PLASMA RENIN ACTIVITY AND ITS RELATION TO DEVELOPMENT OF RESISTANCE DURING CONTROLLED HYPOTENSION

A THESIS

SUBMITTED FOR THE PARTIAL FULFILMENT

FOR THE DEGREE OF (M. D.)

(ANAESTHESIA)

BY

RAAFAT ABDEL AZIM HAMMAD

M.B.,B.Ch., M.Sc. (*Anaesthesia*)

SUPERVISED BY

Prof. Dr. KADRY MERHOM

Prof. and Head of the

Department of Anaesthesia

Prof. Dr. NABIL ABDEL MOATY

Prof. of Anaesthesiology

Prof. Dr. HUSSEIN EL DAMASSY

Prof. of Internal Medicine

and Endocrinology

FACULTY OF MEDICINE

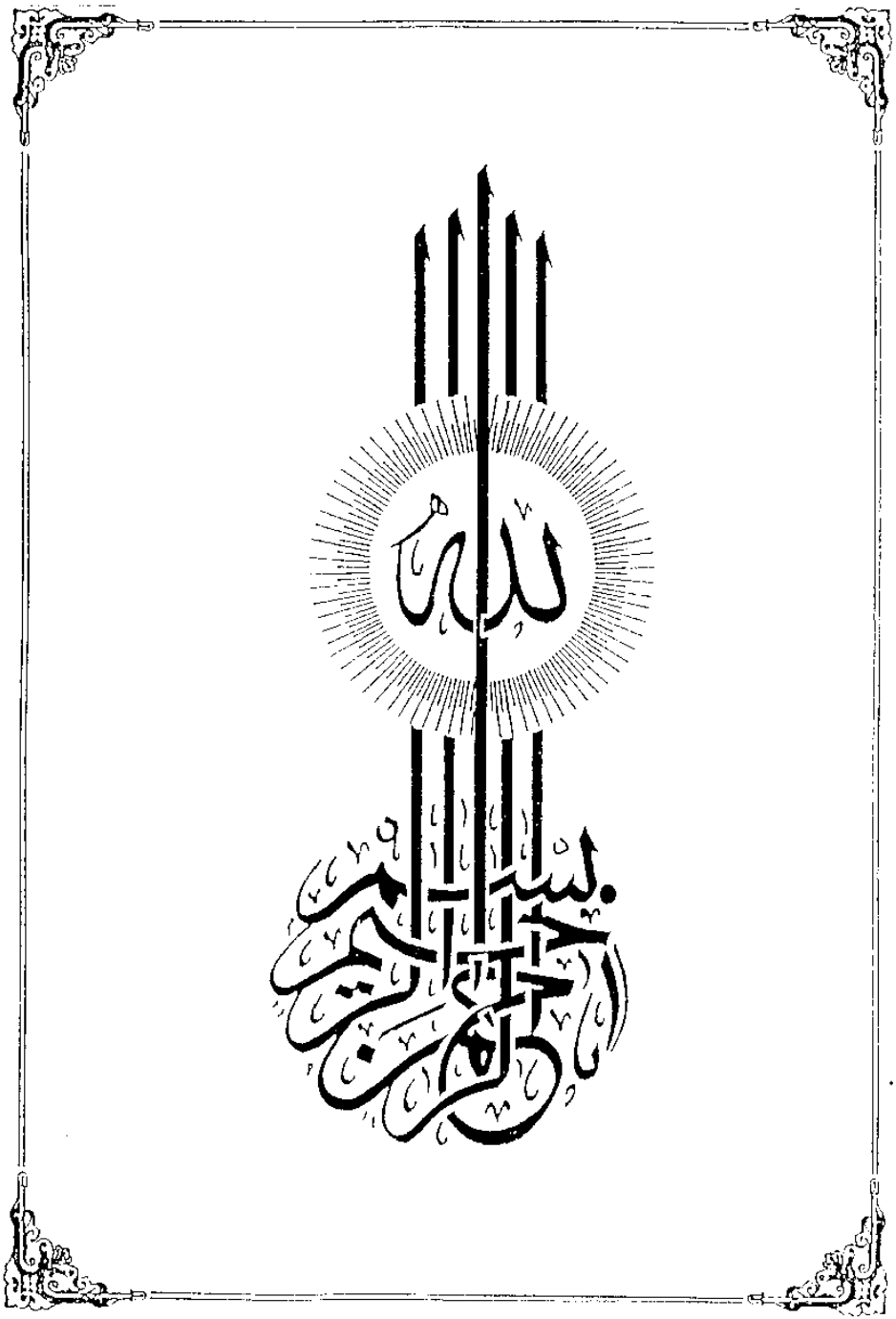
AIN SHAMS UNIVERSITY

1989

وعلمك ما لم تكن تعلم وكان فضل الله عليك عظيما

« صدق الله العظيم »

سورة النساء (آية ١١٣)



ACKNOWLEDGEMENT

It has been my good fortune to carry out this work under the supervision of Professor Dr. Kadri Merhom, Head of the Department of Anaesthesia, Ain Shams Faculty of Medicine. I am grateful to him for his invaluable help, kindness and wisdom. I am proud of being one of his students. He supplied me with a constant paternal help.

I wish to express my sincere appreciation to professor Dr. Nabil Abdel Moaty, Professor of Anaesthesia, Ain Shams Faculty of Medicine, who revised this work several times with patience, constructive criticism, advice, guidance, and continuous encouragement.

My thanks to Professor Dr. Hussein Eldamassy, Professor of Internal Medicine and Endocrinology ,Ain Shams Faculty of Medicine, who gave me a lot of his precious experience and fruitful suggestions, facilitation and assistance throughout this work.

Raafat Abdel Azim Hammad

ABBREVIATIONS

ACE	Angiotensin Converting Enzyme
ARF	Acute renal failure
ECF	Extracellular fluid
CBF	Cerebral blood flow
ICP	Intracranial pressure
JGA	Juxtaglomerular apparatus
MAP	Mean arterial pressure
PCWP	Pulmonary capillary wedge pressure
PG	Prostaglandin
PRA	Plasma Renin Activity
RAS	Renin Angiotensin System
SNP	Sodium nitroprusside
TMP	Trimethaphan
TNG	Nitroglycerin

Introduction & Aim of the Study

INTRODUCTION AND AIM OF THE STUDY

Controlled hypotension has gained a great popularity in the anaesthesiologist's armamentarium of techniques. It is now popular with the development of new hypotensive agents, better understanding of their pharmacologic and physiologic effects and improved monitoring techniques.

