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Histological study of the response of interstitial pancreatic adipose tissue after long-term administration of monosodium glutamate (MSG) food additive

Prof.Dr Amer M Hussin[1]
Lec. Dr. Ali A. Tala'a[2]
Assist.Prof Dr.Ali H Hammadi[3]
Lec Dr.Ayat M Zaydan[4]

(amer17173@gmail .com)

Abstract

In order to study the response of adipose tissue after long-term administration of the food additive MSG, Twenty-four adult male rats were divided into three groups. The first group left as control group, the second and third groups were used as treatment groups. 0.15 mg/kg b.wt of MSG was administered orally for 30 and 75 days respectively. For histological study, The laboratory animals were sacrificed, specimens were collected from pancreas, Routine histological processes were carried out and stained by using the routine H&E stain for routine tissue details and Gomori stain to differentiate between alpha and beta cells of pancreas. Slides were inspected under light microscope.

The main results revealed that the long duration dosage of MSG was adversely affects both exocrine and endocrine pancreatic tissue. Two processes were recognized at the same time, namely the adipose tissue differentiation and the angiogenesis. The result declared that the pancreatic adipose tissue was actively respond and modified to produce a well organized newly-formed islets of Langerhans with well developed beta cells. These islets were embedded within the pancreatic adipose tissue and surrounded by newly formed network of blood vessels. In this respect, five stages of adipose tissue differentiation were noticed. It was concluded that the adipose tissue served as supportive tissue to compensate the damaged pancreatic islets and their beta cells due to the over function load. Moreover, the study concluded that the MSG food additive promotes both processes, adipocytes differentiation and angiogenesis.

Key words: Pancreas, Monosodium glutamate, Adipose tissue

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الملخص

من أجل دراسة استجابة الأنسجة الدهنية بعد تناول المضافات الغذائية على المدى الطويل ، تم تقسيم 24 ذكورًا من الفئران البالغة إلى ثلاث مجموعات. المجموعة الأولى تركت كمجموعة ضابطة ، واستخدمت المجموعة الثانية والثالثة كمجموعات علاج. تم إعطاء 0.15 مجم / كجم من وزن الجسم من مادة MSG عن طريق الفم لمدة 30 و 75 يومًا على التوالي. بالنسبة للدراسة النسيجية ، تم التضحية بالحيوانات المختبرية ، وتم جمع عينات من البنكرياس ، وتم إجراء العمليات النسيجية الروتينية وتلطيخها باستخدام صبغة H&E الروتينية لتفاصيل الأنسجة الروتينية وصمة Gomori للتمييز بين خلايا ألفا وبيتا في البنكرياس. تم فحص الشرائح تحت المجهر الضوئي.

أظهرت النتائج الرئيسية أن الجرعة طويلة الأمد من MSG كان لها تأثير سلبي على كل من أنسجة البنكرياس الإفرازية والغدد الصماء. تم التعرف على عمليتين في نفس الوقت ، وهما تمايز الأنسجة الدهنية وتكوين الأوعية. أعلنت النتيجة أن الأنسجة الدهنية في البنكرياس كانت تستجيب وتعديل بنشاط لإنتاج جزر لانجرهانز حديثة التنظيم جيدة التنظيم مع خلايا بيتا متطورة. تم دمج هذه الجزر داخل الأنسجة الدهنية في البنكرياس ومحاطة بشبكة مكونة حديثًا من الأوعية الدموية. في هذا الصدد ، لوحظت خمس مراحل من تمايز الأنسجة الدهنية. استنتج أن الأنسجة الدهنية كانت بمثابة نسيج داعم لتعويض جزر البنكرياس التالفة وخلايا بيتا بسبب الحمل الزائد للوظيفة. علاوة على ذلك ، خلصت الدراسة إلى أن المضافات الغذائية MSG تعزز كل من العمليات ، تمايز الخلايا الدهنية وتكوين الأوعية.

الكلمات المفتاحية: البنكرياس ، الجلوتامات أحادية الصوديوم ، الأنسجة الدهنية

Introduction:

Monosodium glutamate (MSG) used extensively in the food preparation as flavor enhancer, it is also known as a vesting powder. A previous studies have been reported the effects of MSG when it given at a high dosages (Albrahim and Binobead, 2018; Jubaidi et al., 2019), therefore, the present study was done.

