The Prevention of Bupivacaine-Induced Hypotension with the Addition of Neostigmine in Spinal Anesthesia[11]

SPINAL ANESTEZİDE BUPİVAKAİNE BAĞLI HİPOTANSİYONUN NEOSTİGMİN İLAVESİYLE ÖNLENMESİ

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Summary

We investigated whether the addition of neostigmine to bupivacaine prevents the hypotensive effect of bupivacaine-induced hypotension in spinal anesthesia in patients undergoing minor lower extremity surgical procedures.

19 ASA physical status 1-11 patients were randomly allocated into three groups. Group I (n=6) received bupivacaine 3.0 ml 0.5% plus 100 flgr neostigmine, Group II (n=7) received bupivacaine 3.0 ml 0.5% plus 250 flgr neostigmine and Group 111 (n=6) received bupivacaine 3.0 ml 0.5%> alone (group 111) through a 22 G spinal needle intrathecal!)'. Mean arterial pressure (MAP), Heart Rate (HR) and transcutaneous oxyhemoglobin saturation were recorded before the drugs given intrathecally as baseline values and at every 5 nun. for 30 min., then at 45., 60., 90., 120., 150. ve 180. minutes after the administration of the drugs intrathecally. A decrease in MAP values was observed in group I and 111 from 25. min. to 45. min. after the study agents were administered intrathecally (p<0.05). The addition of neostigmine 100 flgr did not affect the hypotension seen after bupivacaine. In contrast, intrathecal bupivacaine 3.0 ml 0.5%, plus 250 fj.gr neostigmine produced an insignificant increase in MAP beginning within 5 min. and lasting at 45[a] min., then returned to baseline values. One patient in gmup 1 and four patients in group II showed severe emesis.

We concluded that intrathecal neostigmine 250 flgr lessens bupivacaine induced hypotension. We also suggest that despite high incidence of emesis symptoms, this form of anesthesia might be safer in patients undergoing minor lower extremity surgical procedures.

Key Words: Spinal anesthesia, Bupivacaine, Neostigmine, Hypotension

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Özet

Bu çalışmada minör alt ekstremde cerrahisi geçirecek hastalarda spinal anestezi sırasında bupivakain neostigmin ilavesiyle bupivakain kaynaklı hipotansiyonun önlenebilir/iğini, fiziksel durumu ASA I ve 11 olan 19 hasta üzerinde araştırdık. Hastalar rastgele üç gruba ayrıldı. 22 no 'lu spinal iğneyle intratekal olarak 6 hastaya bupivakain 3.0 ml %,0.5 + 100 flgr neostigmin (grup I), 7 hastaya bupivakain 3.0 ml %,0.5 + 250 flgr neostigmin (grup II) ve diğer 6 hastaya sadece bupivakain 3.0 ml %)0.5 (grup III) verildi. Ortalama arter basıncı (MAP), kalp hızı (HR) ve transkütan oksihemoglohiu saturcısyonu ilaçlar intratekal olarak verilmeden önce (başlangıç değerler olarak) ve ilaçlar intratekal olarak verildikten sonra ilk 30 dakika için her 5 dakikada bir ve daha sonra 45., 60.. 90., 120., 150. ve 180. dakikalarda kaydedildi. Grup 1velll'de MAP değerlerinde ilaçlar uygulandıktan sonra 25. dakikadan başlayan ve 45. dakikaya kadar süren düşmeler saptandı (p<0.05). 100 flgr neostigmin ilavesi bupivakaine bağlı hipotansiyonu önlemedi. Buna karşılık intratekal bupivakain 3.0 ml %0.5 + 250 flgr neostigmin verilen grupta; 5 dk içinde başlayan ve 45 dk sürdükten sonra başlangıç değerlerine dönen fakat istatistiksel olarak anlamlı olmayan MAP artışı gözlendi. Grup I'de 1, grup II'de ise 4 hastada ciddi emesis görüldü.

Sonuçta, 250 flgr intratekal neostigminin bupivakain kaynaklı hipotansiyonu azalttığı ve bu anestezi formunun alt ekstremde cerrahisi geçirecek hastalarda güvenle kullanılabileceği sonucuna varıldı.

