The relationships between blood acidity and white blood cells with hypertension before and after atenolol treatment

الطبيب جميل حسن محمد علي – مدرس مساعد المعهد التقني / كربلاء

Abstract:-

In Previous studies, the relationships between blood pressure (B.P) with white blood cells (WBC) and acidity (pH) of blood were studied in a limited way and separately.

In this study we tried to connect between these three parameters in details.

160 patients were chosen and divided into three groups, control, hypertensive, and hypertensive after atenolol treatment. Then each group was subdivided into two subgroups according to the pH.

Blood pressure, WBC differential and total count, and pH of the urine were estimated to each patient.

The results were : Blood pressure elevate with acidity, WBC count increased with mild B.P to decrease with higher B.P , Eosinophils decreased with increasing B.P , Lymphocytes and monocytes increased with increasing B.P., Variable results were shown regarding neutrophils and basophiles, After atenolol treatment all the values in hypertensive patients returned back to almost normal .

الخلاصة: _ هناك بحوث سابقة درست علاقة ضغط الدم مع خلايا الدم البيضاء , و علاقته مع حموضة الدم , و كذلك علاقة

هذاك بحوث سابقة درست علاقة ضعط الدم مع حمي اسم اسيست , و حرف من من من من مع خلايا الدم البيضاء , كلا على انفراد . في هذا البحث ارتاينا الجمع بين هذه المعايير الثلاثة , الضغط الدموي و خلايا الدم البيضاء و حموضة الدم لملاحظة التاثير الحاصل على هذه المعايير قبل و بعد استخدامنا لعقار الاتينولول الخافض لضغط الدم . اختير 160 مريضا بشكل عشوائي و قسموا الى ثلاثة مجاميع . مجموعة السيطرة و مجموعة الضغط الدموي و مجموعة الضغط بعد استخدامها عقار الاتينولول . و قد اجريت الاختبارات التالية على كافة المجاميع : فحص خلايا الدم البيضاء التقريقي و فحص مجموعة الدموي و و قد اجريت الاختبارات التالية على كافة المجاميع : فحص خلايا الدم البيضاء التقريقي و فحص مجموع خلايا الدم البيضاء و قياس حموضة البول (كمؤشر لحموضة الدم) و قياس ضغط الدم .

و كانت النتائج كالتالي : يرتفع ضغط الدم مع زيادة حموضة الدم و يزداد مجموع خلايا الدم البيضاء في الأشخاص و كانت النتائج كالتالي : يرتفع ضغط الدم مع زيادة حموضة الدم و يزداد مجموع خلايا الدم البيضاء في الأشخاص الذين يعانون من ضغط الدم الخفيف ليقل ثانية عند الضغط العالي ينخفض تعداد الخلايا الحامضية عند ارتفاع ضغط الدم بينما يزداد تعداد خلايا المونوسايت و الخلايا اللمفاوية بزيادة الضغط إما بالنسبة للخلايا المتعادلة و القاعدية فكانت النتائج متباينة ، و عند استخدام عقار الاتينولول فان كل المعايير قيد الدراسة قد عادت الى المستوى الطبيعي تقريبا في مرضى ضغط الدم .

Introduction:-

Although in most cases of hypertension the actual reason is obscure (95%), some cases of hypertension are secondary to recognizable diseases, such as Renal disorders, endocrine disorders and pregnancy. In most cases of hypertension the high blood pressure must be secondary to increased peripheral resistance due to vasoconstriction rather than to narrowing of the vessels from organic diseases [1].

The circulating blood contains colourless cells called white cells (5000 – 9000 /m m^{a} of blood). There are three varieties of white cells. The granulocyte series (Neutrophils 60 - 70 %, Eosinophils 2 - 4 % and Basophils 0.5- 0.02 %). the lymphocytes (20-30 %) and Monosytes (2-8%)[2].

Acidosis may be from a respiratory origin (when there is rise in the alveolar and arterial PCo₂ and the result is increase in carbonic acid), or metabolic one (that is excess metabolic hydrogen ion,

or loss of bicarbonate). While alkalosis may be from a respiratory origin (when there is a decrease in alveolar and arterial PCo_2 and the result is decrease in carbonic acid) or metabolic one (that is a deficit of metabolic hydrogen ion or the gain of bicarbonate) [2].

