Studies of the Arterial Pulse Wave

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Previous studies have shown abnormalities of the arterial pulse wave in hypertensive subjects of all age groups. The major change has been diminution to disappearance of the dicrotic wave. The pharmacologic differences between epinephrine and norepinephrine offer a means of studying the mechanism of this change in the dicrotic wave. In the present study, normotensive subjects have had transient hypertension induced by the infusion of epinephrine and norepinephrine. The different effects of these drugs on their arterial pulse waves have been recorded.

IN A previous report,1 describing observations on the arterial pulse wave in human subjects, a new technic was introduced for recording the pulse wave without intra-arterial puncture. The method has been shown to be sensitive and to give reproducible results. The accuracy of the recordings has been demonstrated by the similarity of simultaneous intra-arterial and extra-arterial tracings.

Figures 1 and 2 show typical instances of normal and abnormal arterial pulse waves as recorded by this technic. The major difference in the abnormal cases appears to be diminution to disappearance of the dicrotic wave. These changes in the dicrotic segment of the arterial pulse wave have been found in hypertensive subjects of all age groups as well as in patients with generalized arteriosclerosis, coronary arteriosclerosis, and diabetes mellitus.

The dicrotic wave has been ascribed to a reflected wave from the recoil of the blood column against the closed aortic valve. More recent studies2-7 indicate that peripheral factors also play a role in the formation of the dicrotic wave. The technic described herein seemed to offer another means of studying the mechanism of the dicrotic wave.

The pharmacologic studies of Goldenberg and his group8 have shown that although both epinephrine and norepinephrine produce comparable degrees of hypertension, they do so in different ways. The hypertensive action of epinephrine in man is due primarily to a large increase in cardiac output that overbalances a decrease in total peripheral resistance. On the other hand, hypertension induced by norepinephrine is produced in man by a striking increase in peripheral resistance with little or no change in the cardiac

Fig. 1. Normal arterial pulse waves recorded from the third digit of a healthy 25 year old man. The vertical lines are time signals 0.1 second apart and the horizontal lines represent pressure increments of 10 mm. Hg in the cuff applied about the finger. The cuff pressure (P) is recorded simultaneously but independently of the components of the pulse wave. Note initial wave (I) and well defined dicrotic wave (D).
output. It appeared that investigation of the effect of these 2 drugs, with their different central and peripheral actions, might help to explain the mode of origin of the dicrotic wave. Accordingly, the present study has been carried out on the effect of intravenous infusions of epinephrine and norepinephrine, in quantities sufficient to produce significant hypertension, on the dicrotic wave of presumably healthy, normotensive individuals.

Method and Technic

A sensitive rubber cuff with an inelastic backing is applied to the external surface of the limb or digit. The cuff consists of a thin rectangular membrane 11/2 by 3 inches cemented at the edges to a backing piece of rubberized cloth. A 1/8 inch I.D. nipple attached at the center of the cloth is connected to a 3 foot length of 1/8 inch rubber tubing. This tubing serves the dual purpose of inflating the cuff and connecting it to the recording chamber of a differential pressure transducer. The cuff is attached by an inelastic strap to the extremity to be examined.

The differential pressure transducer consists of a circular beryllium copper diaphragm 0.006 inch thick and 11/2 inches in diameter, separating 2 air chambers. Air pressure required to inflate the cuff is introduced to both chambers, causing no deflection of the diaphragm. Pressure disturbances originating at the cuff, however, are conducted to the recording chamber only. These disturbances cause the diaphragm to deflect according to their intensity and direction.

Deflections of the diaphragm are transmitted by mechanical linkage either to a Statham absolute pressure strain gage or to a piezo-electric crystal cartridge that generates electric energy according to the mechanical motion imposed upon it. The crystal unit (Astatic microphone cartridge D-104) has an output of -45 db. referred to 1 volt per micro bar. Output from the crystal is amplified with a class A balanced push-pull amplifier with continuous variable gain from 0 to 16 db. max. The amplifier feeds a dual-coil string-type mirror galvanometer.

Permanent recordings are made on 12 cm. wide electrocardiographic paper, with a Cambridge 3-speed camera. Camera speeds are 121/2, 25, or 50 mm. per second. Timing marks appear as equally spaced vertical lines. Recordings can also be made intra-arterially and taken on direct-writing electrocardiograph paper.

The frequency response of the entire system from cuff to galvanometer shows the response to be substantially flat to 40 cps., which is well above the 5 to 6 cycle range encountered in studying arterial pulse waves.

