### AUTO TRANSFUSION AND BLOOD PRESSURE ELEVATION BY ELASTIC LEG COMPRESSION IN NORMAL SUBJECTS

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## ABSTRACT

*Study Objective:* This study was aimed to evaluate the physiological and biochemical effects of an autotransfusion tourniquet (ATT) that is intended for the emergency treatment of shock. The ATT is an elastic ring wrapped around by a longitudinal sleeve. When it is rolled up a limb it compresses the tissues beneath it with a pressure that is higher than the systolic blood pressure and remains as an arterial tourniquet at the proximal end of the limb.

*Methods:* In this study we measured the extent of lower limb auto-transfusion and the rise in blood pressure induced by the ATT in 18 normal volunteers (16 male, age range 21-55). In addition, we searched for other cardiopulmonary and biochemical effects of applying the ATT for 20 minutes.

*Results:* When the ATT was applied we found a 17.4; (14.5-20.3) (Mean; (CI))and 13.1; (11.0-15.1) mm Hg rise in systolic and diastolic blood pressures, respectively (p<0.0001). The leg volume dropped by 1040; (863-1216) ml during ATT application (p<0.0001). Ventilation and gas exchange parameters did not change except a slight rise in  $S_pO_2$  (p<0.001). We found small, yet statistically significant, declines in CPK and lactic acid and minute rises in pH and K<sup>+</sup> with no change in Ca<sup>++</sup> and Na<sup>+</sup> concentrations.

*Conclusion:* This study confirmed the hypothesis that elastic leg compression induces significant autotransfusion and blood pressure elevation in normal volunteers. The biochemical data indicate that applying the ATT did not cause significant deleterious tissue ischemia or mechanical crush injury. The usefulness of this new method should be further evaluated in actual treatment of shock victims.

## **Introduction**

Shock continues to be a common cause of death in trauma and non-trauma (medical) patients. It causes inappropriate proportion between blood volume and vascular volume that reduces blood flow and perfusion pressure to the essential organs (brain, heart, gut and kidneys). Shock diminishes the supply of oxygen and metabolic substrates to the tissues, which rapidly result in loss of function, cell destruction and death. This volume - volume discrepancy (VVD) is caused by either diminution of blood volume due to hemorrhage, or dehydration; or by inappropriate expansion of the blood vessels due to anaphylaxis, sepsis or toxins. Substrate reserves and compensatory mechanisms provide a period of time, the "Golden Window", during which adequate treatment aimed at restoring normal or near normal VVD and tissue perfusion can save the life of the shock victim.

Pneumatic and Elastic Anti Shock Garments (ASG) apply external positive pressure of up to 104 mm Hg to the legs and abdomen with the pneumatic version (PASG) and up to about 50 mm Hg with the elastic devices (EASG). Like with the cuff of a sphygmomanometer, the pressure inside the inflated air bladders of the PASG compresses the tissues beneath them and diminishes the transmural pressure (i.e. the pressure inside the vessel minus the pressure outside) acting on the walls of all the blood vessels in the tissue. The theoretical result is marked reduction in vascular volume, and if the transmural pressure falls to zero or below (i.e. the pressure outside is equal to or greater than the blood pressure within), the blood vessels completely collapse and blood flow stops. The presumed ability of the PASG to reverse VVD, by reducing the vascular volume is the underlying rationale of its use in hope for extending the 'Golden Window'. It should be noted that cardiogenic shock is an exception as it is caused by pump failure and the PASG was never shown to be beneficial in this condition (1).

