Egyptian Journal of Anaesthesia (2015) **31**, 291–295

HOSTED BY

ELSEVIER

Egyptian Society of Anesthesiologists

Egyptian Journal of Anaesthesia

www.elsevier.com/locate/egja
www.sciencedirect.com

Research Article

Oral nifedipine as a premedication for induced hypotension in functional endoscopic sinus surgery (FESS)

Ahmed Hassanein [a,*], **Moustafa Talaat** [b]

[a] *Department of Anesthesiology, Al-Minia University, Egypt*
[b] *Department of Otolaryngology, Al-Minia University, Egypt*

Received 17 December 2014; revised 3 June 2015; accepted 15 June 2015
Available online 8 August 2015

KEYWORDS

Induced hypotensive anesthesia;
Oral nifedipine;
Nitroglycerin;
Functional endoscopic sinus surgery

Abstract *Objective:* To evaluate the effects of oral nifedipine as pretreatment, quality of surgical field and amount of hypotensive agent during functional endoscopic sinus surgery (FESS) under general anesthesia.

Methods: Sixty patients ASA I or II scheduled for FESS were randomly allocated into two equal groups. Oral nifedipine 20 mg was given one hour before induction of anesthesia (nifedipine) group and placebo. In the other group (control), all the patients received standard anesthesia and monitoring. Nitroglycerin (GTN) was administrated in a dose of 2 μg/kg/min after induction of anesthesia till it achieved a target mean arterial blood pressure (MAP) of 50–60 mmHg, followed by a continuous i.v. infusion (1 μg/kg/min) intraoperative when needed. Hemodynamic variables were recorded at baseline preoperatively, intraoperatively and till the end of operation. The surgical field score was assessed by average category scale (ACS) and intraoperative blood loss and amount of GTN was estimated. Emergence time and total recovery from anesthesia (Aldrete score $\geqslant 9$) were recorded.

Results: There were no statistically significant differences between two groups with respect to the amount of blood loss and scores for a bloodless surgical field. Emergence time and time needed to achieve 9 of modified Aldrete score were significantly shorter in Control group than nifedipine group (4.46 ± 1.25 min and 7.46 ± 2 min versus 8 ± 1.62 min and 9.5 ± 2.41 min, respectively) ($P < 0.01$). MAP during hypotensive period showed no statistically significant difference ($p > 0.05$) but at 5 and 10 min after stoppage of hypotensive anesthesia, at the end of surgery and after recovery, MAP was significantly lower in nifedipine group than Control group ($p < 0.01$). Heart rate (HR) during hypotensive period showed no statistically significant difference ($p > 0.05$). At 5 and 10 min after stoppage of hypotensive anesthesia, at end of surgery and after recovery, HR was significantly lower in nifedipine group than Control group ($p < 0.001$). The amount of GTN used in nifedipine group was significantly lower than Control group ($p < 0.001$).

* Corresponding author.
Peer review under responsibility of Egyptian Society of Anesthesiologists.

http://dx.doi.org/10.1016/j.egja.2015.06.005

Conclusion: Administration of a single preoperative dose of nifedipine (20 mg) can significantly reduce the blood loss during FESS and improves the visualization of the operative field and it also lowers the amount of GTN needed to achieve target hypotension.

1. Introduction

The introduction of functional endoscopic sinus surgery (FESS) associated with improved surgical dissection due to enhanced illumination and visualization of surgical field, but impaired visibility due to excessive bleeding may present a major complication has been reported for FESS under general anesthesia [1]. Controlled hypotension is defined as a reduction in mean arterial blood pressure to 50–60 mmHg in normotensive subject [2]. Many advantages in controlled hypotension for FESS include reduction in blood loss and improved quality of surgical field. Multiple agents have been used to achieve controlled hypotension e.g., magnesium sulfate, vasodilators (sodium nitroprusside), nitroglycerine, high doses of potent inhaled anesthetics, and beta adrenergic antagonist [3–5]. Although there are numerous approaches to provide controlled hypotension, isoflurane has been an integral part of many reports, and isoflurane lends itself particularly well to the technique of controlled hypotension because of its favorable effects on the systemic and cerebral circulation [6–8]. Nitroglycerin is an organic nitrate that acts principally on venous capacitance vessels to produce peripheral pooling of blood and decrease cardiac ventricular wall tension. As the dose of nitroglycerin is increased, there is relaxation of the arterial vascular smooth muscle. The most common clinical use of nitroglycerin is either sublingual or intravenous administration for the treatment of angina pectoris due to either atherosclerosis of coronary arteries or intermittent vasospasm of these vessels, and also to achieve hypotension by infusion [5]. Nifedipine is a potent vasodilator, which relaxes vascular smooth muscle probably by its inhibitory effect on the transmembrane influx of calcium, and it is very effective in the treatment of severe hypertension and hypertensive emergency. When the conventional form of nifedipine (soft capsule containing 10 mg of dissolved nifedipine) was administered orally, there was a rapid hypotensive effect occurring maximally at 1 h after administration and disappearing within 7 h [9]. The rationale behind using oral nifedipine as an agent for inducing hypotension in our study is to induce gradual smooth hypotension without rapid swing in BP by IV hypotensive agents The current study was designed to evaluate the effect of oral nifedipine on the hemodynamic changes, the quality of the operative field, blood loss and the amount of nitroglycerine used in patients undergoing FESS under general anesthesia.

