

The effect of different vasoconstrictor containing local anaesthetic solutions on plasma glucose in normal and diabetic-volunteers

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ABSTRACT

In this study, the change in plasma glucose half an hour after injection of different vasoconstrictors contained in local anaesthetic solution where measured both in normal and diabetic volunteers. Single cartridge contain (1.8) ml of plain (2%) xylocain or that with (1:80000) concentration of a adrenaline or (3%) prilocain with (0.03) IU of felypressin injected at labial to left maxillary lateral incisor region.

The result showed that half an hour after injection of a adrenaline containing solution, a very highly significant increase in plasma glucose noticed in both study groups from pre-injection base line value ($p < 0.001$). Increase in plasma glucose in diabetic group were significantly greater than that in normal control group ($p < 0.05$). Within diabetic volunteers, this increase were significantly greater in insulin dependent diabetic group than that in non insulin dependent volunteers. After injection of plain solution or that containing felypressin, reduction in plasma glucose noticed.

In conclusion, adrenaline contained within local anaesthetic solution produce hyperglycemic effect even in dose of single dental cartridge. This response enhanced in diabetic patient in general with greater enhancement noticed in insulin dependent patient.

Key Words: Diabetes, vasoconstrictor, local anesthesia.

الخلاصة

في هذه الدراسة تم قياس التغيير بمعدل الجلوكوز بالبلازما بعد نصف ساعة من حقن أنواع مختلفة من المخدر الموضعي الحاوي على قابضات الأوعية الدموية عند متطوعين مصابين وغير مصابين بمرض السكري. ثم استعمال خرطوشة واحدة حاوية على (1,8) مل من المخدر زايلوكانين (2%) بدون مضافات أو زايلوكانين (2%) مع أدرينالين بتركيز (1:80000) أو مخدر البريلوكائين (3%) مع فليبريسين (0.03) وحدة قياسية عالمية وقد حققت لكل متطوع في منطقة السن القاطع الجانبي العلوي الأيسر. الدراسة أو ضحت انه بعد نصف ساعة من حقن المخدر الحاوي على الأدرينالين كانت الزيادة بالبلازما جلوكوز معنوية في مجموعتي الدراسة عن معدلها قبل الحقن كانت هذه الزيادة أكثر معنوية عند مجموعة المتطوعين المصابين بمرض السكري عنها عند الأصحاء. ضمن مجموعة المتطوعين المصابين بمرض السكري الزيادة كانت أكثر عند مرضى السكري غير المعتمد على الأنسولين.

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أوضحت الدراسة انه بعد حقن المخدر الخالي من الإضافات أو المخدر الحاوي على الفلبريسين فإن معدل البلازما جلوكوز قد انخفض بعد نصف ساعة من الحقن.

نستنتج من الدراسة أن جرعة المخدر الواحدة الحاوية على (1,8) مل من المحلول الحاوي على الأدرينالين له تأثير يرفع معدل الجلوكوز بالبلازما وهذا التأثير يكون أكثر عند مرضى السكري عموماً وعند مرضى السكري المعتمد على الأنسولين بوجه خاص.

INTRODUCTION

Addition of vasoconstrictor to local anaesthetic solution have been employed to achieve several advantage including prolongation of duration of action, improving depth of anesthesia, reducing bleeding at operation site, reducing toxic effect of local anaesthetic solutions and finally reducing the dose of local anaesthetic solution needed⁽¹⁻⁶⁾.

In other hand this additive is without the risk of developing adverse effect especially the use of sympathomimetic agent which may absorb systemically in sufficient concentration to cause serious side effect including arise in blood pressure, cardiac arrhythmia and cardiac arrest.⁽⁷⁻⁸⁾ Accordingly, sympathamimetic amine should be used with caution for those patient susceptible to their action.⁽⁹⁻¹¹⁾

Others effects of those agents, are metabolic effects that include hyperglycemic and hyperkalemic effects. Hyperglycemic effect is produced by enhanced level of glycogenolysis and gluconeogenesis (which produced by stimulation of hepatic β_2 receptors) and inhibition of insulin secretion (which produce by stimulation of α pancreatic receptors).⁽¹²⁻¹⁷⁾

Different studies have been attempted to measure the threshold level for adrenaline to produce hyperglycemic effects. The does of these agents within local anaesthetic solution in dental uses is too small to produce serious side effects from transient hyperglycemia produced for half an hour only. However in diabetic patients, enhanced hyperglycemic response that my sustained for long period (about 5 an hour) noticed. This enhanced response is much accentuated in uncontrolled or poorly controlled diabetics which may bring the patient to a condition of hyperglycemic shock or ketoacidosis⁽¹⁸⁻²¹⁾.

