



Dexaject dosage for carriage horses: side effects & fixing

Dr. Abdul-Samad Uleiwi Hassan⁽¹⁾, Dr. Ali Hussein Aldujaily⁽²⁾,
Dr. Shatha Atta Abeed⁽³⁾

1- Al-Forat Al-Awsat Technical University/ Health and Medical Technical Faculty

2- Kufa University/ Veterinary College

3- Al-Forat Al-Awsat Technical University/ Kufa Technical Institution

samadovaabditch@gmail.com 07812322519

Received date: 8 Jan 2018 Accepted: (428) 23 Apr 2018 (59-67) Published: 31 Jun 2018

Abstract:

The instant study clarify excellent treatment response of dexaject with a dose 3.5/2 mg/ml in fixing musculoskeletal injuries imaged by x-rays to get a statistical probability less than 0.001 ($P < 0.001$) put it in progress for uses without serious side effects mentioned or noticed in carriage horse models.

Keywords: Dexaject, Carriage horses, Musculoskeletal inflammations, Side effects.

جرعات الديكساجكت المعطاة لخيول الأحمال: اثارها الجانبية ومدى الشفاء
د. عبدالصمد عليوي حسن⁽¹⁾، د. علي حسين الدجيلي⁽²⁾، د. شذى عطا عبيد⁽³⁾

1- جامعة الفرات الاوسط التقنية/ كلية التقنيات الصحية والطبية

2- جامعة الكوفة/ كلية الطب البيطري

3- جامعة الفرات الاوسط التقنية/ المعهد التقني الكوفة

الخلاصة:

بيّنت الدراسة الراهنة ان افضل استجابة علاجية للعقار الديكساجكت كانت بجرعة 2/3.5 ملغم-مل في حالات الاصابات العضلية-الهيكلية المشخصة بواسطة أشعة أكس وبمستوى معنوية إحصائية اقل من 0.001 ($p < 0.001$) وهذا ما سّمه عملية الإستخدام لعدم إظهاره آثاراً عرضية خطيرة تذكر او تلاحظ في عينات خيول الأحمال المعالجة.

Introduction:

Dexaject medication is a type of corticosteroid potent anti-inflammatory with curative exertion used in all types horses with acute musculoskeletal inflammations. It also furnishes helpful therapy in a wide variety of cases, such as influenza, heat exhaustion, retained placenta and laminitis, concerned that the primary cause is diagnosed and rectified. It is not species specific and a veterinarian should be entailed in all treatments using dexaject. It is

considered to be a superior anti-inflammatory than many pharmaceutical steroids^(1,2).

Veterinarians authorise dexaject for use in treating osselets, bursitis, myositis, carpalitis, sprains, and tendonitis in horses. In addition, it is used in supportive therapy in cases of influenza, heat exhaustion and fatigue, retained placenta, and laminitis, along with diagnosis and treatment of the primary cause^(3,4).

Side effects from using dexaject divided into three categories; common ones includes weight loss, enzyme elevations, laminitis and anorexia. The second ones are the unknown incidence includes sodium and water retention, skin atrophy, osteoporosis, candidiasis, seizures, muscular atrophy, and allergic reactions including anaphylaxis. Some horses may show withdrawal evidence after long-term treatment with corticosteroids like fever, lethargy or drowsiness. Lethargy usually diminishes in approximately 20-24 hours ^(5,6).

Carriage horses exposed to many hurts and disorders of the musculoskeletal system most often disturb their ability to work and move. How harshly movement is debilitated banks on the type and asperity of the problem. Skeletal and joint anarchies are the most common, but bad cases in the musculoskeletal system can also signify diseases of the muscles, neurologic troubles, hormonal aberrancies, poisons or toxins in

the body, infectious or contagious diseases, metabolic disorders, blood and vascular clutters, poor or bad nutrition, and birth imperfection. This is demanding, fast revision and treatment by the veterinarians ^(7,8).