Continuously variable gain control enables the operator to standardize the amplitude of recordings without affecting the configuration of the arterial pulse wave. This feature is of value in comparative studies over a period of time on the same subject. Recording at the same basic amplitude permits standardized conditions insofar as the instrument itself is concerned. The only variables then lie with the patient.

\[ \text{Fig. 2. Left. Abnormal arterial pulse wave. Note diminished size of dicrotic wave (D). The cuff pressure (P) is also recorded. Right. More severely abnormal arterial pulse wave showing a complete absence of the dicrotic wave.} \]
STUDIES OF ARTERIAL PULSE WAVE

All arterial pulse wave tracings during this study were recorded intra-arterially. A Cour- nand needle (18 gage, 2 3/64 inch. no. 488 LNR) was introduced into a brachial artery. Pulse pressure waves were transmitted to a Statham P-23A absolute pressure strain gage and a continuous intra-arterial pulse wave tracing was begun. After a control period lasting from 2 to 5 minutes, a previously introduced infusion of glucose and water was changed to an infusion containing either norepinephrine (Levophed) or epinephrine (Suprarenin, Winthrop). The blood pressure was taken by cuff at 1 minute intervals and in some cases was also recorded on the tracing. After 3 minutes of sustained elevation of systolic and diastolic pressures, the intravenous infusion was discontinued but the continuous intra-arterial pulse wave recording was maintained until the configuration of the pulse wave had about returned to its control appearance. This usually took 10 to 15 minutes. The blood pressure invariably fell to its baseline levels before the control pulse wave configuration was restored.

Fig. 3. Effect of intravenous infusion of norepinephrine on the arterial pulse wave of a 32 year old normotensive male subject. Note the diminution of the dicrotic wave (D) in 2 and its virtual disappearance in 3. It starts to return in 4 after the blood pressure has returned to control levels.

RESULTS

With Norepinephrine

Nine normotensive, presumably healthy subjects were given norepinephrine by intravenous infusion. In all individuals, as the blood pressure rose, the well defined dicrotic wave of the control intra-arterial pulse wave became smaller and finally disappeared completely. Upon discontinuing the norepinephrine, the dicrotic wave reappeared within minutes of the return of the blood pressure to control levels.

Figure 3 is illustrative of these changes. The subject was a 32 year old male hospital porter with no clinical evidences of vascular disease. His resting blood pressure was 120/80, and a well defined dicrotic wave is seen on his initial pulse tracing. The blood pressure rose to 170/110 after 1 minute of intravenous norepinephrine in doses of 0.4 µg. per Kg. per minute and the dicrotic wave became markedly smaller. The double peaking of the anacrotic wave has been seen in other subjects with hypertension, whether natural
or induced. Its cause remains unexplained. After 3 minutes of sustained hypertension, the dicrotic wave completely disappeared. Five minutes after stopping the norepinephrine infusion, the blood pressure had returned to its control level of 120/80 and the dicrotic wave had started to become evident again. The study was discontinued in this patient before the dicrotic wave had recovered its full height.

With Epinephrine

Four normotensive, presumably healthy subjects were given epinephrine intravenously. Despite elevations of the systolic and diastolic blood pressure comparable to those seen in the experiments with norepinephrine, no basic change was noted in the configuration of the dicrotic wave. Specifically, the dicrotic wave was neither diminished nor had disappeared in any of the subjects studied, even though the over-all amplitude of the pulse wave increased as the blood pressure rose.

Figure 4 illustrates these changes in a 21 year old female hospital technician. Epinephrine was infused intravenously in doses of 0.4 μg. per Kg. per minute for a total of 8 minutes. During this time the blood pressure rose from 122/80 to a sustained peak of 220/110. Although the form of the arterial pulse wave reflected this change in the blood pressure, the dicrotic wave remained clearly defined in all tracings.

In one of the normotensive subjects (a 30 year old male technician) epinephrine and norepinephrine were given consecutively, with a 15 minute interval between the administration of the 2 drugs to permit return of the control pattern. The typical difference between the effects of epinephrine and norepinephrine are demonstrated in this case (fig. 5). Both drugs produced approximately the same elevation of blood pressure. Norepinephrine caused a complete disappearance of the dicrotic wave, whereas the dicrotic wave was undisturbed after the administration of epinephrine.