Therefor the greater risk of development of hyperglycemia and ketoacidosis must be avoided for such patient by avoiding the administration of large dose of adrenaline is those susceptible patient and other vasoconstrictor such as felypressin could be used safely.

So this study designed to determine the change in plasma glucose after administration of different vasoconstrictor contained in local anaesthetic agent in normal and diabetic volunteers to determine the hyperglycemic effect of adrenaline in normal & diabetic volunteers half an hour after injections.

MATERIALS AND METHODS

Clinical trial conducted at Al-Waffa clinic of diabetes in Mosul and Collage of Dentistry / University of Mosul.

In this study of (117) volunteers participated (97) were diabetic volunteers and (20) where normal. Of diabetic volunteers, (61) were non-insulin dependent and (36) where insulin dependent.

Each diabetic group divided in to (3) subgroup according to the type of local anaesthetic solution to be injected and volunteers distributed on different solution according to the table of random number.

For control group, each volunteer receives (3) type of injection on (3) separate days thus representing (3) subgroup.

Local anaesthetic solutions used were either plain (2%) xylocain or xylocain (2%) with (1:80000) concentration of adrenaline or prilocain (3%) with (0.03) IU of felypressin.

Each volunteer seated at the morning after an over night fasting, area of cubital fossa scabed several times with cotton saturated with hibitane. Then (2) ml of venous blood aspirated for plasma glucose determination and placed into fluoride oxalate tube to prevent glycolysis and coagulation. After short period of rest, (1.8) ml of proposed anaesthetic solution injected at area labial to the left maxillary lateral incisor to reduce the possibility of intravascular injection, as that site is less vascular than other region⁽²²⁾. Half an hour later another (2) ml of venous blood aspirated for plasma glucose determination and placed into another fluoride oxalate tube.

Plasma glucose determination performed at the same day by using specific glucose oxidase method using Randex enzymatic kit.

Two ml of reagent solution added to (20) microliter of plasma or standard solution and the solution left to react at room temperature for (25) minutes. Then spectrophotometer used to measure the absorbency of standard or sample solution against blank solution at (500)-nm absorbency. Then following equation used to measure plasma glucose:

$$\begin{aligned} \text{Plasma glucose} &= \frac{\text{Absorbency of sample}}{\text{Absorbency of standard}} \times 100 \\ &= \text{mg/dl} \end{aligned}$$

Statistical analysis performed after determination of pre and post injection plasma glucose. Measurement of change in plasma glucose performed. Following statistical test performed to determine the significance of change in plasma glucose:

- 1-t-test to determine the significance of change of plasma glucose from pre injection base line value at (0.05), (0.01) and (0.001) level of significance.
- 2-ANOVA test to determine if there is significance in difference of change in plasma glucose among different study group.
- 3-Dunces Multiple Range test to determine the highest & lowest group in their change of plasma glucose when F- test show significance.

RESULTS

In this study, of total (97) diabetic volunteers the mean age of them was (43) years, (28) years for insulin dependent volunteers and (51) years for non-insulin dependent volunteers. Ratio of male to female in diabetic volunteers was (1:1.3). For control group all volunteers were male with age range of (21) years.

After measurement plasma glucose change in two study group, increase in plasma glucose noticed half an hour after injection of adrenaline containing solution. This increase being very highly significant comparing to pre injection base line value ($p < 0.001$). Following injection of plain solution or that containing felypressin there were a reduction in plasma glucose in (3)-study group with no significant difference noticed between (2) type of solution injected.

Within control study group increase in plasma glucose after injection of adrenaline containing local anaesthetic solution where very high significantly greater than the reduction noticed after injection of both other (2) solution ($p < 0.001$) (table 1, and figure 1).