2. Methods

A prospective, randomized, single blinded study was done in Minia University Hospital, during the period from October 2012 to November 2013. After obtaining the informed consent from patients and approval of the local ethical committee, sixty ASA physical status I or II patients aging 18–55 years were scheduled for elective FESS. All patients had bilateral nasal polyposis with opacity of most paranasal sinuses. We exclude patients with recurrent sinus surgery, history of hypertension, coronary artery diseases, patients with coagulopathies or receiving drugs influencing blood coagulation, renal, hepatic or cerebral insufficiency, morbid obese patients, patients with neuromuscular diseases, pregnancy, and patients with prior treatment with calcium channel blockers or beta blockers. All surgical procedures were done by the same surgeon, and he was blinded to the hypotensive agent used. The patients were examined clinically and investigated by ECG, chest X-ray and laboratory tests.

Sample size calculation was based on our primary endpoint of keeping the mean arterial pressure (MAP) between 50 and 60 mmHg, while the normal MAP ranged between 70 and 105 mmHg. For this purpose, a difference of 20 mmHg in MAP between study and control groups was deemed clinically relevant. The calculation determined that 60 patients (30 in each group) would be required for a study with a power of 1 and an alpha of 0.05 set for significance. The study design was parallel grouping; each patient was randomly assigned to either receive oral nifedipine 20 mg (Epilat 10 mg capsules, Eipico Pharmaceuticals, EGYPT) ($n = 30$) or Placebo ($n = 30$), receiving placebo one hour before induction of anesthesia by sips of water, the placebo was identical to nifedipine capsules and prepared by the pharmacy to maintain double blind study, and an appropriate code number was assigned to each patient, with an allocation ratio of 1:1. Patients were randomized in block size of 4 to either receive oral nifedipine 20 mg or placebo. Patients were assigned to the next sequence at the time of surgery. It was impractical to blind the anesthesiologists.

In the operating room 500 ml lactated Ringer's solution i.v. infusion was started in all patients and an intra-arterial line was inserted under local anesthesia in the radial artery for direct measurement of arterial blood pressure. One hour preoperative in the recovery room the patient connected to continuous routine monitoring included ECG, pulse oximetry and invasive blood pressure were measured using (Spacelabs; model 90364, USA). All patients were premedicated with IV midazolam 0.05 mg/kg and fentanyl 1 μg/kg. Patients received standard anesthetic technique with propofol 2 mg/kg, and intubation was facilitated with atracurium 0.5 mg/kg with suitable sized cuffed tube. Anesthesia was maintained with isoflurane 1–3% and neuromascular blocker was atracurium with incremental dose 0.15 mg/kg every 25 min IV, respiration was controlled with tidal volume 6–9 ml/kg and respiratory rate 12–15 cycle/min, and the tidal volume used was mostly guided by the end tidal CO_2 (between 33 and 36 mmHg) (Drager medical AG/COKGaA; model 23542, Germany). Patients were placed in a 15° reverse Trendlenburg position to improve venous drainage, and cottonoids soaked with epinephrine in a concentration of 1:100.000 were inserted into the nasal cavity and in between the polyps to reduce blood loss. Nitroglycerin (GTN) (Nitronal aqueous, Global Napi