The aim of this study set up on assessment the best dose of dexaject uses to cure musculoskeletal inflammations in carriage horses in order to fixing the worst side effects arose when made a choices to the dosage concentrations used in such cases.

Materials and method:

1- study included 30 carriage horse models subjected to the veterinarian investigation and care to restrict their injury with severe musculoskeletal inflammation.

2- models gave dexaject by three tested doses applied equally on 10 animals for each group to compare curing state upon the duration of a week and list of side effects appeared (see table-1).

Table-1: the dosages, concentration of dexaject per period given for treating horses models injured with musculoskeletal inflammation.

Dexaject method	Dosage	Concentration	Period	Duration
1- Intramuscular	2 mg	2 mg/ml	1/day	
2- Intramuscular	3.5 mg	2 mg/ml	1/day	
3- Intramuscular	5 mg	2 mg/ml	1/day	

3- In all crisis of musculoskeletal injuries and inflammation, indicative procedures applied to dictate the nature, extent, and exact location of the injury. Checking up the prominent side effects appeared in the treated models according to the applied dosage by using medical manners like checking up vital or life signs and accomplish underlying medical cues about horses. Checking involves horse’s weight, eyes, ears, routine cross-examination of the mouth and teeth, and observing the horse’s movements.

Veterinarian used a stethoscope to auscult for anomalistic heart, lung, or alimentary system tones that may signify problems with these organs.

Veterinarians use palpation process to check for the propotions and sites of internal organs such as the liver, spleen, kidneys, and urinary bladder. They will also check for enlargement of lymph nodes located throughout the body ⁽⁹⁾.

4- Data statistical inquiry: all the inputs and issues tabulated and scheduled by computerized statistical programme (SPSS)

established on the interact articles to get fine assessment⁽¹⁰⁾.

Results:

1- The most severe musculoskeletal inflammation affected regions captured in the horse body include all the pointed ones shows in the plastic coated figure-1 explained down.



Figure-1: plastic coated sample explain the 25 musculoskeletal injuries and inflammations that's diagnosed in the carrying horses.

The most prominent musculoskeletal cases recorded in our models of study are the sesamoid injuries, kissing spines and olecranon fracture respectively. By using radiographical X-rays we try to illustrate those three main injuries (see image-1, -2 and -3 down).



Image-1: Sesamoid injuries captured radiographically by X-rays. Fracture is obvious due to overstressed.

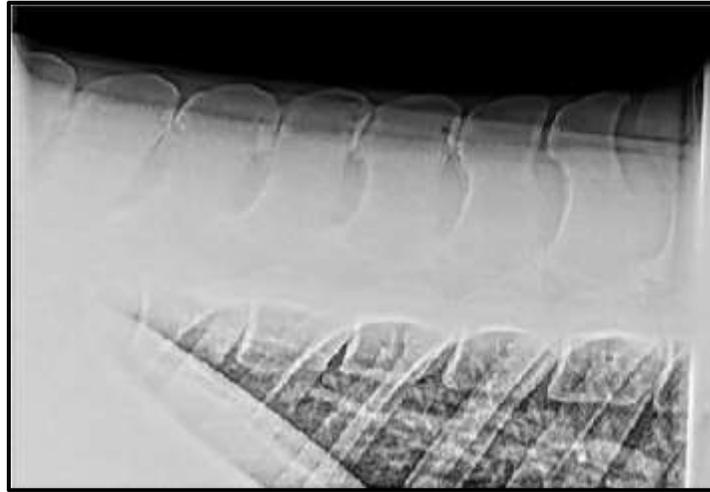


Image-2: Kissing spines captured radiographically by X-rays. Spinous processes affixed to the vertebrae, are adjoining together and bear upon each other.



Image-1: Olecranon fracture captured radiographically by X-rays. fractures involved the olecranon bone.