Adipocytes arise from mesenchymal stem cells (MSCs) by a sequential pathway of differentiation. MSCs develop either from ectoderm or mesoderm and commit into different undifferentiated precursors, which upon the expression of key transcription factors enter a differentiation program to acquire their specific functions. In mammals, the adipose tissue is composed of white adipocytes (primary site in energy storage) and of brown adipocytes (specialized in thermogenesis)(Laharrague and Casteilla, 2010)

Adipose tissue is now recognized as the body's largest endocrine organ, controlling many aspects of systemic physiology by secreting hormones (adipokines), lipids, cytokines and other factors (Nawrocki and Scherer, 2014 ; Gesta et al., 2007).

Adipose tissue-derived stem cells (ADSCs) are mesenchymal cells, which have a capacity for self-renewal and which can also be differentiated into adipocytes, chondrocytes, myocytes, osteoblasts and neurocytes among other cell lineages (Thomson et al., 1998) which has resulted in them being used in clinical trials for the treatment of conditions such as diabetes mellitus, liver disease, corneal lesions, articular and cutaneous lesions, among others (Gimeno et al., 2011 ; Hur et al. 2017) . In addition, stem cells and, in particular, adipose tissue-derived cells, play a key role in reconstructive or tissue engineering medicine as they can be used to develop new treatments. (Zimmerlin et al., 2013).

Materials and methods:

Animals:

Twenty-four adult wistar male rats aged between (6-8) weeks old and weight between (190-250 g). Animals were housed in an individual cages during autumn months (September, October and November) and evaluated clinically by physical examination before initiation of experiment. Animals were provided with food and water ad libitium [3]

and maintained in the animal house of veterinary medicine collage\university of Baghdad. Animals were divided into three groups. First group (A) included eight (8) mature male rats served as a control group and supplied only by water . Second group (B) included eight (8) mature male rats that were given a daily oral dose of MSG (15mg/ kg /BW) for 30 days and then they were scarified. Third group (C) included eight (8) mature male rats that were given a daily oral dose of MSG (15mg/ kg /BW) for 75 days and then they were scarified.

Histological study:

Samples from pancreas were preserved in 10% Neutral buffered formalin for 72 hrs then the specimen were processed by routine histological processing method (Weiss et al., 2011). H & E stain for routine tissue details, Gomori stain to differentiate between alpha and beta cells of pancreas (Alturkistani et al., 2016). A Histomorphometric measurements Were done by aid of optica view7 image analysis software, Which is a professional image analysis software that perform a series of processing or measurements and incorporates with optica camera (Ballesteros-Tato et al., 2012). The histomorphometric measurements of the pancreas include, diameter of the islet of Langerhans and nuclei of alpha and beta cells, Number of alpha & beta cells per islet of Langerhans, and Percentage of small and large diameter of Langerhans. All data presented as mean ± standard error. The comparisons of the data were done between groups at the same age. The significance of the differences between means was estimated with one way ANOVA by using SPSS version 20 at level ($P>0.05$).

Results:

The study focused on the interstitial adipose tissue present between the exocrine pancreatic lobules and the incidents of cellular specialization that occurred in it. After long- term administration of MSG, two processes were recognized at the same time, the differentiation of adipose tissue and the angiogenesis. Both these processes were thrown into five stages. In stage 1, Linear arrangement of pancreatic adipose tissue was observed (figure2). In stage 2, formation of polygonal beta cells with reddish cytoplasm and dark nuclei when stained with Gomori stain (figure 3). In stage 3, Beta cells were arranged at the periphery of the newly-formed islets of Langerhans (figure 4). In stage 4, a network

of newly-formed blood vessels was observed in the centre of adipose tissue indicating the onset of angiogenesis process (figure 5). In stage 5, beta cells were intermingled with different sizes blood vessels (Mature islet of langerhans beside large blood vessel) (figure 6). In the last stage there were Large functional islet of Langerhans packed mostly with alpha and beta cells embedded in adipose tissue (figure 7).