Pharmaceuticals, Egypt) 1 mg/ml:10 ml of GTN was added to 40 ml of 5% dextrose (1 ml of this solution containing 0.2 mg of GTN). The hypotensive agent (GTN infusion) was given after the induction of anesthesia intravenously by using a syringe pump (Pilote A2 10 CCIs; model 36590, France) when MAP is above 60 mmHg, but not given when MAP is less than 65 mmHg, GTN infusion was started with a rate of 2 μg/kg/min and then decreased to 1 μg/kg/min to maintain the target level of MAP ranged between 55 and 65 mmHg, when MAP becomes less than 55 mmHg we stop GTN, and when MAP persists below 55 mmHg more than 5 min, reduction in inhalational anesthetic and rapid iv fluids administered to the patient, then incremental low doses of ephedrine were given when needed. At the end of the operation, the hypotensive agent was stopped before packing the nose and the residual effect of atracurium was reversed by neostigmine in a dose of 0.04 mg/kg and atropine sulfate in a dose of 0.02 mg/kg. Extubation was carried out when adequate tidal volume and good cough reflex were observed. The patients were transferred to the recovery room and assessed for any side effects associated with induction or during maintenance of anesthesia or during recovery such as persistent hypotension, rebound hypertension or any excessive nasal bleeding were recorded and compared in both groups.

2.1. Measured parameters

Assessed parameters include the following: (1) *hemodynamics* (heart rate, mean arterial blood pressure, and O_2 saturation) was recorded preoperatively as a baseline, postinduction, postintubation every minute for 5 min and intraoperative every 15 min till the end of operation; (2) *amount of blood loss* was measured from the suction apparatus and number of completely socked gauzes (10–15 ml blood); (3) *quality of the surgical field*: by using average category scale for the assessment of surgical field: 0 = no bleeding, 1 = slight bleeding – no suctioning of blood required, 2 = slight bleeding – occasional suctioning required. Surgical field not threatened, 3 = slight bleeding – frequent suctioning required, bleeding threatens surgical field a few seconds after suction is removed, 4 = moderate bleeding – frequent suctioning required, bleeding threatens surgical field directly after suction is removed, 5 = sever bleeding – constant suctioning required, bleeding appears faster than can be removed by suction, surgical field severely threatened and surgery not possible. The ideal category scale values for surgical conditions were predetermined to be two and three, the surgeon assessed the quality of surgical field by category scale adopted from that of [10]; (4) *total amount of hypotensive agent* (*GTN*) for every patient in both groups; (5) *emergency time*, is the time between the discontinuation of anesthetics to response of eye opening to verbal command [11]; (6) *recovery character* by measuring time to reach score 9 of modified Alderat score [12].

2.2. Statistical analysis

The statistical analysis was carried using a statistical package (SPSS, version 0.11. interface). Descriptive and analytical statistics were performed. Numerical data were presented as mean ± standard deviation (±SD). Paired *t*-test was used to compare parametric data inside the group and unpaired *t*-test between the groups. Rank test Mann Whitney *U*-test was used to compare nonparametric data between the two groups and Wilcoxon test inside the group. Categorical data were presented as numbers and percent and Chi square test was used to compare group of categorical data. A *P*-value was calculated and considered to be significant if <0.05.

3. Results

Sixty patients ASA I and II patients (26 females and 34 males) undergoing FESS were included (control, $n = 30$; nifedipine, $n = 30$). There were no statistically significant differences between two groups with respect to patient demographic and operative characteristics (age, gender, weight, ASA, duration of surgery and amount of blood loss) ($p > 0.05$) (Table 1). The amount of nitroglycerine used in nifedipine group was significantly lower than Control group ($p < 0.001$); 12 patients (40%) of nifedipine group achieved hypotension without the need for GTN, and the remaining 18 patients (60%) of this group achieved hypotension with significant low amount of GTN.

Scores for a bloodless surgical field using the average category scale (ACS) (Table 2) during hypotensive period (MAP = 55–65 mmHg) were low in both groups; there was no significant difference in scores between both groups. The median range of scores was 2 (1–3) in both groups. No patients presented with excessive blood loss. Emergence time and time needed to achieve >9 of modified Aldrete score (Table 3) were significantly shorter in Control group than nifedipine group (4.46 ± 1.25 min and 7.46 ± 2 min versus 8 ± 1.62 min and 9.5 ± 2.41 min, respectively) ($P < 0.01$).