The physiological rationale behind the introduction of PASG to widespread clinical use for treatment of shock in the mid- 1970s was based on these arguments. However, contrary to these potential advantages of PASG, several concerns were presented regarding its use. These include delay in transport by approximately 5 minutes when used by well-trained paramedics (2), and interference with breathing (3,4), especially in chest trauma victims (5). Moreover, use of PASG during air transport, where ambient air pressures change significantly, is not desired (6). Sudden removal of the PASG or loss of bladder pressure was associated with rapid deterioration of the patient's condition. Also, PASG application limits the access to the lower body of the patient. In addition, it is possible that if the patient's systolic blood pressure increases above the PASG bladders pressure, blood may escape beyond the inflated abdominal or leg cuffs and will not return, effectively causing reduction in central blood volume (7). Finally, there are now data showing that optimal blood pressure in trauma victims prior to definitive hemorrhage control is approximately 80-100 mm Hg,

not higher (8). Maintaining this blood pressure reduces bleeding and helps prevent dislodging of early soft clots that were formed at the injury site. The PASG does not readily permit titration of its effect to achieve the desired blood pressure. Thus, it is not surprising that large-scale outcome studies on the usefulness of PASG in shock showed virtually no benefit (9-11).

In the present study we evaluated the physiological effects of an alternative Auto-Transfusion Tourniquet (ATT) device (ATT Model 1979, Oneg HaKarmel Haifa, Israel 34331). The new device is an elastic sleeve that is rolled upon itself over a thick elastic ring (Figure 1A). When rolled onto the limb of a person, the sleeve unfolds while the ring is exerting radial pressure on the limb. The length and material thickness of the sleeve are such that when the ATT is up-rolled and the sleeve is unfolded all the way up to the upper thigh the ring maintains essentially uniform radial force on the leg that exceeds systolic blood pressure. The working hypothesis tested in this study is that the rolling-up action squeezes the blood from the veins, arteries, and capillaries of each extremity into the central circulation. Thus, effecting autotransfusion of the subject's own blood. In addition, the residual toroid acts as an arterial tourniquet to increase systemic vascular resistance, cardiac afterload and blood pressure, while directing the cardiac output away from the lower extremities towards the essential organs. In addition we measured biochemical markers to assess muscle and other tissue ischemia and/or crush damage to evaluate the safety of applying the ATT.



Figure 1

The Auto-Transfusion Tourniquet

A. the device

- B. the applied ATT on a subject
- C. the change in skin color due to squeezing of blood
- D. the post-removal reactive-hyperemia

### **Methods**

#### Population

Eighteen normal adult volunteers were recruited for this study. The subjects were screened for prior or present orthopedic, cardiovascular, or cutaneous diseases or malformations. Israel Ministry of Health National Human Use Committee and the Israel Defense Force (IDF) Helsinki committee approved this study. Each subject signed an informed consent. Inclusion criteria were freedom of any active disease, normal blood pressure and leg pulses and normal cardiac stress test for those volunteers who were older than 40 years. Exclusion criteria included use of vaso-active or cardiac medications, vascular malformations, history of deep vein thrombosis or varicose veins, leg deformation of gait abnormality.

#### Procedure

The study included three consecutive phases: PRE before application of the ATT, During (DUR) - the application period (Figure 1B), and POST - after the removal of the ATT. Each segment was 20 minutes long and included measurements of the following parameters: blood pressure, heart rate, SpO<sub>2</sub>, respiratory rate, sensation of touch in both feet and pain level using the 0-10 Borg's scale. These parameters were recorded manually every 5 minutes during each phase of the study. We also measured the minute ventilation, oxygen consumption, CO<sub>2</sub> production, the respiratory exchange ratio, and the O<sub>2</sub>-pulse (oxygen consumption divided by the heart rate). These measurements were done once in each phase of the study during a 3 - minute recording while the subject was connected to a metabolic analyzer (Technion Exercise Lab Model 101, Haifa, Israel). The arterial pulse in the drosalis pedis and tibialis posterior arteries was monitored with a Doppler stethoscope at each phase of the study. At the beginning of the PRE phase and at the end of each of the other phases (DUR and POST) we collected venous blood for lactic acid, K<sup>+</sup>, Ca<sup>++</sup>, CPK, Hemoglobin, and pH.