2- Side effects correlated with a low dose of dexamethasone included weight loss,

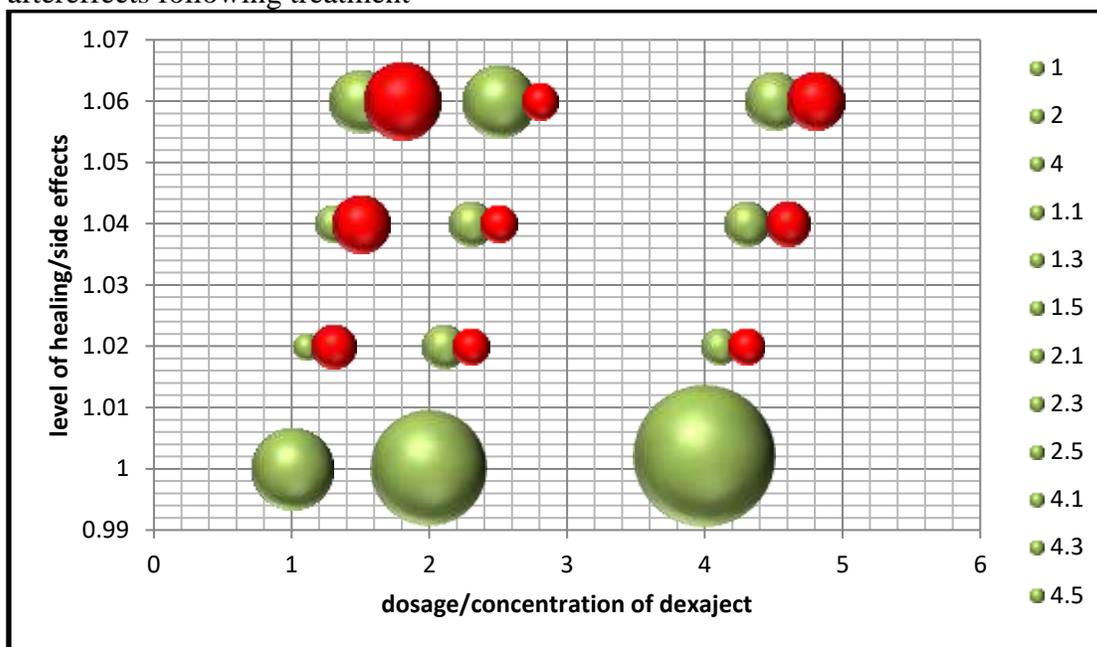
enzyme elevations, laminitis, sodium and water retention, skin atrophy, [osteoporosis](#),

[candidiasis](#), seizures, muscular atrophy, allergic reactions, some horses may show withdrawal evidence.

On the other hand, high dose of dexaject causes a dangerous side effects continece with laminitis, anorexia, [anaphylaxis](#), fever, lethargy or drowsiness and painful itchy skin nodules.

At the same time we noticed that perfect dose given for tested models show little aftereffects following treatment

3- Statistical calculations submit that when contemplate with their relatives, the application of dexaject requiring smart protocol that will significantly reduce the level of musculoskeletal inflammation; however, the other relatives had significantly more aftereffects when applied on the likewise level (look the scheme-1 down here).



Scheme no. 1: Healing levels (green bubble) and aftermath of dexaject doses applied participation side effects (red bubble) arose later.

Discussion:

The aftereffects of our tests arrayed that dexamethasone as pharmacologic doses, abolishes inflammation and shift gears of the normal immune feedback due to dexamethasone considered as a glucocorticoid agonist ⁽¹¹⁾. Disengage dexamethasone captious cell outer layer and gets a tight spot with high closeness to specific cytoplasmic glucocorticoid receptors. This multiplex sticks to nucleic acid DNA elements (glucocorticoid response part or elements) which sequels in a modificational changes of transcription and,

away, protein synthesis in contemplation of achieve embargo of leukocyte infiltration at the point of inflammation, conflict in the mission of mediators of inflammatory response, beats down of humoral immune responses, and attrition in edema or scar tissue ⁽¹²⁾. The antiinflammatory agility of dexamethasone are theorized to involve phospholipase A₂ inhibitory proteins, lipocortins, which subordination the biosynthesis of potent mediators of inflammation such as leukotrienes and prostaglandins ^(13,14).