Regarding measurements of mean arterial blood pressure (MAP) (Fig. 1), nifedipine group showed no statistically significant difference when compared to control group at basal measurement (92.73 ± 4.77 vs 92 ± 3.84, $P = 0.51$), after induction (80.63 ± 5.17 vs 78.90 ± 5.47, $P = 0.21$) and during hypotensive period (59.33 ± 3.23 vs 60.20 ± 3.17, $P = 0.29$), while MAP in nifedipine group was significantly lower than control group at 5 min after HA (hypotensive

Table 1 Patient demographic and operative characteristics.

Characteristics	Nifedipine ($N = 30$)	Control ($N = 30$)	*P*-value
Age (years)	37(19–56) 35.1 ± 8	32(20–52) 37 ± 9	0.38
Gender (M/F)	16/14	18/12	0.43
Weight (kg)	68(31–99) 70 ± 15.7	51(52–103) 73.9 ± 11.8	0.27
ASA (I/II)	14/16	17/13	0.43
Duration of surgery (min)	62(62–124) 90 ± 15.3	51(66–117) 92 ± 12.9	0.60
Amount of blood loss (ml)	110(80–190) 129.6 ± 25.9	80(90–170) 132 ± 20	0.70
Amount of Nitroglycerine (mg)	3(0–9.5) 3.3 ± 3.4	16.5(8–30) 16 ± 6.4	0.0001[a]

Data are expressed as median (range) and mean ± standard deviation or number.

[a] Significant difference.

anesthesia) (62.96 ± 3.81 vs 80.73 ± 5.89, $P < 0.001$), 10 min after HA (66.10 ± 4.38 vs 81.86 ± 5.11, $P < 0.001$), at end of surgery (76.56 ± 3.85 vs 85.80 ± 5.46, $P < 0.001$) and after recovery (80.73 ± 5.89 vs 83.56 ± 4.19, $P = 0.03$). Two patients of nifedipine group needed ephedrine 5 and 10 mg to elevate MAP above 55 mmHg.

Regarding measurements of heart rate (HR) (Fig. 2), nifedipine group showed no statistically significant difference when compared to control group at basal measurement (85.60 ± 2.60 vs 85.16 ± 3.20, $P = 0.56$), after induction (70.23 ± 5.67 vs 70 ± 5.81, $P = 0.87$) and during hypotensive period (72.36 ± 5.68 vs 71.70 ± 6.24, $P = 0.66$), while HR in nifedipine group was significantly lower than control group at 5 min after HA (77.13 ± 4.09 vs 67.30 ± 4.45, $P < 0.001$), 10 min after HA (77.56 ± 4.65 vs 69.33 ± 3.75, $P < 0.001$), at end of surgery (75.43 ± 5.96 vs 71.56 ± 5.90, $P = 0.01$) and after recovery (73.33 ± 5.58 vs 68.13 ± 4.29, $P < 0.001$).

4. Discussion

During FESS, nasal and the sinus mucosa are very vascular and bleed easily, which would interfere with the visualization of the surgical field through the endoscope, and this could result in inadvertent tissue injury leading to adhesions and scarring and even severe complications such as orbital and brain injury [13–17]. A number of techniques/agents have been advocated to achieve hypotension during FESS. Among the pharmacological agents nifedipine was chosen as it is a vasodilator. We examined the use of nifedipine 10 mg in 3 pilot cases before starting in the study, but we noticed minimal reduction in MAP, and then we decided to examine nifedipine 20 mg. The result of our study showed that oral nifedipine (20 mg) one hour before induction of anesthesia markedly reduces the amount of GTN required to decrease MAP during FESS by 80% used in control group (3.3 ± 3.4 mg in nifedipine versus 16 ± 6.4 mg in control) These findings confirm a previous study by Ahmad1 et al. they investigated the pharmacokinetic of nifedipine in healthy adult male human volunteers which showed that use of oral nifedipine reduced MAP [18], is also in agreement with our study, and Imai et al. examined the effect of nifedipine in essential hypertensive patients, when the conventional form of nifedipine (soft capsule containing 10 mg of dissolved nifedipine) was administered orally, there was a rapid hypotensive effect occurring maximally at 1 h after administration and disappearing within 7 h [9]. The probable mechanism of reducing blood pressure by promote vasodilator activity (and reduce blood pressure) by reducing calcium influx into vascular smooth muscle cells by interfering with voltage-operated calcium channels (and to a lesser extent receptor-operated channels) in the cell membrane [23]. The study by Puri and Batra showed that administration of nifedipine before induction, can reduce arterial pressure but not HR in responses to laryngoscopy and intubation [19], and this coincides with our results but significant tachycardia was not recorded in the study group may be due to midazolam and fentanyl premedication; also, Kale and colleagues showed that oral nifedipine 10 mg is a useful pretreatment to prevent the pressor response to laryngoscopy and tracheal intubation in

Table 2 Scores for bloodless surgical field (average category scale).