In addition to these physiological parameters and biochemical markers, we measured the volume of the legs in each phase of the study. To do so we horizontally submerged the subject's lower body in a water tub at 32°C while measuring the water level before and during the submersion. The measurements of the water level were done with an accurate slanted graduated both manually burette. and photographically. The difference between the two water levels represents an estimate of the volume of the subject's lower body. We estimated the volume of the subjects' legs by measuring the circumference of each leg using a measuring tape at four standard levels (12): lower calf (1/3 of the ankle to knee distance), mid calf (2/3 of the ankle to knee distance), lower thigh (7 cm above the knee) and mid thigh (14 cm above the knee). The measurements were done in duplicates. The leg volumes were calculated using a four - compartment truncated cones model, where each compartment represents a segment of the leg.

### Statistical analysis

Differences between the means were evaluated using repeated measures analysis of variance (repeated measure ANOVA) comparing the three phases (PRE, DUR and POST). All values are presented as means and 95% confidence internals (CI). Differences were considered as statistically significance when p < 0.05.

# Results

We studied the effects of the Auto-Transfusion Tourniquet (ATT) in 18 healthy subjects (male 16, female 2). The age distribution was 21 to 55  $(30.1\pm11.8 \text{ mean}\pm\text{SD})$ . The subjects were  $180\pm7 \text{ cm}$ tall and weighed  $78\pm10$  kg. The calculated leg volumes were 13.7+2.0 liter. All subjects completed the study and no significant side effects were observed. The main positive observations were reduction of leg volume and increases of both systolic and diastolic blood pressures during ATT application. The application of the device was done by one person and was graded as 'easy' in a scale of 'easy', 'moderate' and 'difficult'. It took 6 to 12 seconds to apply the ATT to each legs with the completion of the application and securing of the ATT to both legs lasting no longer than 120 seconds in all of the subjects. All subjects experienced compressive pain and/or discomfort in the calf and the thigh during the up-rolling of the ATT. Most subjects reported that the pain somewhat diminished 1-3 minutes after the uprolling (Borg scale 4.5 [3.2-6.8]: Mean [CI]) and remained at this level until after the device was removed. In addition, most of the subjects reported tingling in the feet/toes toward the end of the 20 minutes ATT application period with 14 of them also reporting reduced sensation to touch at the 20 minutes point. Within a minute after the removal of the ATT most subjects reported intense "waking-up" tingling sensations that lasted 3-6 minutes. Four subjects also developed shivering within 2-4 minutes after the ATT removal ATT lasting for 4-6 minutes. All subjects were free of any symptoms or discomfort within 10 minutes after the removal of the ATT.

## Physiological measurements

We found substantial increases of the systolic and diastolic blood pressures (BP) during the application of the ATT (p<0.0001)(Figure 2, Table 1). The initial BP readings were the highest immediately after the application of the device, probably due to combination of the direct hemodynamic effect and doloric stress. The BP readings then stabilized with similar values at 10, 15, and 20 minutes. The DUR phase systolic values were 17.4 [14.5-20.3] mm Hg higher than the PRE phase values (p<0.0001) and 15.4 [12.4-18.4] mm Hg higher than the POST phase values (p<0.0001). The DUR diastolic pressures values were 13.1 [11.0-15.1] mm Hg higher than the PRE (p<0.0001) and 11.3 [9.3-13.2] mm Hg higher

than the POST (p<0.0001). The differences of BP values between the PRE and the POST phases were not statistically significant (NS). The only other physiological parameter that exhibited a systematic change (p<0.001 PRE to POST) was the  $S_pO_2$ , which increased from 97.2 [96.8-97.5] (PRE) to 97.5 [96.9-98.0] (DUR) and to 97.9 [97.5-98.3] (POST)(Table 1). The changes from PRE to POST were statistically significant (p<0.001). The heart rate (HR), respiratory rate (RR), minute ventilation (V E), oxygen consumption (V<sub>O2</sub>) and carbon dioxide production (V<sub>CO2</sub>) did not differ significantly throughout the study.

