The effect of sulcular injection of meloxicom on biochemical parameter of rabbit

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ABSTRACT

Background: Meloxicam is an NSAID of the oxicam class that acts by inhibiting prostaglandin synthesis and inducible COX-2, thereby exerting anti-inflammatory effect. This study aimed to evaluate the level of alkaline phosphetase and high sensitivity C - reactive protein as response to sulcular injection of meloxicom using a rabbit model.

Material and method: Forty five male rabbits of the same species were divided into three groups. Group 1 which included 20 rabbits that injected with meloxicon in a dose equal to the human therapeutic dose /kg .Group 2 which included 15 rabbits that injected with normal saline. Group 3 which included 10 rabbits used as control group. Five ml of blood was collected from the rabbits ear vien for biochemical analysis at deferent time interval. Biochemical analysis included alkaline phosphetase (ALP) which analyzed by using Biolabo kit and High sensitivity C- reactive protein (hs- CRP) was measured using ELISA technique.

Results: The result showed that the level of ALP after 1 day of sulcular injection in group 1 was 101.25 then it was decrease to 97.50 after 14 days while mean of ALP in group 2 was 70.33 After 1 day of injection and reach to 74.67 After 14 days and this almost near to the mean value of control group

Statistic description of hs-CRP for group 1 was decreased. The mean value from 11.617 after 1 day to 3.639 after 14 days. For group 2 also there was decreased in the mean from 11.556 after 1 day to 3.536 after 14 days, while for the control group the mean value was 3.170 .

Conclusions: The sulcular injection of NSAIDs seems to be of particular interest. This may help to further reduce adverse systemic effects of NSAIDs in treatment of periodontal disease safely.

Key word: Meloxicom, sulcular injection, biochemistry. (J Bagh Coll Dentistry 2012; 24(4):88-91).

INTRODACTION

Nonsteroidal anti-inflammatory drugs (NSAID's) have been used by humans in various forms for more than 3,500 years.. Despite this long history and large volume, the mechanisms of how NSAID's achieve their actions are still not completely unravelled.[1]

Some 30 years ago, it was first revealed that these drugs all reduced the formation of prostaglandins and that this ability was associated with inhibition of the enzyme cyclo-oxygenase (COX), which converts arachidonic acid to the prostaglandin precursor prostaglandin H2 (PGH2). In the early 1990's the existence of two isoforms of COX, COX-1 and COX-2, was demonstrated, leading to the categorization of all NSAID's according to their specificity to each of these isoforms.[2]

The effect of anti-inflammatory drugs on bone healing has been evaluated in several studies[3,4] Non-steroidal anti-inflammatory drugs (NSAIDS) interfere with aracdonic acid metabolism by blocking prostaglandin synthesis through cyclooxygenase pathway inhibition, which has a fundamental role in bone healing[5]

Meloxicam is an NSAID of the oxicam class, that acts by inhibiting prostaglandin synthesis and inducible COX-2, thereby exerting antiinflammatory, anti-exudative, analgesic and antipyretic effects [6, 7].

Meloxicam is an NSAID of the oxicam class that acts by inhibiting prostaglandin synthesis and inducible COX-2, thereby exerting antiinflammatory, anti-exudative, analgesic and antipyretic effects [6, 7]. The molecule is highly plasma protein bound, when circulating in the body (95-99%). It has a long plasma half-life, enabling less frequent dosage schemes.

Selective COX-2 inhibitors have emerged with the objective of reducing stomach and renal toxicity. Additionally, they can also promote effects on bone healing inhibiting prostaglandins[8]. It has been shown that the COX-2 enzyme participates in early phases of osteogenesis and that it is more related to osteoblast maturation in later stages. COX-2 inhibitors reduce the osteoblastogenesis process and alter genes activities responsible for osteoblastic differentiation[8,9].