Selective B1-receptor antagonist (Atenolol) reduce the workload on the heart and help in regulation of heart beats, this medicine is used to treat high blood pressure and to prevent chest pain as well as used to protect the heart durineg heart attack [3].

Till now the picture is not clear about the relationships between blood picture, pH and hypertension. We tried here to connect these parameters together and examining the effects of atenolol on them .

Materials and methods:-

160 persons from both sexes aged above 40 years were chosen randomly and divided into three groups, 80 persons in each one according to following schedule:-

1 – control group A: 80 persons with normal blood pressure.

2 – Hypertensive group B: 80 patients with hypertension without treatment.

3 – treated group C: it is group B after two weeks of atenolol treatment one tablet 50 mg / day.

Each group was subdivided into 2 subgroups. 1 and 2 according to the acidity(pH). Subgroup 1 with higher pH(less acidity), 40 patients.

Subgroup 2 with lower pH (higher acidity), 40 patients.

So we have 3 groups (A. B. C) and 6 subgroups (A1 A2, B1 B2, C1 C2).

The following tests were done to each patient:-

- 1. White blood cells differential count. according to Geimsa stain (Cresent company) [4].
- 2. White blood cells total count.
- 3. Urine pH (as indicator to blood pH) [5][6][7].we used pH meter (Indian)
- 4. Blood pressure.
- 5. SPSS program (one-way ANOVA & bivariate correlations) was used for statistical evaluation.

Results:-

In table 1, when comparing groups (B, C) with group A we found :-

Blood pressure (B.P) increase with the decrease of pH in group B, But B.P will decrease when pH starts to increase in group C. So B.P increase with increasing acidity .result 1 (R 1)

Eosinophils cells was decreased significantly p<0.01 in group B with the increase of B.P. But eosinophils increase with the decreasing B.P in group C ,so there is a reversed relationship between eosinophils and B.P. result 2 (R2)

Regarding the other values we found :-

In group B: increase in B.P , WBC count p<0.05, lymphocytes and monocytes p<0.05. But little changes in neutrophils and basophiles (R3).

In group C: B.P was decreased but still higher than B.P in group (A). WBC, lymphocytes and monocytes decreased again. But still little effects in neutrophils and basophiles here .

So all the values in group C (after a tenolol) where returned back to almost $% \left({R4} \right)$. result 4 (R4)

B.P mm. Hg	105/70	153/95	142/87
WBC cells / m ^{m^a} of blood	6500	7500 **	6800
EOSINOPHILS CELLS %	3	1.7 *	1.8
LYMPHOCYTE CELLS %	31.8	33	31.8
NEUTROPHIL CELLS %	62.3	61.5	62.8
MONOCYTE CELLS %	2.7	3.7 **	3.5
BASOPHILCELLS %	0.11	0.12	0.11
pH of urine	6.1	5.7	5.8
	GROUP A CONTROL	GROUP B HYPERTENSION	GROUP C TREATED

Table 1:- the changes in groups (A, B, C)

* P<0.01 ** p<0.05

In table 2 :- when comparing with subgroup A1, there were high blood pressure with low pH in subgroups (A2,B2,B1,C1,C2), this support the result in groups A,B,C (B.P increase with increasing acidity). Result 5 (R5)

In subgroups (A2,B2,C2) comparing with the subgroup (A1), eosinophil cells increase (p<0.01) with the decreasing pH, B.P is higher than the B.P in subgroup(A1). Result 6 (R6)

Comparing with subgroup (A1) , In subgroups (B1,C1) , with highest level of B.P , eosinophils was decreased (p<0.05), pH here was increased comparing with subgroups (A2, B2 , C2) but was still less than pH in subgroup (A1). Result 7 (R7)

Regarding other white blood cells, comparing with A1, we found elevation of: - result 8 (R8)

- Eosinophils (p<0.01) and lymphocytes (p<0.05) in subgroup A2.
- WBC count, (p<0.05) and monocytes (p<0.05) in subgroup B2.
- Lymphocytes (p<0.05) and monocytes (p<0.05) in subgroup B1.
- WBC count and neutrophil in subgroup C1.
- Monocytes (p<0.05) and lymphocytes in subgroup C2.

A part from the mentioned cells above we found little changes in the remaining white cells (basophils) .