Time of hypotensive anesthesia (min)	Nifedipine ($N = 30$)	Control ($N = 30$)	P-value
15	2(1–3) 1.86 ± 0.57	2(1–3) 1.80 ± 0.61	0.63
30	2(1–3) 1.90 ± 0.54	2(1–3) 1.96 ± 0.61	0.67
45	2(1–3) 2.03 ± 0.66	2(1–3) 2.13 ± 0.68	0.55
60	2(1–3) 2.26 ± 0.63	2(1–3) 2.23 ± 0.62	0.82

Data are expressed as median (range) and mean ± standard deviation. Mann–Whitney test was used.

Table 3 Recovery characteristics.

Recovery characteristics (min)	Nifedpine ($N = 30$)	Control ($N = 30$)	P-value
Emergence time	7(4–11) 8 ± 1.62	5(2–7) 4.46 ± 1.25	0.0001[a]
Time to modified Alderet score >9	9(5–14) 9.5 ± 2.41	9(2–11) 7.46 ± 2	0.001[a]

Data are expressed as median (range) and mean ± standard deviation.
[a] Significant difference.

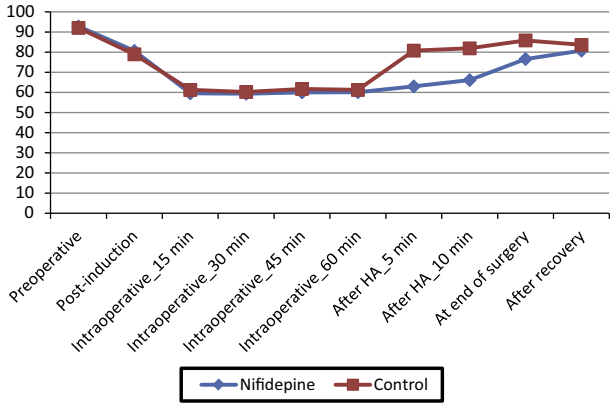

Figure 1 Mean values of mean arterial blood pressure (mmHg). HA: hypotensive anesthesia.

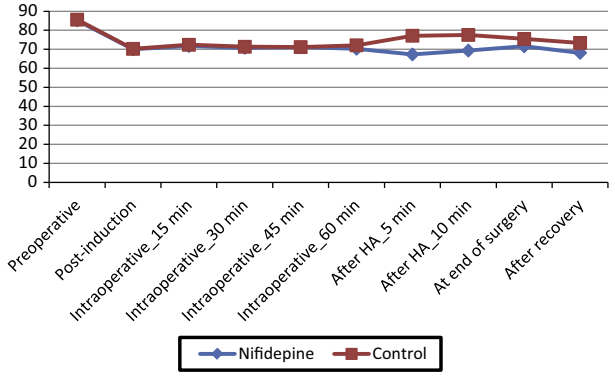

Figure 2 Mean values of heart rate (Bpm). HA: hypotensive anesthesia.

patients with coronary artery disease [20]. Nitroglycerin induced hypotension is related primarily to a direct effect of the drug on vascular smooth muscle. Both resistance and capacitance vessels are dilated, but the effect on the veins is predominant [21]. In the study by Nabil and Fahmy, nitroglycerin offers certain advantages over sodium nitroprusside. It produced a smooth and gradual decrease in blood pressure, and it is easy to control the dose and blood pressure response with minimal danger of producing severe hypotension [22]. In the present study, it is evident that patients receiving oral nifedipine had a nonsignificant difference regarding surgical field and amount of blood loss as compared to patients receiving placebo, and the amount of GTN used in nifedipine group was 20% of total amount of GTN used in control group to induce hypotension ($p < 0.001$), 12 patients (40%) of nifedipine group achieved hypotension without the need for GTN, this is explained by the fact that nifedipine produces vasodilatation, resulting in lower blood pressure and thereby decreasing blood loss at the surgical site and improving the quality of surgical field. In our study, the recovery time and time to reach Aldrate score 9 were significantly higher than control group, this may be explained by delayed return of skeletal muscle power under effect of nifedipine as calcium channel blockers augment the effect of nondepolarizing muscle relaxant. *In conclusion*, this study has demonstrated that administration of a single preoperative dose of nifedipine (20 mg) can significantly reduce the blood loss during FESS and improve the visualization of the operating field and it also lowers the amount of GTN needed to achieve hypotensive anesthesia.