The enzyme Alkline phosphetase (ALP) plays a role in bone metabolism. It is a membrane-bound glycoprotein produced by many cells, such as polymorphonuclear leukocytes, osteoblasts, macrophages, and fibroblasts within the area of the periodontium and gingival crevice[10] Gao J et al.[11] found that ALP activity was highest in osteoblasts, moderate in periodontal ligament PDL fibroblasts, and lowest in gingival fibroblasts. No activity was detected in cementoblasts. In the periodontium, ALP is very important enzyme as it is part of normal turnover of periodontal ligament, root cementum and

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maintenance, and bone homeostasis. Some forms of enzyme are also produced by plaque bacteria. [12]

C-reactive protein is one of the best know members of a group of acute –phase proteins, which increase their concentration during certain inflammatory disorders. It has widely been used as a bio-marker of inflammation in the body .In recent years C.R.P has received a lot of attention because of its apparent ties to cardiovascular disease, and it has also been linked to a number of other disease, including hypertension, diabetes, cancer and autoimmune disorders[13]

As elevated C.R.P values are always associated with pathological changes, the C.R.P assay provides useful information for diagnosis, therapy and monitoring of inflammatory process and associated disease [14].

Sick people admitted to a hospital had average salivary C.R.P levels 25 times higher than healthy people .salivary C.R.P may largely reflect local inflammation in the mouth, but some serum CRP can enter saliva through gingival tissue, especially if periodontal disease is present [15].

The aim of this study was to evaluate the level of alkaline phosphetase and high sensitivity C - reactive protein as response to sulcular injection of meloxicom using a rabbit model.

MATERIALS AND METHODS

This study was carried out at the Duhok Medical University, College of Dentistry, Department of Periodontology and department of basic science, during the period from 1st Jan 2012 up to 30th June 2012. Forty five (45) male rabbits of the same species and weight (1-2 kg) were left to acclimatization for seven days before starting the experiments, to maintain their standard diet and environmental condition were equal among all animals. Rabbits housed in an air –conditioned room (23-25˚C) with a 12 h light dark cycle. They had free access to water and standard food during the experimental period, tags with different numbers were fixed on the rabbit's ear to mark them.

The animals were divided into three groups:

Group 1 which included 20 rabbits that injected with meloxicon in a dose equal to the human therapeutic dose /kg.

Group 2 which included 15 rabbits that injected with normal saline.

Group 3 which included 10 rabbits used as control group.

Sulcular injection technique was used through the labial gingival tissue of lower right central incisor.

Five ml of blood was collected from the rabbits ear vein for biochemical analysis which measured at deferent time interval, After 1,3 ,7,10 and 14 days of giving sulcular injection.

Biochamical analysis included: Alkaline phosphetase (ALP) which anlysed by using Biolabo kit (REF 80014) in clinical chemistry analyzer KENZA 240.

High sensitivity C- reactive protein (hs- CRP) was measured using ELISA technique

Statistical analysis

Statistic description was done for Biochamical analysis of all the three groups. ANOVA was performed for the data obtained from all three groups

RESULTS

The result showed that the level of ALP after 1 day of sulcular injection in group 1 was 101.25 then it was decrease to 97.50 after 14 days as shown in table 1.

Table 2 showed the mean of ALP in group 2. It was 70.33 after 1 day of injection and reach 74.67 After 14 days and this almost near to the mean value of control group which was 71.80 as shown in table 3.

Statistic description of hs-CRP for group 1 was shown in Table 4 which included decreased the mean value from 11.617 after 1 day to 3.639 after 14 days.

For group 2 also there was decreased in mean of hs-CRP from 11.556 after 1 day to 3.536 after 14 days. 3.536 as shown in table 5 , while for the control group the mean value was 3.170 as in table 6.

The inter and intra group comparison for both ALP and hs-CRP were highly significant $P<0.001$ as shown in table 7.

DISCUSSION

The non steroidal anti-inflammatory drugs (NSAIDs) belong to the group of the most abused drugs by virtue of combining the pharmacological actions of anti-inflammatory and analgesia and because they can easily be bought over the counter.

The result of this study showed that sulcular injection of gingival tissue of rabbit with meloxicom caused significant increase of AP in compared to normal saline and control group and this result is in agreement with Duncan et al [16]; Klaassen, [17] whom they found that all the NSAIDs used produced significant increase in the level of ALP.

The result showed significant decrease of ALP during different time interval in meloxicom group in compared to other groups

Since ALP is among the enzymes most commonly associated with bone metabolism[18].

ALP is enriched in the membranes of mineralizing tissue cells (e.g. osteoblasts) and is also present in polymorphonuclear leukocytes (PMN) granules. Changes in enzymatic activity of ALP reflect metabolic changes in the gingiva and periodontium, in the inflammation

Study done by Oliveria et al[19] showed that Systemic therapy with meloxicam can modify the progression of experimentally induced periodontitis in rats by reducing alveolar bone loss, and this is in agreement with Gurgel et al[20] who concluded that selective cyclooxygenase-2 inhibitors may reduce bone loss associated with experimental periodontitis and that no remaining effect can be expected after its withdrawal.