B.P mm. Hg	66\104	76\112	90\130	105\170	107\146	84\140
WBC cells / m ^{m^a} of blood	6900	6100	8500 **	6100	7100	6800
EOSINOPHILS CELLS %	2	4.5 *	2.5	1.1 *	1 *	2.1
LYMPHOCYTE CELLS %	29.7	35 **	28.5	35 **	30	32.1
NEUTROPHIL CELLS %	65	57	64	60.5	65.5	62.2
MONOCYTE CELLS %	2.8	2.6	4 **	3.5 **	3.7	3.5 **
BASOPHILCELLS %	0.10	0.11	0.13	0.12	0.11	0.12
pH of urine	6.5	5.7	5.6	5.8	5.9	5.6
	Subgroup A1 HIGHER PH	Subgroup A2 LOWER PH	SUBGROUP B2 LOWER PH	SUBGROUP B1 HIGHER PH	SUBGROUP CI HIGHER PH	SUBGROUP C2 LOWER PH

Table 2 :- the changes in subgroups (A1,A2,B2,B1,C1,C2)

* P<0.01 ** P<0.05

The results were arranged here according to the increasing B.P

Discussion:-

High blood pressure with increasing of blood acidity (R1)(R5) was found in many diseases ex: - (in chronic glomerulo – nephritis,the blood become acidic and blood pressure increase) [1]. The high B.P here may be due to either high adrenaline level (epinephrine after intravenous infusion there is a moderate increase in systolic pressure, diastolic blood pressure usually falls) [8], or due to activation of ionized calcium (ionized Ca^{++} reduced due to alkalosis) [8], but here we have acidic pH so ionized activated calcium may be the reason for hypertensive effect. The hypertensive effects due to Ca^{++} can be blocked by Ca^{++} channel blockers [8] [9]. To differentiate between these two effects, we have (adrenaline infusion showed a marked eosinopenia) [10] (R2)(R7). So high B.P in group B may be due to high adrenaline level because low level of eosinophils here.

In group C when atenolol is used, B.P falls (atenolol is a selective B1-receptor antagonist which reduce the workload on the heart and used as antihypertensive drug) [8]. So atenolol decrease the effect of adrenaline therefore eosinophils start to increase here (R4) (R6). The increased eosinophils in group C, with still high B.P (R4), may be also due to activated Ca^{++} or due to the acidic pH. (studies now demonstrate that acidity increase eosinophil cellular viability in a dose - dependent manner) [11]. (Acute inhibition of calcium – calmodulin will block a specific aspect of eosinophil motility) [12] (R2). So in group C we have hypertension with increasing eosinophils this may be due to some decrease in the level of adrenaline (atenolol effect) or activated Ca^{++} or both. (Many patients with primary pulmonary hypertension had an unusually high eosinophil count) [13].

The increased number of lymphocytes , monocytes and WBC count with decrease eosinophils in group B (R3) may be due to the hypertensive effect of adrenalin (recent evidence suggests that the lnflamatory response involving T – lymphocyte may be associated

with blood pressure elevation) [14]. (preactivated peripheral blood monocytes was detected in hypertensive patient) [15]. (several studies have shown that high WBC count is a risk factor for hypertension) [16].

These previous changes in white cells started to disappear in group C. which may be due to the low effects of adrenaline after atenolol treatment. (R4)

So the increased B.P in subgroups (A2,B2, C2) mostly due to the effects of activated Ca^{++} in acidic pH, because adrenaline decrease eosinophils [14], but here eosinophils were high (R6).and In subgroups (B1, C1), high B.P with decreasing eosinophils and acidic pH mostly due to the action of adrenalin [10] (R7).

The relationships between hypertension with adrenalin [8], and Ca^{++} , hypertension with W.B. cells. [14] [15] [16], may explain the relationships between adrenalin, Ca^{++} and hypertension with different types of infections and stress: - as following (R9)

- The increased numbers of eosinophils and lymphocytes in subgroup A2 may be due to allergic reactions or viral infection [17].
- The Increased WBC count, neutrophils and monocytes in subgroup B2 may be due to acute infection or stress [17].
- The Increased lymphocytes and monocytes in subgroup B1 may be due to chronic infection, viral infection or stress [17].
- The Increased WBC count and neutrophils in subgroup C1 may be due to acute infection. [17].
- The Increased monocytes and lymphocytes in C2 may be due to chronic infection, viral infection or stress [17].