Conflict of interest

Author states that there is no conflict of interest.

References

[1] Stankiewicz JA. Complication of endoscopic intranasal ethmoidectomy. Laryngoscope 1987;97:1270–3.

[2] Lavoie J. Blood transfusion risks and alternative strategies in pediatric patients. Pediatr Anesth 2011;21(14–24):4.

[3] Degoute CS et al. Remifentanil and controlled hypotension; comparison with nitroprusside or esmolol during tympanoplasty. Can J Anaesth 2001;48:20–7.

[4] Elsharnouby NM, El Sharnouby MM. Magnesium sulphate as a technique of hypotensive anesthesia. Br J Anaesth 2006;96:727–31.

[5] Degoute CS et al. Effect of posture, hypotension and locally applied vasoconstriction on the middle ear microcirculation in anaesthetized humans. Eur J Appl Physiol Occup Physiol 1994;69:414–20.

[6] Lam AM, Gelb AW. Cardiovascular effects of isoflurane induced hypotension for cerebral aneurysm surgery. Anesth Analg 1983;62:742–8.

[7] Newberg LA, Milde JH, Michenfelder JD. Systemic and cerebral effects of isoflurane-induced hypotension in dogs. Anesthesiology 1984;60:541–6.

[8] Newman B, Gelb AW, Lam AM. The effect of isoflurane induced hypotension on cerebral blood flow and cerebral metabolic rate for oxygen in humans. Anesthesiology 1986;64:307–10.

[9] Imai Y et al. Pharmacokinetics and pharmacodynamics of conventional and slow release forms of nifedipine in essential hypertensive patients. Tohoku J Exp Med 1986;148(4):421–38.

[10] Fromme GA et al. Controlled hypotension for orthognatic surgery. Anesth Analg 1986;65:683–6.

[11] Chung F. Are discharge criteria changing? J Clin Anesth 1993;5:645.

[12] Alderete JA. The post anesthesia recovery score revisted. J Clin Aesth 1995;7:89.

[13] Tewfik MA, Wormald PJ. Ten pearls for safe endoscopic sinus surgery. Otolaryngol Clin North Am 2010;43:933–44.

[14] Baker AR, Baker AB. Anaesthesia for endoscopic sinus surgery. Acta Anaesthesiol Scand 2010;54:795–803.

[15] Nair S et al. The effect of beta-blocker premedication on the surgical field during endoscopic sinus surgery. Laryngoscope 2004;114:1042–6.

[16] Boezaart AP, van der Merwe J, Coetzee A. Comparison of sodium nitroprusside and esmolol-induced controlled hypotension for functional endoscopic sinus surgery. Can J Anaesth 1995;42:373–6.

[17] Albu S, Baciut M. Failures in endoscopic surgery of the maxillary sinus. Otolaryngol Head Neck Surg 2010;142:196–201.

[18] Ahmad1 M et al. Trop J Pharm Res 2009;8(5):385.

[19] Puri GD, Batra YK. Effect of nifedipine on cardiovascular responses in laryngoscopy and intubation. Br J Anaesth 1988;60(5):579–81.

[20] Kale SC et al. Nifedipine prevents the pressor response to laryngoscopy and tracheal intubation in patients with coronary artery disease. Anaesthesia 1988;43(6):495–7.

[21] Mason DT, Zelis R, Amsterdam EA. Actions of the nitrates on the peripheral circulation and myocardial oxygen consumption: significance in the relief of angina pectoris. Chest 1971;59:296–305.

[22] Nabil R, Fahmy MD. Nitroglycerin as a hypotensive drug during general anesthesia. Anesthesiology 1978;49:17–20.

[23] Fleckenstein et al. Bay a 1040-emn hoch-aktiver Ca^{++}-antagonistisher inhibitor der electromechanishen Kopplungsprozesse im Warmbluter-Myokad. Arzneimittel-Forsch 1972;22:22–33.