In study showed a remarkably increased activity of ALP in the acute phase of periodontal disease, and after periodontal therapy, the activity of these enzymes was restored to the value found in healthy persons. [21]

NSAIDs are mainly responsible for the stabilization of periodontal conditions by reducing the rate of alveolar bone resorption. This is achieved through local inhibition of both enzymes (e.g. COX-1 and COX-2) responsible for the synthesis of arachidonic acid metabolites. Evidence shows that the effects of NSAIDs drop off rapidly after drug withdrawa[22]

This study showed significant increased in hs-crp in group 1 and group 2 in compare to group 3 and this in agree with Rader who said that C-reactive protein is one of many proteins produced by the liver in response to cellular injury due to trauma, infarction or infection [23]. Release of CRP from the liver into the circulation after cell injury is stimulated by the proinflammatory cytokine interleukin-6 (IL-6) [24]

The result showed significant reduction of hs-crp in group 1 in compare to group 2 during different time interval. This result is agreement with study[25] found that Taking nonsteroidal anti-inflammatory drugs or stations may reduce CRP levels in blood. Anti-inflammatory drugs and statins may help to reduce the inflammation, thus reducing CRP.

Therefore, the sulcular injection of NSAIDs seems to be of particular interest. This may help to further reduce adverse systemic effects of NSAIDs in treatment of periodontal disease safely.

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Table 1: Statistic description of ALP in group 1 at deferent time interval

Days	N	Minimum	Maximum	Mean	Std. Deviation	Std. Error
After 1 day	4	80	130	101.25	21.061	10.521
After 3 days	4	168	198	176.75	14.268	7.134
After 7 days	4	138	159	147.75	8.770	4.385
After 10 days	4	85	101	94.00	7.071	3.536
After 14 days	4	79	112	97.50	15.716	7.858

Table 2: Statistic description of ALP in group 2 at deferent time interval

Days	N	Minimum	Maximum	Mean	Std. Deviation	Std. Error
After 1 day	3	62	79	70.33	8.505	4.910
After 3 days	3	63	78	69.67	7.638	4.410
After 7 days	3	49	82	62.00	17.578	10.149
After 10 days	3	60	79	70.00	9.539	5.508
After 14 days	3	56	86	74.67	16.289	9.404

Table 3: Statistic description of ALP in group 3 at deferent time interval

N	Minimum	Maximum	Mean	Std. Deviation	Std. Error
10	51	101	71.80	15.091	4.772

Table 4: Statistic description of hs-CRP in group 1 at deferent time interval

Days	N	Minimum	Maximum	Mean	Std. Deviation	Std. Error
After 1 day	4	9.880	13.250	11.617	1.427	0.713
After 3 days	4	7.311	9.805	8.596	1.056	0.528
After 7 days	4	5.754	7.155	6.273	0.770	0.385
After 10 days	4	3.754	5.033	4.414	0.542	0.271
After 14 days	4	2.964	4.637	3.639	0.796	0.398

Table 5: Statistic description of hsCRP in group 2 at deferent time interval

Days	N	Minimum	Maximum	Mean	Std. Deviation	Std. Error
After 1 day	3	10.230	13.230	11.556	1.529	0.883
After 3 days	3	8.860	9.120	8.963	0.137	0.079
After 7 days	3	6.910	7.560	7.126	0.375	0.216
After 10 days	3	4.260	5.210	4.810	0.492	0.284
After 14 days	3	3.450	3.64o	3.536	0.096	0.055

Table 6: Statistic description of hs-CRP in group 3 at deferent time interval

N	Minimum	Maximum	Mean	Std. Deviation	Std. Error
10	1.870	4.613	3.170	0.902	0.285

Table 7: Inter and intra group comparison for ALP and hs-CRP

		Sum of Squares	df	Mean Square	F	Sig.
ALP	**Between Groups**	21859.700	4	5464.925	26.760	.000
	Within Groups	3063.250	15	204.217		
	Total	24922.950	19			
hsCRP	**Between Groups**	169.341	4	42.335	45.274	.000
	Within Groups	14.027	15	.935		
	Total	183.368	19			