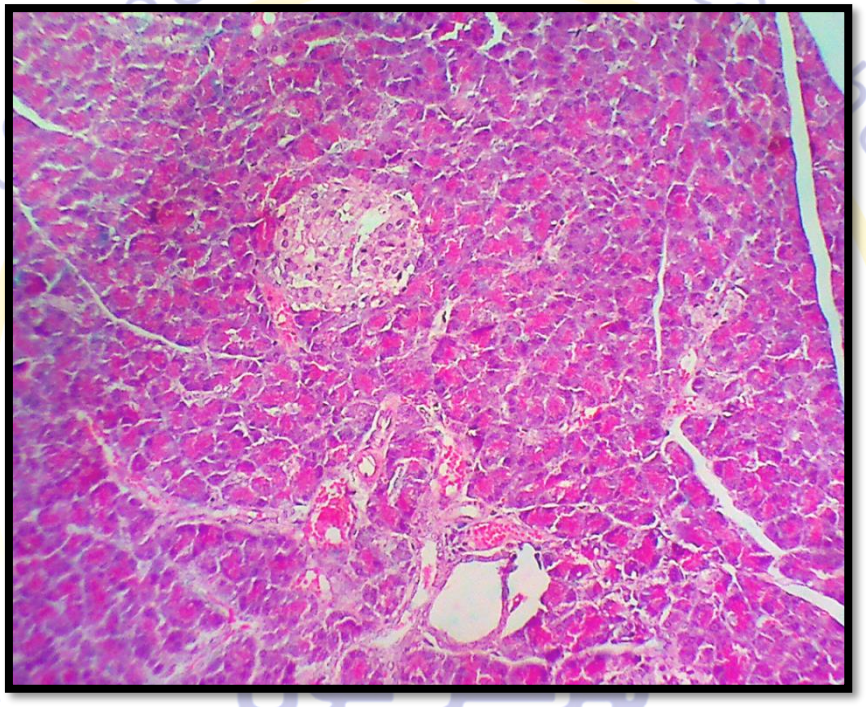
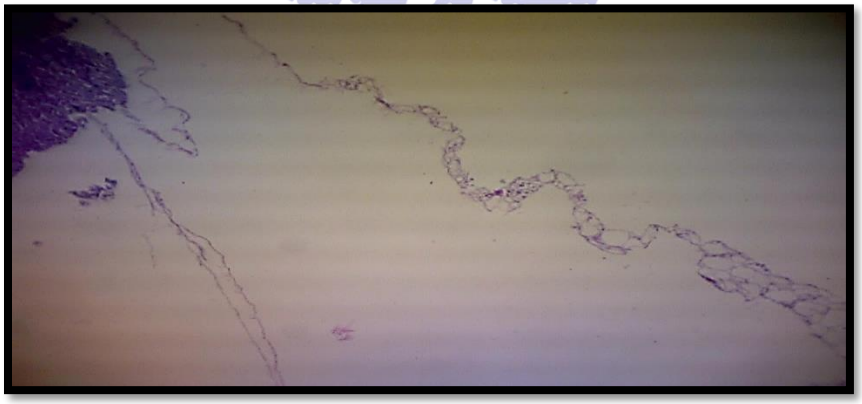


Figure (1) Histological section of pancreas of control group after 30 days showing normal architichture of the exocrine and endocrine parts of pancreas. H&E stain (100 X).



[5]

Figure (2): Histological section of pancreas of MSG treated group after 30 days (stage 1) showing linear arrangement of adipocytes. GOMORI'S stain. (100X).