DISCUSSION

The mode of origin and propagation of the dicrotic wave has been investigated for years but remains incompletely understood. The
Fig. 5. Effect of epinephrine and norepinephrine given consecutively to the same patient after a 15 minute interval. Note persistence of the dicrotic wave (D) in the epinephrine tracings and its disappearance after norepinephrine. Both drugs gave comparable elevations of blood pressure.

classic theory explains the dicrotic peak as a reflected wave initiated by the recoil of the arterial blood column against the closed aortic valve. The studies of Hamilton, Remington, and Dow,\(^2\)\(^-\)\(^5\) Wiggers,\(^6\) and Alexander\(^7\) have shown that the arterial pulse wave is progressively transformed in its passage down the aorta and its arterial branches, suggesting that the physiologic state of the peripheral vessels may play an important part in influencing the appearance of the dicrotic wave. Our initial studies\(^1\) also suggested that changes in the peripheral arteries determine the presence or absence of the dicrotic wave of the arterial pulse. It was found, for example, that the dicrotic wave was markedly abnormal in hypertensive subjects of all age groups, in patients with peripheral arteriosclerosis, and in diabetic patients as young as 14 years of age.

The results of the present study would seem to support this view. In the 4 subjects given epinephrine, the dicrotic wave was not basically altered although the blood pressure rose significantly. On the other hand, in all 9 patients who received norepinephrine, the dicrotic wave was abolished or markedly reduced in size, despite a similar rise in blood pressure. These findings are well explained by what is known of the pharmacologic differences between the 2 drugs. Goldenberg and others\(^8\) have shown that the actions of epinephrine and norepinephrine in man are similar only in that they both produce significant elevations of blood pressure. The hypertensive effect of norepinephrine is due to an increase of total peripheral resistance, with no significant change in cardiac output. Epinephrine, on the other hand, raises the blood pressure predominantly by a central action on the heart, increasing the rate and force of cardiac contractions and the cardiac output. The peripheral resistance actually decreases, because of an over-all vasodilating action.

The marked difference between the effects of epinephrine and norepinephrine on the dicrotic wave thus support the hypothesis that changes in the tonus of the arterial wall have significant effects on the configuration of the distinctive waves seen in arterial pulse tracings.
SUMMARY

Previous studies have shown a diminution to disappearance of the dicrotic wave in the presence of clinical evidences of arteriosclerosis, diabetes mellitus, and hypertensive vascular disease.

Transitory hypertension was induced in 13 normotensive subjects by intravenous infusions of either norepinephrine or epinephrine. A continuous intra-arterial pulse-wave tracing was recorded from the brachial artery before, during, and after the infusions in most instances.

The pulse waves of all 9 subjects given norepinephrine demonstrated disappearance of the dicrotic wave as the blood pressure rose. The dicrotic wave reappeared as the blood pressure returned to normal. Contrariwise, 4 subjects given epinephrine had no change in the dicrotic wave despite comparable elevation of the blood pressure.

The different effects on the dicrotic wave may be related to the pharmacologic differences between the 2 drugs. Epinephrine hypertension is produced by an increased cardiac output in spite of a reduced total peripheral resistance; norepinephrine hypertension is caused by an increased peripheral resistance with little or no change in cardiac output.

The evidence presented lends support to the theory that peripheral factors play an important role in the production of the dicrotic peak of the arterial pulse wave.

SUMMARIO IN INTERLINGUA

Previe studios ha monstrate un diminution o dispariton del unda dicrotic in le presentia de manifestationes clinic de arteriosclerosis, diabe mellite, e hypertensive morbo vasculare.

Hypertension transitori esseva inducita in 13 subjectos normotensive per infusiones intra-venose de norepinephrina o de epinephrina. Un registration continue del unda del pulso intra-arterial essava effectuate pro le arteria brachial ante, durante, e post le infusiones (in le majoritate del casos).

Le undas de pulso del 9 subjectos recipiente norepinephrina exhibiva disparition del unda dicrotic in association con le augmento del pression de sanguine. Le unda dicrotic re-appareva quando le pression de sanguine retornava a nivels normal. Del altre latere, 4 subjectos recipiente epinephrina exhibiva nulle alteration del unda dicrotic in despecto de comparabile augmentos del pression de sanguine.

Le differentia inter le effectos exerce e super le undas dicrotic es possibilemente relationate al differentias pharmacologic inter le duo drogas. Hypertension a epinephrina es producita per un augmento del rendimento cardiac in despecto de un reduceit total resistentia peripheric. Hypertension a norepinephrina es causata per un augmento del resistentia peripheric con pauc o nulle alteration del rendimento cardiac.

Le datos presentate supporta le theoria que factores peripheric ha un rolo importante in le production del culmine dicrotic que characterisa le unda del pulso arterial.

REFERENCES