Table (1): Plasma glucose before and after injection of different solutions in control group

Type of Injected Solution	Plasma Glucose Before Injection mg/dl	Plasma Glucose After Injection mg/dl	t-value
Xylocain (2%) Plain Solution	95	91	5.7
Xylocain (2%) with Adrenaline (1:80000)	95	111	18.3
Prilocaine (3%) with Felypressin (0.03) IU	95	90	7.8

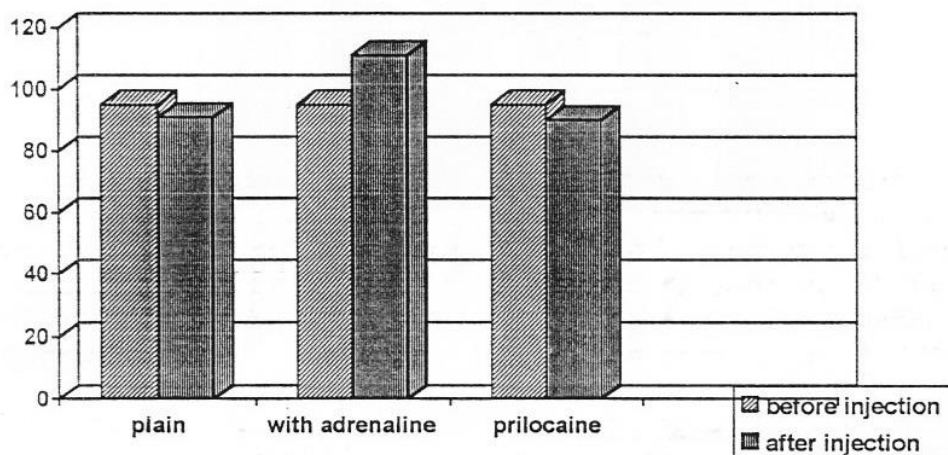


Figure (1): Plasma glucose before and after injection of different solutions in control group

Within both diabetic groups increase in plasma glucose after injection of adrenaline containing local anaesthetic solution where very high significantly greater than the reduction noticed after injection of both other (2) solution ($p < 0.001$) (table 2, and figure 2).

Table (2): Plasma glucose before and after injection of different solutions in diabetic groups

Type of Injected Solution	Plasma Glucose Before Injection mg/dl	Plasma Glucose After Injection mg/dl	t-value
In Insulin Dependent Group			
Xylocain (2%) Plain Solution	232	226	3.67
Xylocain (2%) with Adrenaline 1:80000	230	254	25.04
Prilocaine (3%) with Felypressin (0.03) IU	233	226	7.01
In Non-insulin Dependent Group			
Xylocain (2%) Plain Solution	221	216	4.2
Xylocain (2%) with Adrenaline (1:80000)	218	238	16.1
Prilocaine (3%) with Felypressin (0.03) IU	214	208	7.8

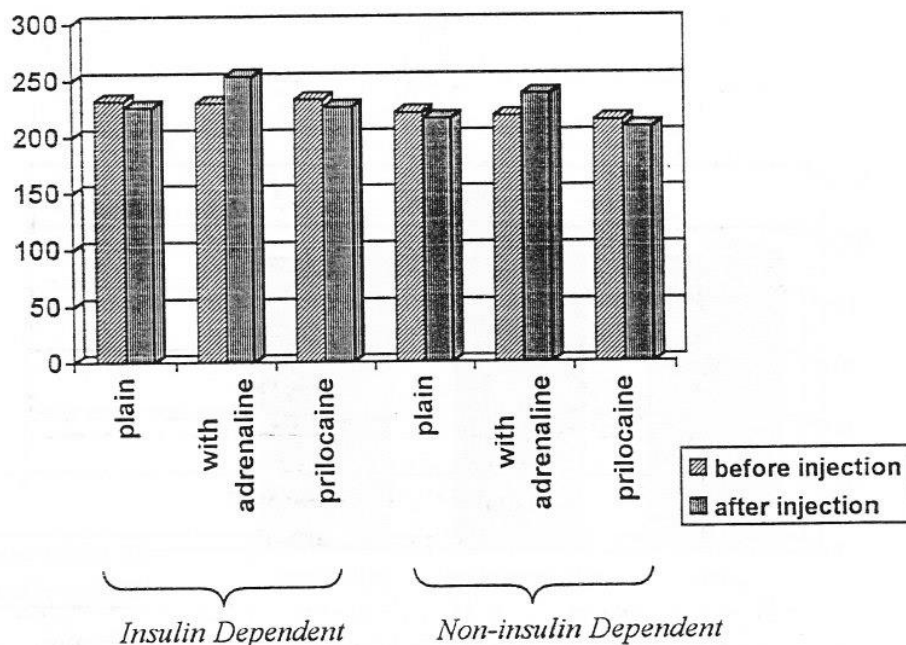


Figure (2): Plasma glucose before and after injection of different solutions in diabetic groups

For group injected with adrenaline containing local anaesthetic solution, mean increase in plasma glucose after such injection in diabetic volunteers was about (22) mg/dl. Whereas in normal volunteers, increase in plasma glucose after injection of adrenaline containing solution was significantly less than that in diabetic volunteers ($p < 0.05$) and was about (15) mg/dl.