The using of a dosage 3.5 mg/ml by a concentration 2 mg/ml gives the best requests because it is related to special dose (exposure) - response linear relationship. So, behindhand of how a drug aftereffect occurs –buttoned up sticking or chemical intercommunication- the concentration of the drug at the spot of action dominations the effect. However, riposte to concentration may be complicated and is often nonlinear. The affiliation between the drug dose, behindhand of way used, and the drug concentration at the cellular plain is even more complex according to pharmacokinetics principles ⁽¹⁵⁾.

Dose-response brass tacks are as is usual graphed with the dose or dose affair (eg; \log_{10} dose) on the x-axis and the measured aftermath (i.e. response) on the y-axis. As long as a drug aftereffect is a function of both dose and time, such a graph delineate the dose-response whole relationship autarchical of time. Admeasured effects are as a rule archived as maxima at time of peak aftereffect or under steady-state circumstances (eg; during continuous intravenous infusion). Drug aftermaths may be calibrated at the level of molecule, cell, tissue, organ, organ system, or organism as a whole ⁽¹⁶⁾.

A hypothetical-assumptive dose-response curve has attributes that vary (see down hypothetical dose-response curve figure.):

- Potency or dominion (location of curve along the dose axis)
- Maximal competence or ceiling aftereffect (greatest accomplishable response)
- Slope or abruptness (conversion in response per unit dose) ⁽¹⁷⁾.

Biologic aberration (variation in grandeur of response among test subjects in

the same population accustomed the same dose of drug) also occurs. Delineate dose-response curves of drugs tested under interchangeable conditions can assist compare the pharmacologic contours of the drugs (see down: comparison of dose-response curves figure). This enlightenment helps determine the dose bottom-line to achieve the admiration aftereffect ⁽¹⁸⁾.

Dose-response, which comprehend the assumption of pharmacokinetics and pharmacodynamics, arbitrate the desired dose and frequency as well as the therapeutic index or formula for a drug in a population. The therapeutic index (correspondence of the minimum lethal concentration of the median persuasive concentration) assist arbitrate the efficacy and assurance of a drug. Raising the dose of a drug with a little therapeutic index increases the likelihood of toxicity, harmful or abortiveness of the drug. However, these characters differ by population and are afflicted by patient-related factors, such as pregnancy, age, and organ function (eg; estimated glomerulo-filtration rate GFR) ^(19,20).

Figure-1: Hypothetical dose-response curve by [Merck & Co., Inc., Kenilworth, NJ, USA](#)