The value of controlled bypotension is to decrease the operative bleeding and so can be used to achieve two important goals:

1) Improve operating conditions.

2) Decrease blood transfusion requirements and complications.

The use of new hypotensive agents made the technique safer than before. Blood flow to vital organs is maintained with the vasodilator drugs.

Hypotension stimulates different compensatory mechanisms to maintain the blood pressure, these include release of catecholamines, renin , angiotensin, vasopressin and corticosteroids. The more active these compensatory mechanisms, the more will be the dose requirements of the hypotensive drug.

Of these compensatory mechanisms , the renin angiotensin system has a great importance.The function of this system can be estimated by measurement of plasma renin activity using a radioimmunoassay technique to measure the rate of generation of angiotensin I in ng/ml/hour.

Aim Of The Study

The aim of the study is to measure the plasma renin activity as a reflection of resistance during controlled hypotension in patients receiving trimethaphan , sodium nitroprusside or nitroglycerin infusions.

Review of Literature

INDICATIONS AND CONTRAINDICATIONS TO INDUCED HYPOTENSION

Hypotensive anaesthesia (= controlled hypotension = induced hypotension = deliberate hypotension) has three potential benefits : (1) reduced blood loss with a consequent reduction in risks associated with blood transfusion , (2) improved quality (dryness) of the operative field , allowing more accurate dissection and improved surgical results, and (3) reduced operative time. For the most part, studies of controlled hypotension have shown a reduced blood loss that has been statistically significant (Sivarajan et al 1980, Donald 1982). Reductions in operative time have also been statistically significant in some (Thompson et al, 1978), but not all studies (Grundy et al, 1982).

Controlled hypotension should be applied only when its advantages will be of certain benefit to the patient and when these are likely to outweigh the accepted risks.