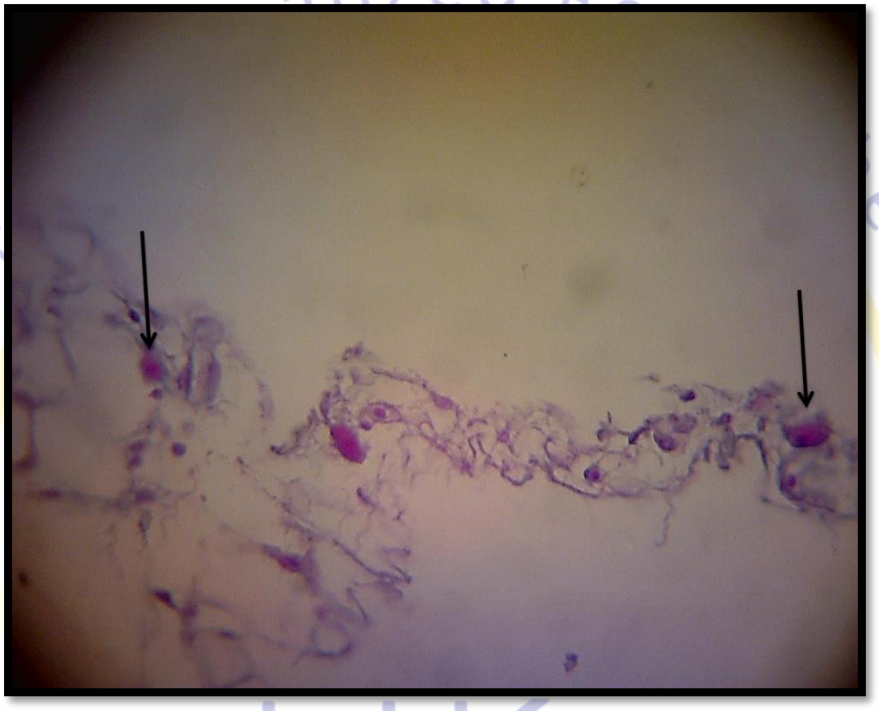


Figure (3): Histological section of pancreas of MSG treated group after 30 days (stage 2) showing formation of irregular elongated beta cells with reddish cytoplasm and dark nuclei (arrows). GOMORI'S stain. (400X).

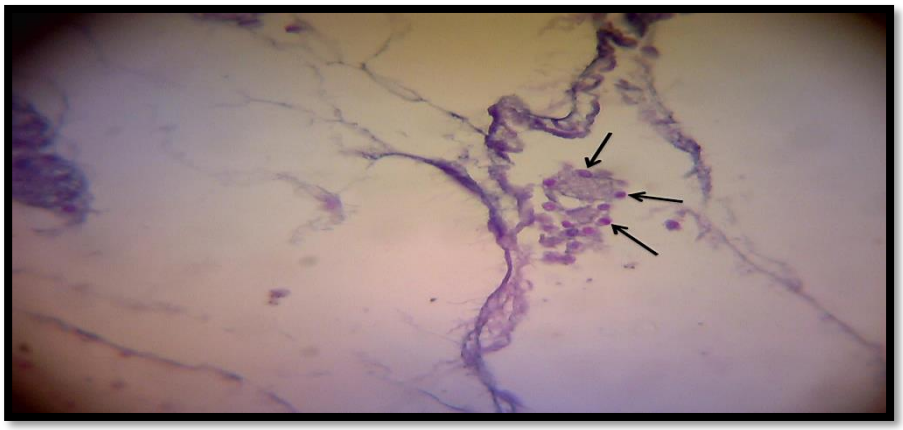


Figure (4): Histological section of pancreas of MSG treated group after 30 days (stage 3) showing Beta cells arranged at the periphery of the newly - formed islet of langerhans (arrows). GOMORI'S stain. (400X).