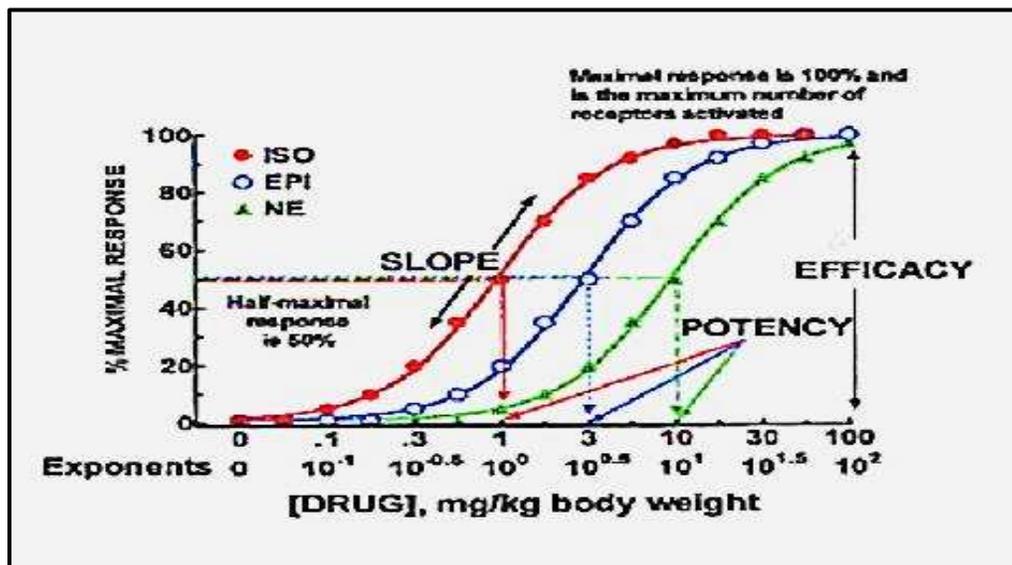
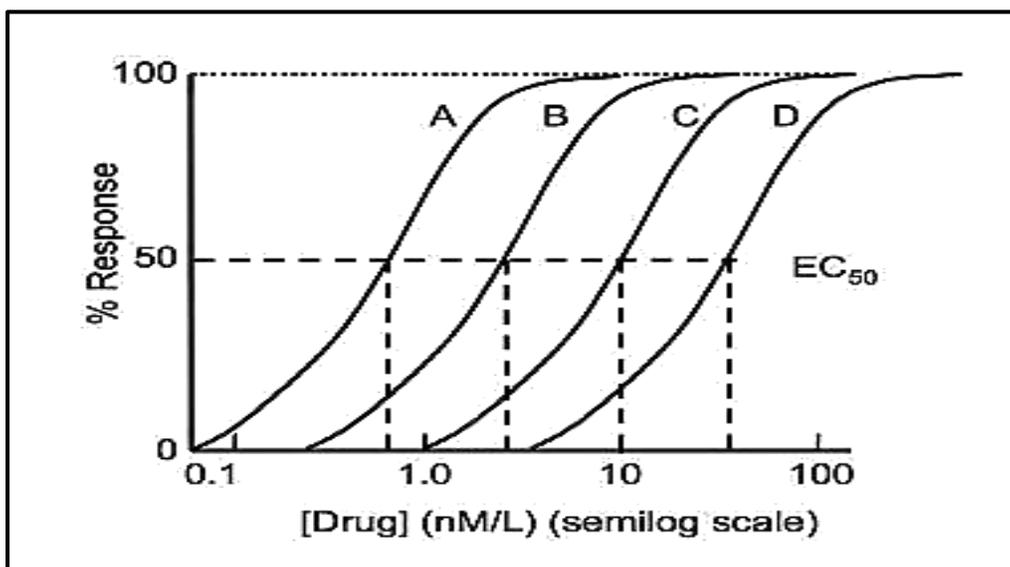


Figure-1: [Comparison of dose-response curves](#) by [Merck & Co., Inc., Kenilworth, NJ, USA](#)



Our conclusion about this study is that dexaject by a dosage/concentration 3.5mg/2mg-ml was accomplished clear

response in treatment musculoskeletal disorders in carriage horses, this was award an idea to employ the perfect dose of

dexaject according to dose-response linear relationship based on pharmaceutical levels to ensure that will convey **favorable**, definitely and beneficially without side effects recorded.

References:

1- Ekstrand, C. (2017). Dexamethasone in Horses. Doctoral Thesis Swedish University of Agricultural Sciences Uppsala. ISBN (print version) 978-91-576-8835-4. Print: SLU Service/Repro, Uppsala 2017.

2- The American Society of Health-System Pharmacists. (2017). Dexamethasone. Archived from the original on 2017-09-08 by Drug.com.. Retrieved Jul 29, 2015.

3- Bond, S. L., Timsit, E., Workentine, M., Alexander, T. and Léguillette, R. (2017). Upper and lower respiratory tract microbiota in horses: bacterial communities associated with health and mild asthma (inflammatory airway disease) and effects of dexamethasone. *BMC Microbiology*; 17:184.

4- United States Equestrian Federation. (2017). Equine Drugs and Medications Program. 2017 GUIDELINES FOR DRUGS AND MEDICATIONS. 800.633.2472.

