertumbuhan dan pengaruh penurunannya dipengaruhi oleh kenaikan dosis asam mefenamat.

Penelitian ini menyimpulkan bahwa pemberian asam mefenamat menyebabkan panjang femur lebih pendek, panjang lempeng pertumbuhan menjadi lebih pendek dan menyebabkan jumlah sel yang tersusun memanjang dari lempeng pertumbuhan menjadi lebih sedikit dan makin tinggi dosis asam mefenamat makin besar pengaruhnya terhadap penurunan panjang femur, panjang growthplate dan jumla sel dalam growthplate.

## SUMMARY

### The Effect of Mefenamic Acid on Longitudinal Development of Growth plate in Young Male White Rats

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NSAIDs are one of commonest used drugs. Not all of them recommended by drugs federation used for children. Even thought almost all of NSAIDs common used for children. There are not clear data available , but we predict there are many kind of NSAIDs given for children. NSAIDs decrease prostaglandin production by inhibit cyclo-oxygenase enzim. Prostaglandine has rule in the chondrocyte proiiferation and differentiation of growth plate, by activation of PKC ( protein kinase C )

The design of this study was The *Separate pretest, Posttest Only Control Group Design*. The research was done using 40 one month old male wistar strain white rats. These rats were randomly divided into four groups. They consists of one pretest group, one control group and two treatment groups. The pretest group directly measure body weight and length of femur (K0). The control posttest group were given orally 2 ml of distilled water/200 g BW/day (K1). The treatment groups were given mefenamic acid orally in the dose of 27 mg/200 g BW/day (K2), and 54 mg/200 g BW/day (K3) respectively, all of which were dissolved in 2 ml of distilled water. After 4 weeks, the length of femur, length of growth plate and number of longitudinal cell of growth plate are noticed. the measurement was undertaken using manual and light microscope.

The results showed the mean of length of femur in pretest group was  $24.010 \pm 1.003$  mm, where as the mean of growth plate length and number of growth plate cell were  $144.2650 \pm 69.5197$  micron and  $17.3670 \pm 7.1430$  cell. The control posttest groups, showed the mean of femur length , growth plate length and number of growth plate cell were  $30.410 \pm 0.711$  mm,  $89.9120 \pm 23.6441$  micron and  $11.2230 \pm 2.7285$  cell. At the

group was treated that were given mefenamic acid 27 mg, showed the mean of femur length, growth plate length and number of growth plate cell were  $29.230 \pm 0.835$  mm,  $64.5930 \pm 13.8842$  micron and  $7.9340 \pm 1.3312$  cell. The last treatment group showed the mean of femur length, growth plate length and number of growth plate cell were  $29.388 \pm 1.146$  mm,  $41.2012 \pm 6.7291$  micron and  $5.0000 \pm 0.5036$  cell.

The result was subsequently showed descriptively and analyzed using multi analysis variants and pair wise comparisons. It showed in all of experimental animals with had a significant difference to control ( $p < 0.05$ ). Pair wise comparisons showed that significant difference ( $p < 0.05$ ) occurred in all of groups except between mefenamic acid 27 mg and mefenamic acid 54 mg that not significant difference.

Linear regression analysis resulted in linear equation that showed all of variables had a significant difference ( $p < 0.05$ ). This study show that mefenamic acid treatment cause decrease of femur length, decrease of growth plate length and decrease number of growth plate cell and increase doses of mefenamic acid will make decrease bigger.

## ABSTRACT

### The Effect of Mefenamic Acid on Longitudinal Development of Growth plate in Young Male White Rats

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**Introduction :** The past epidemiologic studies did not have definite explanation about the effect of consuming Mefenamic Acid on Longitudinal Bone Development .

**Objective :** To explain the effect of Mefenamic Acid on Longitudinal Bone Development

**Method :** The design of this study was The *Separate pretest, Posttest Only Control Group Design*. The research was done using 40 one month old male wistar strain white rats. These rats were randomly divided into four groups. They consists of one pretest group, one control group and two treatment groups. The pretest group directly measure body weight and length of femur (K0). The control posttest group were given orally 2 ml of distilled water/200 g BW/day (K1). The treatment groups were given mefenamic acid orally in the dose of 27 mg/200 g BW/day (K2), and 54 mg/200 g BW/day (K3) respectively, all of which were dissolved in 2 ml of distilled water. After 4 weeks, the length of femur, length of growth plate and number of longitudinal cell of growth plate are noticed. the measurement was undertaken using manual and light microscope. The result was subsequently showed descriptively and analyzed using Manova. It showed in all of experimental animals with had a significant difference to control ( $p < 0.05$ ). Pair wise comparisons showed that significant difference ( $p < 0.05$ ) occurred in all of groups except between mefenamic acid 27 mg and mefenamic acid 54 mg that not significant difference. Linear regression analysis resulted in linear equation that showed all of variables had a significant difference ( $p < 0.05$ ) . This study show that mefenamic acid treatment cause decrease of femur length, decrease of growth plate length and decrease number of growth plate cell. The following studies with different methods and measurement devices needed as comparison as well as to know the doses that can effect the Longitudinal Development of Growth plate and increase doses of mefenamic acid will make decrease bigger

**Keywords:** mefenamic acid, chondrocyte, growth plate, experimental study.