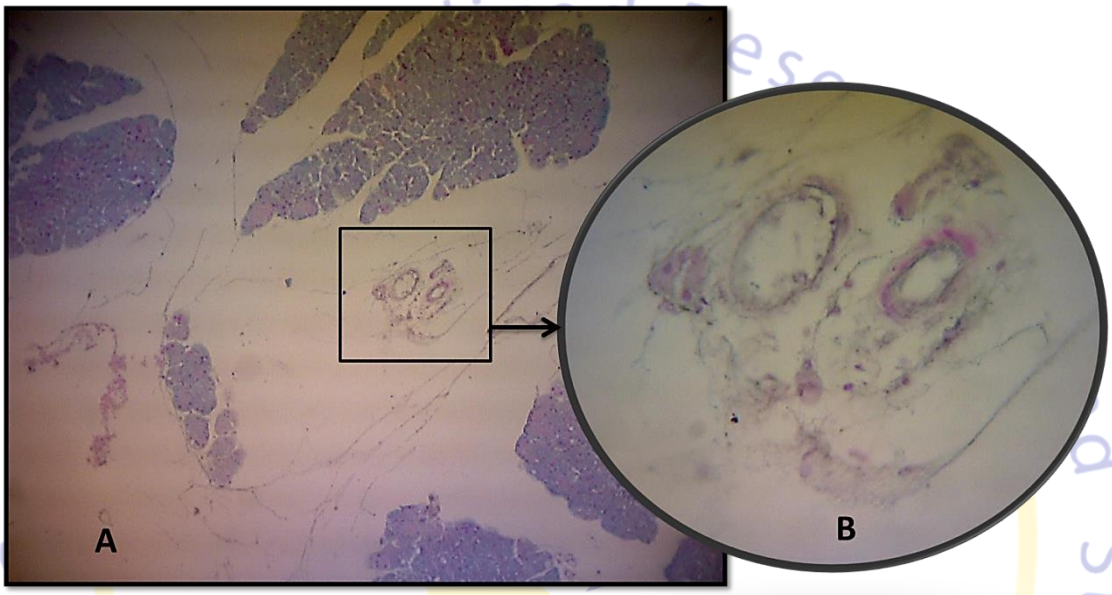


Figure (5): (A) Histological section of pancreas of MSG treated group after 75 days (stage 4) showing Network of newly- formed blood vessels observed in the center of adipose tissue indicating the onset of angiogenesis process. GOMORI'S stain. (100X). (B) showing high magnification power of network of newly- formed blood vessels. GOMORI'S stain. (400X).

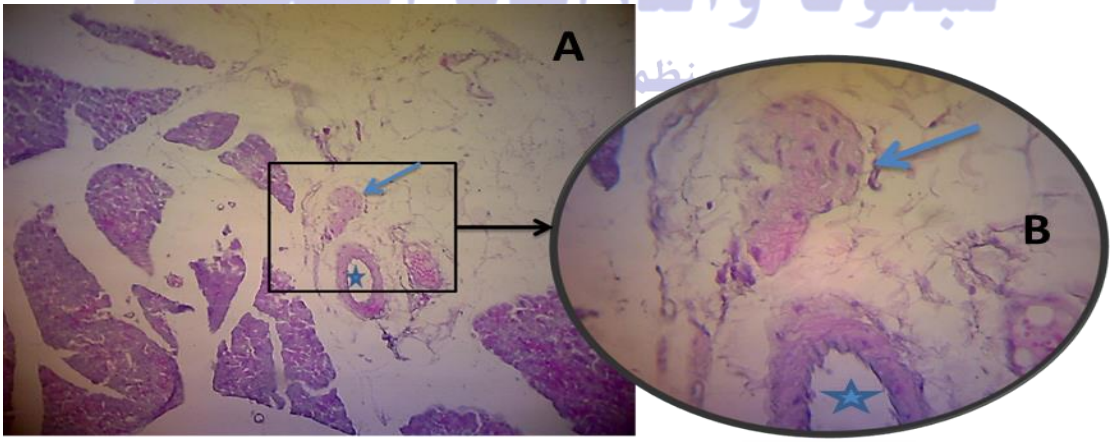


figure (6): (A) Histological section of pancreas of MSG treated group after 75 days (stage 5) showing Mature islet of langerhans (Blue arrow) beside large blood vessel (star). GOMORI'S stain. (100X). (B) showing high magnification power of islet of langerhans beside large blood vessel. GOMORI'S stain. (400X).