Anahtar Kelimeler: Spinal anestezi, Bupivakain, Neostigmin, Hipotansiyon

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It is well known that one of the clinically important side effects of spinal anesthesia is hypotension. The hypotensive effect of spinal block is thought to be the result of decreased activity of preganglionic sympathetic nerves produced by this technique (1). Intraspinal administration of bupiva-

caine holds the potential for providing excellent analgesia but also decreases blood pressure as a results of the sympathetic blockade. This side effect is generally well tolerated in normal individuals, but is bothersome and could be dangerous in cardiac and elderly patients.

Intrathecal administration of cholinergic agonists has been shown to increase spinal preganglionic sympathetic nervous system activity with a resultant increase in blood pressure (2-6). This vasopressor effect appears to be mediated by activation of muscarinic receptors within the central nervous system (3-6). Neostigmine, a cholinesterase inhibitor, has been shown to prevent the hypotensive effect of spinal block (6,7). Therefore, the present study is designed to investigate whether the addition of neostigmine to bupivacainc prevents the hypotensive effect of spinal block in patients undergoing minor lower extremity surgical procedures.

Material and Methods

After instutional review board approval and informed constent, 19 ASA physical status I-II patients were studied. The patients were randomly allocated into three groups. Group I (n=6) received bupivacaine 3.0 ml 0.5% (no: 709443, Astra Sweden) plus 100 (Igr neostigmine (Neostigmine mctylsulphatc, no: 013, Adeka, TR) (group I), Group II (n=7) received bupivacaine 3.0 ml 0.5% plus 250 (igr neostigmine (group II) and Group III (n=6) received bupivacaine 3.0 ml 0.5% alone (group III) through a 22 G spinal needle. Patients were monitored with an automatic blood pressure cuff, three lead ECG and pulscoximetry. A peripheral intravenous catheter was inserted to all patients. L_{v4} or $L^{\wedge}{}_{s}$ lumbar space were selected for the administration of drugs intrathecally. Mean arterial pressure (MAP), heart rate (HR) and oxyhemoglobin saturation were recorded before the drugs given intrathecally as baseline values and at every 5 min. for 30 min., then at 45., 60., 90., 120., 150. and 180. minutes after the administration of drugs intrathecally. A 30%) decrease in MAP was treated with an intravenous fluid bolus of lactated Ringer's solution and/or a vasopressor (ephedrine). Analysis of variance (ANOVA) and Student's t-test were used for statistical analysis. $p<0.05$ was considered significant.

Results

There were no significant differences in demographic characteristics among the groups. The onset, duration and height of the sensory and motor level of the spinal block and MAP and HR baseline values were similar in all groups (Table 1) (Figure 1,2). The heart rate was not affected in all groups during the procedure (Figure 2). A decrease in MAP values was observed in group I and III from 25 min. to 45 min. after the study agents were ad-

Table 1. Patients demographics and the onset, duration and level of analgesia

	Group I (n:6)	Group II (n:7)	Group III (n:6)
Age (yr)	39.3±8.7	40.5±6.9	39.8±9.1
Weight (kg)	76.3±9.0	73.5±8.3	78.2±4.9
Height (cm)	163.4±7.8	168.0±6.5	165.3±8.0
Onset of analgesia (min)	3.6±0.8	3.9±1.1	3.7±0.7
Duration of analgesia (min)	124.5±34.3	118.8±27.8	129.3±30.0
Level of motor block	Th-11	Th-11	Th-11

**Values were given as ± SD*

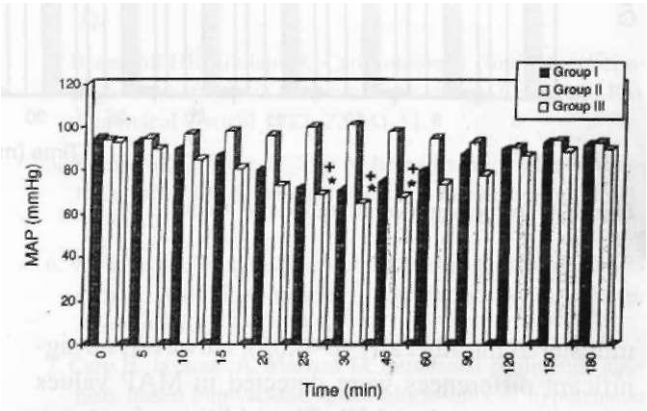

Figure 1. Mean arterial blood pressure (MAP) values.