Controlled hypotension can be used effectively in the following operations:

(1) Total hip arthroplasty and major hip surgery: During total hip arthroplasty, blood loss can be

Rosberg et al (1982) reported that patients undergoing surgery ~~in~~ under epidural anaesthesia did lose a smaller amount of blood than with neuroleptanaesthesia. The sum of intra- and postoperative blood losses was also significantly reduced in epidural analgesia compared with normotensive halothane anaesthesia. Advantages claimed with regional versus general anaesthetic techniques include, apart from reduced surgical blood loss, a possibly reduced incidence of postoperative thromboembolism (Thorburn et al, 1980), the pulmonary dysfunction during the first postoperative days is of a minor degree, and mental disturbances are fewer (Hole et al, 1980).

Donald (1982) showed that the phenomenon of " bloodless field" occurred over a wide range of arterial pressure and had little or nothing to do with induced hypotension, he suggested that a "step-down" phenomenon exists, a level of arterial pressure below which no further reduction of blood loss occurs.

Bernard et al (1987) studied the effects of isoflurane during hypotensive anaesthesia for total hip arthroplasty and they concluded that it is a good alternative to SNP.

(2) Intracranial aneurysm surgery:

Surgery on the cerebral vasculature frequently requires the induction of controlled arterial hypotension to facilitate surgical exposure and reduce the risks of intraoperative haemorrhage (Lam , 1984). During the dissection and clipping of cerebral arterial aneurysms, controlled hypotension is often required in order to reduce the aneurysm wall tension, thus minimizing the risk of rupture and bleeding and the mortality rate attributable to this type of surgery (Ferguson , 1982).However, the choice of technique and the ideal arterial pressure remain controversial. The advantage of having a reduced pressure in the arterial system when the aneurysm is about to be clipped must be weighed against a possible negative effect on cerebral haemodynamics. Thus , inherent in all intracranial operations is the possibility of arterial vasospasm, which may be present due to a local vascular disease per se or may be secondary to digital or instrumental manipulations. It is of the utmost importance that all parts of the brain are ensured an adequate blood supply during the surgical procedure , and reducing mean arterial pressure might accentuate regions with critically low cerebral blood flow (C B F) (Henriksen et al, 1983).

Rudehill et al (1979) studied the use of SNP as a hypotensive agent in intracranial aneurysm surgery . They showed that there is a risk of impairment of cerebral autoregulation after the use of SNP, it is important to avoid sudden and prolonged blood pressure fluctuations, and to continue with controlled hyperventilation in the postoperative period to reduce the risk of brain oedema and high ICP.

Deep controlled hypotension (hypotension below 60 mmHg of systolic arterial pressure) with SNP in the surgical treatment of intracranial arterial aneurysms was studied by Da pian et al (1979). Surgical results were excellent with no complications. However, the authors stressed the risks of deep hypotension in the early surgery, due to the possible association to vascular spasm.

SNP was used during anaesthesia with enflurane in patients operated for cerebral aneurysm or angioma (Vandesteene et al, 1980).

Henriksen et al (1983), studying controlled hypotension with SNP in patients operated for cerebral aneurysms, concluded that SNPhas only a minor influence on cerebral haemodynamics in the anaesthetized state. In

their study , CBF remained unchanged during SNP hypotension, indicating that the autoregulation was preserved. C B F slightly increased following discontinuation of S N P infusion. In conclusion, the use of S N P infusion for controlled hypotension during surgery for intracranial aneurysm seems safe. Neither a decrease in average hemispheric blood flow nor disclosed focal ischaemia were observed during the hypotension .

Guggiari et al (1985) showed that T N G can be used to induce moderate degrees of hypotension (MAP 50 - 60 mmHg) during surgery for intracranial aneurysm.

Nitroprusside and nitroglycerine have been shown to increase intra cranial pressure , provided that the arterial blood pressure is not greatly reduced (Shapiro 1975, Morsh et al 1979, Ghani et al 1983). This effect is dose and administration rate dependent. The increase in intracranial pressure will be severe when large doses are rapidly given.

Isoflurane - induced hypotension in patients subjected to surgery for cerebral aneurysms was studied by Newman et al (1986) and Madsen et al(1987). They concluded that cerebral metabolic rate for oxygen