## Auto-transfusion

The application of the ATT induced compression of the legs and transfer of volume of blood from the lower extremities to the central circulation. This was visually evident by observing the pale color of the legs and the collapsed veins in the dorsum of the feet (Figure 1c). No pulse or blood flow was detected using a Doppler stethoscope when the ATT was worn. Accurate measurements of the volume of the legs before, during and after the application of the ATT were obtained in 11 of the subjects. The leg volume during the application was 1040 [863-1216] ml lower than the PRE volume (Figure 3); (p < 0.0001). The volume and the normal color of the legs were restored immediately after the removal of the ATT and became hyperemic approximately 30 seconds later. The dorsalis pedis and the tibialis posterior pulses were easily detected immediately after the removal of the ATT in all subjects. The hyperemia lasted for 4-5 minutes with return to normal color not later than 10 minutes after the removal.

## Biochemical parameters

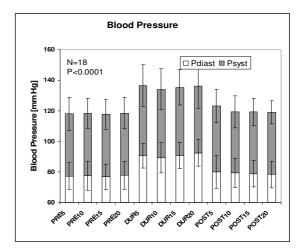
We found small, yet statistically significant changes in the biochemical parameters that we measured (Table 1). These changes were predominantly in the opposite direction to the expected. We found that the venous lactic acid dropped from 2.89 [2.53-3.25] mmol/l (PRE) to 2.15 [1.90-2.40] mmol/l (DUR) (p=0.004) and 2.21 [1.89-2.54] mmol/l (POST) (p=0.013 PRE to POST). Similarly, the CPK fell by 5.7% from PRE to DUR and by 7.6% from PRE to POST (p<0.01). The venous pH increased slightly by 0.035 pH units from PRE to DUR (p=0.04) and then fell back by 0.018 pH units from DUR to POST (p<0.0001). We also found a small, yet statistically significant rise in K<sup>+</sup> levels from 3.84 [3.77-3.92] (PRE) to 3.98 [3.90-4.06] (DUR) (p<0.0001) and 4.00 [3.90-4.10] (POST) (p=0.003). There was a 5.7% increase in hemoglobin level from PRE to DUR (p=0.028). The serum ionic Ca<sup>++</sup> and Na<sup>+</sup> did not change during the study.

Study phase	n	PRE	DUR	POST
Physiological		Mean	Mean	Mean
parameters		[CI]	[CI]	[CI]
Heart Rate [b/min]	18	68* [64-73]	69* [64-74]	64* [59-68]
Systolic Blood Pressure [mm Hg]	18	118** [114-123]	136* [130-141]	120** [116-124]
Diastolic Blood Pressure [mm Hg]	18	77** [73-81]	90* [86-94]	79** [75-83]
O <sub>2</sub> – pulse [ml/beat]	12	4.9* [4.0-5.7]	4.5* [3.6-5.4]	4.8* [3.7-5.9]
Respiratory Rate [b/min]	18	15.8* [14.0-17.6]	15.6* [13.5-17.7]	15.2* [13.4-17.1]
S <sub>P</sub> O <sub>2</sub> [%]	18	97.2* [96.8-97.5]	97.5** [96.9-98.0]	97.9* [97.5-98.3]
Minute ventilation [l/min]	12	9.7* [8.6-10.9]	9.8* [7.6-12.0]	8.4* [7.5-9.3]
Oxygen consumption [ml/min]	12	332* [271-392]	311* [242-379]	289* [229-349]
CO <sub>2</sub> Production [ml/min]	12	282* [240-324]	277* [211-343]	225* [184-266]
Biochemical Parmeters				
CPK [U/I]	18	158** [117-199]	151** [110-192]	147** [107-188]
K <sup>+</sup> [mmol/l]	18	3.84** [3.77-3.92]	3.98** [3.90-4.06]	4.00* [3.90-4.10]
Lactic acid [mmol/l]	18	2.89** [2.53-3.25]	2.15** [1.90-2.40]	2.21* [1.89-2.54]
рН	18	7.37** [7.34-7.40]	7.404* [7.40-7.41]	7.39** [7.37-7.40]
Hemoglobin [g/dl]	14	14.1** [13.2-15.0]	14.8* [13.9-15.7]	14.6* [13.8-15.3]
Na <sup>+</sup> [mmol/l]	18	140.3* [139-142]	140.4* [139-142]	141.5* [140-143]
Ca <sup>++</sup> [mmol/l]	17	1.17* [1.15-1.19]	1.19* [1.16-1.22]	1.20* [1.18-1.22]