**The decrease in MAP values was significant in group I and III compared to baseline values ($p<0.05$).*

+The decrease in MAP values was significant in group I and III compared to group II ($p<0.05$).

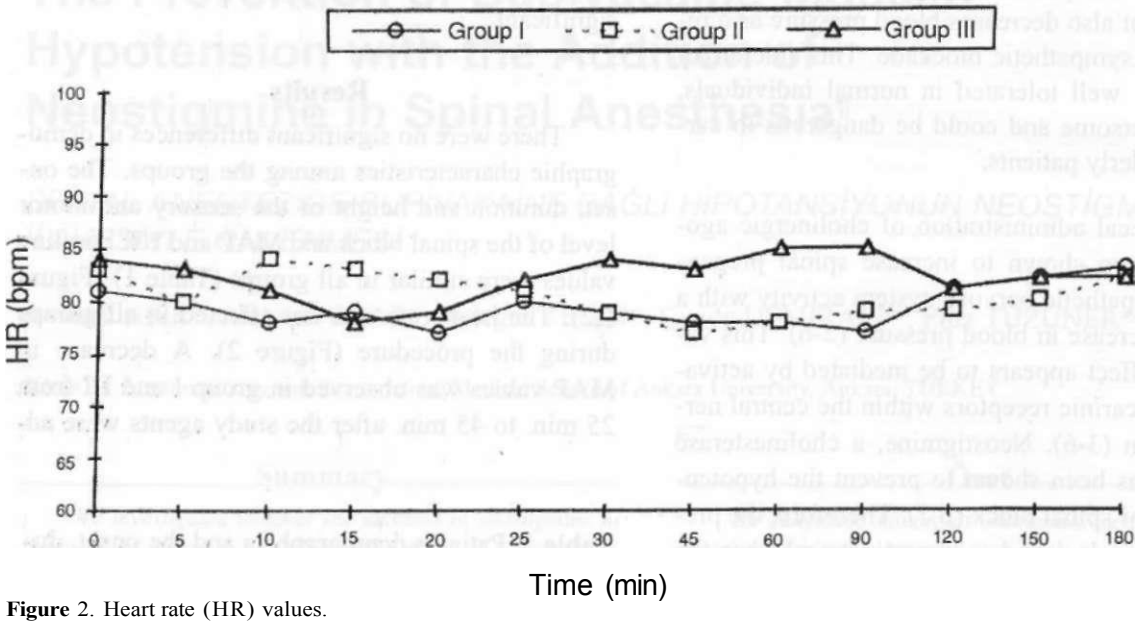

Figure 2. Heart rate (HR) values.