Conclusion :-

From our results (result 6, 7). Ca^{++} action is increased in more acidic blood with increased number of eosinophil. So it is ideal to use calcium channel blocker antihypertensive drugs to hypertensive patient with such blood characters. But we can use beta-blocker antihypertensive drugs in patient with less acidic blood and less number of eosinophils because the higher activity of adrenalin in such patients. This idea needs further studies.

References:-

- 1. Macleod, J, in *Davidson's principle & practical of medicine*. Eleventh edition, Churchill Livingstone. New York. (1974). pp: 273-274. pp: 507-508.
- George H.Bell.J.Norman Davidson. Donald e\Emslie Smith. *Text book of physiology and Biochemistry*. Eighth edition. Churchill Livingstone. Edinburgh and London (1972). pp: 429-431. pp: 699-702. pp: 217
- 3. Cariberh B, Samuel sson O, lindholm LH. "Atenolol in hypertension is it a wise choice ? " *Lancet* -(2004) .364 (9446) pp: 1684-9.
- 4. Gerard J, Tortora N. principles of *anatomy and physiology*. 5th edition .(1987).
- 5. CHARLES R. BRASSFIELD and VIVIAN G. BEHRMANN."A CORRELATION OF THE pH OF ARTERIAL BLOOD AND URINE AS AFFECTED BY CHANGES IN PULMONARY VENTILATION " *Am J physiol* (1941).132 pp:272-280.
- 6. Celso Akio Maruta , Marta Lizandra Doregor, Daniel Mendes Netto etal"The measurement of urine pH to predict the amount of buffer used in the treatment of acute rumen lactic acidosis in cattle"*Cienc . Rural* (2008). 38(3).

- 7. LUBETSKAYA, T.MELNICHUK" Urine pH as an index for calculating the amount of bicarbonate for treatment of acidotic calves " *Journel of animal and feed sciences*(1999). 8 pp:247-254.
- 8. Alfred Goodman Gilman, Louis S.Goodman. Alfred Gilman, *The pharmacological basis of therpeutice*. Sixth edition. Macmillan. Publishing Coilnc . New York. (1980).
- 9. Ob Nelson, Mark. "Drug treatment of elevated blood pressure" Australian prescriber (2010). (33) pp: 108-112.
- 10. Z.Z Goblowski M.D. "Eosinopenia caused by adrenalin infusion and by insulin hypoglycaemia" *British medical journal* (1948). pp: 46.
- 11. Leah c.kottyan, Aunr. Collier. khanh H. Cao, kathrgn A.niee megan Hedgebeth, caius G.Radu, Owen N.witte, Gurjitk, khurana Hershey, Marc E.Rothenberg, and Naves Zimmerman " Eosinophil Viability is increased by acidic pH in a CAMP and GPR 6s dependent manner " *Blood*, September (2009). vol. 114. No.13 pp: 2774-2782.
- 12. Jwwalker "Acute inhibition of calcium calmdulin blocked specific aspect of eosinophil motility" <u>www.pnas.org/content/qs/41 1568.full.1998</u>.
- 13. Ivor obeyeseker and Neil soysa "primary pulmonary hypertension, eosinophilia , and filariasis in Ceylon "*Br heart J.* July, (1970) . 32 (4). pp: 524-536.
- 14. Rhian M.Touy2."Pathophysiology of hypertension " *Current Opinion in Nephrology & hypertension* March(2010). vol.19 issue 2 . pp181-186.
- 15. Yvonne Dorffel, christoph Latsch, Bruno stahlmuller, Susann scholze, Gerd R, Burmester, Jurgen Scholze, "preactivated peripheral blood Monocytes in patient with Essential Hypertension "*Hypertension* (1999). 34:pp:113-117.
- 16. Yoshimi Tatsukawa, Wan ling Hsu, Michiko Yamada John B cologne, Gen Suzuki, Hideya Yamamoto, Kiminori Yamane, Masazumi Aka hosi, Saeko Fujiwava and Nobuoki kohno. "White blood cell count, especially Neutrophil count, as a predictor of hypertension in a Japanese population" *Hypertension research* (2008). 31. pp: 391 1397.
- 17. Galdmanl. "Leukopenia and Leukocytosis" *Cecil Medicine* 23rd philadelphiai sauuders Elsevier (2007) .chap 173.