#### Discussion

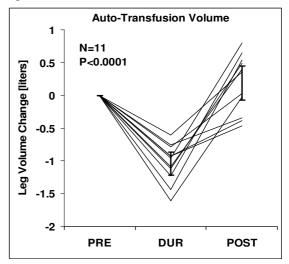
Table 1

This study clearly demonstrates the substantial rise in blood pressure induced by shifting blood away from the lower extremities to the central circulation and by blocking the re-entry of blood into the lower limbs. The systolic and diastolic pressures were substantially and proportionally increased (Figure 2), indicating a combined contribution of elevated preand after- loads of the heart. The rise in cardiac preload is probably due to the auto transfusion effects of squeezing the blood from the legs into the central



### Figure 2

Systolic and diastolic blood pressures before (PRE), during (DUR) and after (POST) application of the ATT at 5 minutes intervals. Note the substantial rise in both systolic and diastolic pressures. Error bars represent confidence intervals.



### Figure 3

Difference in leg volume during (DUR) and after (POST) application of the ATT relative to the baseline (PRE). Note drop of approximately one liter in the volume of the legs. Error bars represent confidence intervals.

circulation. The rise in cardiac after-load is caused by the elevated total peripheral resistance due to the tourniquet effect of the elastic toroid around the thigh.

The up-rolling of the ATT on healthy volunteers induced an auto transfusion of about one liter or approximately two units of whole blood from both legs into the central circulation (Figure 3). This volume corresponds well to estimates of lower limb blood volume ( $V_{Blood}$ ) based on previously published values of blood volume of 81 ml/kg (13, 14) and the

measured legs volumes ( $V_{Legs} = 13.7$  liter) of our subjects ( $V_{Blood} = 81 \times V_{Legs} = 1110$  ml). It is difficult to predict what will be the extent of auto transfusion that will be induced by elastic leg compression in shock victims. It is likely to be lesser during the initial ('compensated') phase of the shock while sympathetic tone induces peripheral vasoconstriction. However, application of the device when the compensatory mechanisms have already failed may induce auto-transfusion of larger volumes of blood.

Other cardiovascular and respiratory physiological parameters did not show statistically significant changes while the ATT was on the subjects. The respiratory rate, minute ventilation, O<sub>2</sub> consumption and CO<sub>2</sub> production were all within the normal range and remained so throughout the study. The only parameter that showed a statistically significant difference was the  $S_PO_2$  that increased by less than 1% in this group of normal subjects (Table 1). This rise may be explained if the ATT increases pulmonary vascular pressure with sustained reopening of pulmonary capillaries in the upper lung lobes and an improvement of ventilation-perfusion distribution in the lung. Additional studies are needed to evaluate the validity and clinical significance of this unexpected observation.

In this study we also evaluated the effects of ATT application on biochemical markers of ischemia (lactic acid, pH) and tissue/muscle crush injury (CPK,  $K^+$ ,  $Ca^{++}$ ). (Table 1). We found no indication that leg ischemia was of a significant factor. As a matter of fact lactic acid declined and pH increased slightly after the application of the ATT. We do not have a solid physiological explanation to this finding. Chiu et al who measured the effects of inflating a tourniquet to 300 mm Hg observed no rise in CPK levels after one hour of continuous use, but did find a rise in CPK when the tourniquet was applied for 2 and 3 hours continuously (15). We did not notice a significant change in ventilation and CO<sub>2</sub> output, so that respiratory alkalosis is not a likely explanation. Since we did not measure hepatic and renal blood flow, we cannot conclude that these changes are due to a rise in hepatic activity or GFR. Additional studies are needed to explore this unexpected finding. We found a small, yet statistically significant rise in Potassium level. This rise could indicate reduce efficiency of the Na/k ATPase pump, due to tissue compression or ischemia or to slight hemolysis. The Na<sup>+</sup> and Ca<sup>++</sup> did not change significantly during the study. We noted a systematic small decline of CPK that was statistically significant. This obviously reflects reduced CPK flux into the blood and/or higher rate of its elimination from the blood. Either way we did not find in any of the subjects a rise in CPK levels as would have been expected if muscle crush injury was caused by the elastic compression of the limbs. Thus, we did not find any indication that significant tissue ischemia or injury was caused by the application of the ATT.