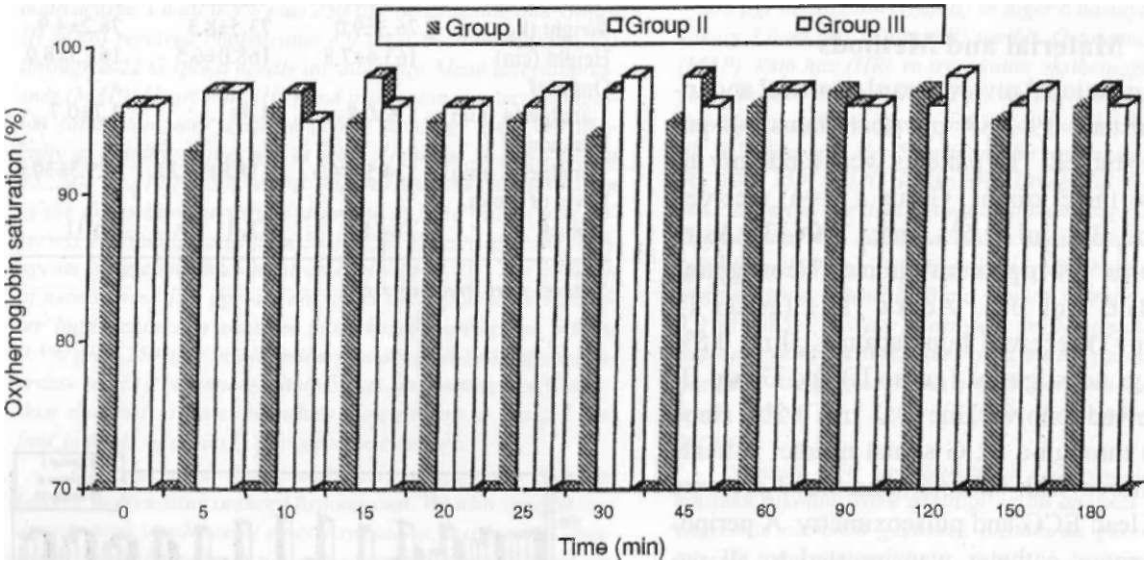

Figure 3. Oxyhemoglobin saturation (%) values.

ministered intrathecally ($p<0.05$). However, no significant differences were detected in MAP values between groups I and III. The addition of neostigmine 100 |Xgr did not affect the hypotension seen after bupivacaine. In contrast, intrathecal bupivacainc 3.0 ml plus neostigmine 250 u,gr produced an insignificant increase in MAP beginning in 2-3 min. and lasting 45 min., then returned to baseline values (Figure 1). A non-significant decrease was observed in oxyhemoglobin saturation, 5 minutes after the study agents were given in group 1. However, oxyhemoglobin saturation values were similar in all groups during the procedure (Figure 3). One patient in group I and four patients in group

II showed severe emetic symptoms. No patients in group III had nausea and vomitting.

Discussion

The present study has shown that the use of spinal neostigmine with a local anesthetic combination demonstrates a dose related prevention of spinal block induced hypotension and side effects.

The current study agrees with the results of previous work in rats and sheep demonstrating a vasopressor effect after cholinergic stimulation at a spinal site (2-6). The observation that cholinergic ligands bind densely within the spinal cord intermediolateral cell column (8) and that activation of these neurons by iontophoretic application of cholinergic agonists at this site has a potent vasopressor effect (9), supports the probability that there is a spinal site of action for the antihypotensive effect of neostigmine (7).

In addition to spinal sites of action, cholinergic agonists may also increase blood pressure through effects on central nervous system sites involved in blood pressure regulation (2-4). The rostral ventrolateral region of the medulla oblongata contains cholinergic receptors that are capable of producing increases in arterial blood pressure when activated by cholinergic agonists (4,10).

Our results demonstrate that intrathecal neostigmine with a dose of 250 (igr lessens bupivacaine induced hypotension while 100 figr does not prevent the hypotensive effect of bupivacaine. This effect is thought to be the result of activation of spinal cord preganglionic sympathetic neurons by neostigmine using a muscarinic dependent pathway (7). It might be speculated that despite emetic symptoms, this form of anesthesia can be used more safely in hypotensive patients.

It has been postulated that cholinergic agonists or cholinesterase inhibitors have respiratory stimulant effects near pontine centers of respiratory control (II). However, we observed no stimulant effects of spinal neostigmine on respiration and oxyhemoglobin saturation.

Lauretti et al (12) investigated the analgesic and antiemetic efficacy of intrathecal neostigmine in patients undergoing orthopedic surgery. He indicated that although the patients were hemodynamically stable, 100 ugr subarachnoid neostigmine was associated with a high incidence of nausea and vomiting. Similary, nausea and vomiting occurcd in a dose related manner after spinal neostigmine in the present study. The most likely site of this effect is in the brainstem as it appeared approximately 60 min. later after intrathecal injection. It has been proposed that the use of hyperbarique solutions with neostigmine such as 5% Dextrose might prevent the cephalad spread of neostigmine and so emesis (11).

The results of the present study suggest that the addition of neostigmine to local anesthetic solutions used for spinal anesthesia could result in greater hemodynamic stability after spinal block. However, nausea and vomiting could limit the utility of spinal neostigmine.

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