Within diabetic volunteers this increase was more significant in insulin dependant group than in non-insulin dependent group ($p < 0.05$). Using ANOVA test it shows significant difference both with in and in between three groups injected with adrenaline containing solution ($F_{2, 51} = 14.8$). Using Duncan Multiple Range test, maximum increase in plasma glucose noticed in insulin dependent group followed by non insulin dependent group and finally normal control group (table 3, and figure 3).

Table (3): Plasma glucose change after injection of adrenaline containing local anaesthetic solution in three study groups

Group	No. of Volunteers	Change in Plasma Glucose After Injection of Adrenaline (mg/dl)	Significance of Change
Insulin Dependent	12	20	V.H.S
Non-insulin Dependent	20	25	H.S
Control	20	15	S

$F_{2, 51} = 14.8$

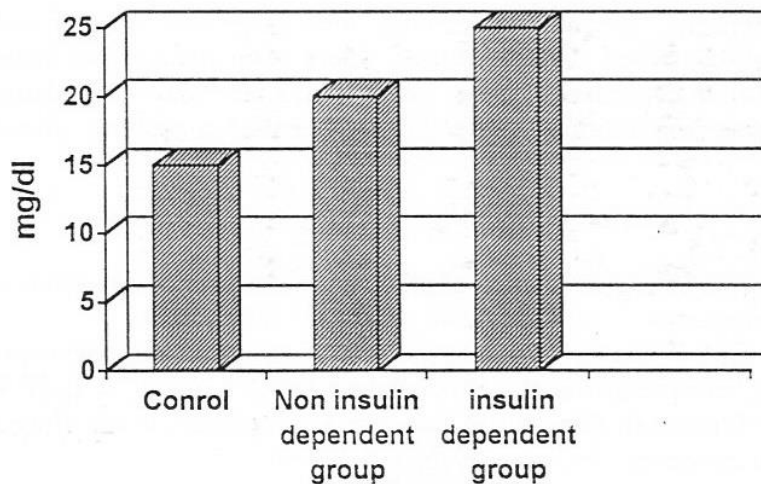


Figure (3): Plasma glucose change after injection of adrenaline containing local anaesthetic solution in three study groups

DISCUSSION

Hyperglycemic effect of adrenaline produced by increasing level of liver gluconeogenesis and glycogenolysis as well as enhancing glucagon secretion and inhibition of insulin secretion^(12,13,16)

Most of study demonstrated a threshold level for adrenaline as hyperglycemic agent and found that its equal to (150-200) pg/ml of blood which is produced by injection of (3) dental local anaesthetic cartridge containing (1:100000) concentration of adrenaline^(13,5). Other studies show that even smaller doses of adrenaline may elevate plasma glucose^(23,24).

In this study increased in plasma glucose half an hour after injection of adrenaline containing solution from base line pre injection level noticed and was purely attributed to the effect of adrenaline it self and not other factor as stress or pain of injection. This based on comparison with group injected with plain solution, which show reduction in plasma glucose although they are exposed to the same stress or pain.

For diabetic patients, enhanced hyperglycemic response noticed for adrenaline. This accentuated response caused by increase cyclic adenosine monophosphate response to epinephrine due to inhibition of insulin secretion^(21,25,26). This accentuated response was also sustained for (5) hours rather than transient response that noticed in normal individual⁽¹⁹⁾.

Within diabetic volunteers increase in plasma glucose after injection of adrenaline containing solution were more significant in insulin dependent volunteers and this may attributed to completely inhibited insulin pancreatic or pancreas destruction of β cell occur which accentuate the response of A cell to epinephrine to secrete glucagon. This result agreed with that performed by other studies^(18,20).

Accordingly, the chance of hyperglycemic shock and ketoacidosis may occur in uncontrolled diabetics (specially in insulin dependent diabetics) after injection of adrenaline containing solution and this agree with Perruse *et al.*⁽¹⁰⁾. Other solution (Plain or felypressin containing) showed a reduction in plasma glucose so that could be used safely for diabetic patients.

In conclusion adrenaline containing local anaesthetic solution could be used safely for well-controlled diabetic patient where as in uncontrolled diabetic patient (especially insulin dependent) -when use of local anaesthetic is mandatory- plain or felypressin-containing solution is preferable to adrenaline containing solution.

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