The ATT was applied in this study for 24 + 3minutes. Most subjects noted tingling of the toes and feet and reduced tactile sensation towards the end of this period. These sensations were quickly reversed after the removal of the device and all subjects were free of any symptoms or discomfort within up to 10 minutes from the removal of the ATT. It is of interest to estimate the duration of safe application of an elastic leg compression device. It is common practice for orthopedic surgeons to use an inflatable thighlevel tourniquet during knee and ankle surgical procedures at 175 to 305 mm Hg for up to two hours to maintain a bloodless surgical field (16). An estimated 40 minutes are then required for the tissues to return to normal after prolonged use of the tourniquet (17). Similarly, it is common teaching in emergency medicine to leave arterial tourniquets in place for up to 2 hours without danger of irreversible damage. The most common side effect of the bloodless field pneumatic tourniquet is nerve paralysis (18). It was estimated that paralysis occurs once in 5000-8000 operations with the rate being dependent on the inflation pressure and the duration of application. The dimensions of the tourniquet cuff were also found to be important, with wider cuffs being more effective at lower pressure (19). These clinical and experimental studies indicate that the deleterious effects of the tourniquet are due to direct mechanical compression of the nerves just beneath the cuff, rather than to ischemic effects to the muscle, nerves and other tissues distal to the occlusion point. Therefor, lower shear forces at the tourniquet edges are desired. In addition, Shaw et al found that the percentage of tourniquet pressure reflected in the underlying tissue varied inversely with the circumference of the thigh (20). This observation supports the design of the ATT as an elastic ring, since larger thigh circumference stretches the ring more, which generates the needed higher compression pressure on the thigh tissues.

The ATT is a simple 'low tech' device that can be easily applied by minimally trained personnel. It is intended for a single use and does not pose a contamination risk. It requires little storage space and fits persons of a broad range of sizes. The effect of the unfolding sleeve is to counter-balance the normal taper of the human leg, so that the applied pressure is uniform from the ankle up to the upper thigh. Once the ring is in place at the upper thigh level the sleeve can be cut away to facilitate access to the leg for treatment of wounds. The ATT is designed to generate compressive pressure that depends on the circumference of the thigh: approximately 140 mm Hg in very slim individuals to 180 mm Hg in subjects who have thick thighs. These differences are due to the degree of tension that develops in the elastic ring when applied to legs of different circumference. However, the higher compressive pressure in heavyset individuals is probably beneficial since their vessels are deeper in the tissue and require higher compression pressure to be squeezed and occluded (20). The ATT may be applied to a single limb or to knee level when titration of the patient's blood pressure to ~100 mm Hg is desired. The major drawback of the ATT, in comparison to the PASG, is due to the fact that the former does not provide counter-pressure and/or stabilization to the abdomen and the pelvis.

The present study documented the substantial rise in blood pressure and the auto-transfusion induced by the ATT in a group of normal volunteers. No other significant cardio-pulmonary effects were observed. The biochemical changes observed in this study do not suggest significant ischemic or tissue crush side effects. The pain and discomfort associated with the application were mainly due to direct pressure on the thigh and to numbness and were relieved soon after the removal of the device. This study demonstrates the potentially beneficial physiological effects of the ATT. Additional clinical studies will help in determining the usefulness of this device in emergency medicine.

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