5- McGowan, C., Cooper, D. and Ireland, J. (2016). No evidence that therapeutic systemic corticosteroid administration is associated with laminitis in adult horses without underlying endocrine or severe systemic disease. *Veterinary Evidence* Vol 1, Issue 1: 1-17. ISSN: 2396-9776.

6- Cornelisse, C.J., Robinson, N.E., Berney, C.E., Kobe, C.A., Boruta, D.T. and Derksen, F.J. (2005). Efficacy of oral and intravenous dexamethasone in horses with recurrent airway obstruction. *Equine Vet J.*; 37(1):36.

7- Bolwell, C., Rogers, C., Gee, E. and McIlwraith, W. (2017). Epidemiology of Musculoskeletal Injury during Racing on New Zealand Racetracks 2005–2011. *Animals*; 7, 62: 1-9.

8- Dallas, R.S. 2013. Musculoskeletal Injury in Arabian Racehorses: A Study of Injury Distribution and Prevalence in One Training Yard in the United Kingdom (2005–2012). *Equine veterinary science*; Volume 45, Issue S44: Page 10.

9- Costa, L.R.R. and Paradis, M.R. (2017). *Manual of Clinical Procedures in the Horse*. (illustrated edition). John Wiley & Sons Co., USA. ISBN: 978-0-470-95927-5.

10- Wagon, B. 2017. *Veterinary Biostatistics*. (2ed). Cbs pvt ltd, Delhi. ISBN-13: 978-9386217707.

11- Flower, R.J. and Gavins, F. (2008). Dexamethasone. xPharm: The Comprehensive Pharmacology Reference. *Editors-in-Chief: S.J. Enna and David B. Bylund* ISBN: 978-0-08-055232-3. Last update, February 2011. Elsevier, USA.

12- Tsurufuji, S., Kurihara, A. and Ojima F. (1984). Mechanisms of anti-inflammatory action of dexamethasone: blockade by hydrocortisone mesylate and actinomycin D of the inhibitory effect of dexamethasone on leukocyte infiltration in inflammatory sites. *J Pharmacol Exp Ther.* ;229(1): 237-43.

13- Elahian, F., Kalalinia, F. and Behravan, J. (2010). Evaluation of indomethacin and dexamethasone effects on BCRP-mediated drug resistance in MCF-7 parental and resistant cell lines. *Drug Chem Toxicol*; 33 (2): 113-9.

14- Coutinho, A.E. and Chapman, K.E. (2011). The anti-inflammatory and immunosuppressive effects of glucocorticoids, recent developments and mechanistic insights. *Mol Cell Endocrinol.*; 15, 335 (1): 2–13.

15- Links, J.M. (2006). Principles of Exposure, Dose, and Response. Johns Hopkins Bloomberg School of Public Health. Johns Hopkins University. USA. ocw.jhsph.edu/courses/EnvironmentalHealth/PDFs/Lecture5.

- 16- Peper, A. (2009). Aspects of the Relationship Between Drug Dose and Drug Effect. *Dose Response*; 7(2): 172–192.
- 17- Parris, G.E. (2015). A Hypothesis Concerning the Biphasic Dose-response of Tumors to Angiostatin and Endostatin. *Dose Response*; 13(2): 14-020.
- 18- Fu, Z., Hu, X., Wu, Y. and Zhou, Z. (2016). Is There a Dose–Response Relationship of Cement Volume With Cement Leakage and Pain Relief After Vertebroplasty?. *Dose Response*; 14(4): 15593258-16682867.
- 19- Bogen, K.T. (2017). Low-Dose Dose–Response for In Vitro Nrf2-ARE Activation in Human HepG2 Cells. *Dose Response*; 15(2): 15593258-17699696.
- 20- González-Sales, M., Nekka, F., Tanguay, M., Tremblay, P. and Li, J. (2017). Modelling the dose–response relationship: the fair share of pharmacokinetic and pharmacodynamic information. *British Journal of Clinical Pharmacology*; Volume 83, Issue 6: Pages 1240–1251