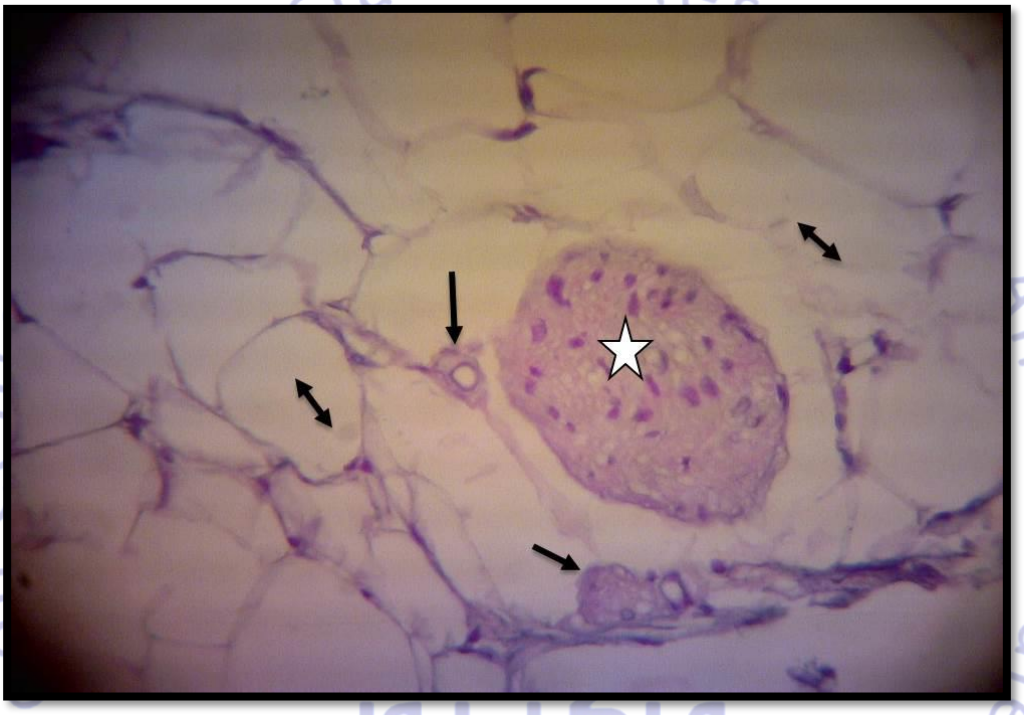


Figure (7): White star refers to Large functional islet of Langerhans packed mostly with alpha and beta cells. Arrows refer to smaller newly-formed two islets. All islets were embedded in adipose tissue (two-headed arrows). GOMORI'S stain. (400X).

Discussion:

MSG increases the appetite capability and obesity which in turn leads to over function and over load on the pancreas. These results were in agreement with results of Itoh et al. (2011) who stated that the Obesity is now viewed as a state of systemic, chronic low-grade inflammation. It has been recognized by recent studies that obesity (waist circumference) has a strong impact on adipokine secretion and insulin resistance (Stepień et al., 2011).

On the other hands, Boonnate et al. (2015) showed an increase in number of beta cells. Also, it has been reported that the number of alpha cells were increased due to MSG intake (Araujo et al., 2019). Last decade, the adipose tissue attracts the attention of many researchers and many researches were carried out many researches on the new functions of adipose tissue. Adipose tissue secretes many enzymes and growth factors and behaves as a large endocrine organ. These results were in agreement with results of Ahima and Flier, (2000) who showed that through the discovery of the ability to secrete hormones, great importance has been attributed to the role of adipose tissue . White adipose tissue may represent the largest endocrine tissue of humans. Its pleiotropic nature is based on the ability of fat cells to secrete numerous hormones, growth factors, enzymes, cytokines, complement factors and matrix proteins. Adipose tissue also expresses receptors for most of these factors that are implicated in the regulation of many processes including food intake, energy expenditure, metabolism homeostasis, immunity and blood pressure homeostasis (Costa and Duarte, 2006 ; Matsuzawa, 2006). The present study reported firstly that the adipose tissue can modified and differentiated into endocrine tissue. The present study declared that the process of adipose tissue differentiation thrown into five stages. The current study also demonstrated that both processes, adipocytes differentiation and angiogenesis takes place in the same manner and the same time. These results were in agreement with results of Chandra et al., (2009) who stated that the adult stem cells can be derived from adipose tissue and have the potential to differentiate into insulin producing cells

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