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Comparison of Efficacy of Intrathecal 0.5% Levobupivacaine Heavy Versus 0.5% Bupivacaine Heavy in Patients for Lower Abdominal Surgeries.

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1. Introduction

Levobupivacaine is an enantiomer or isomer of racemic bupivacaine. Bupivacaine is a local anesthetic drug with a long duration of action which has been commonly used in obstetric surgeries and other lower abdominal surgeries. Usually epinephrine is used in addition to local anesthetic drugs to increase their duration of action but bupivacaine does not require adding epinephrine as bupivacaine is a long acting drug.[1] Bupivacaine produces motor as well as sensory blockade and there is a distinct difference between the motor and sensory block which can be appreciated well with bupivacaine. There is no requirement for continuous dosing with bupivacaine. Adverse reactions such as tachyphlaxis which is commonly seen with [lidocaine] is not seen with bupivacaine. In spite of having many advantages bupivacaine had its downfall with reported cases of cardiac toxicity associated with it. The order of cardiac toxicity occurrence was thought to be initiated with simple anesthetic toxicity such as convulsions, then convulsions would progress to cardiac depression which is eventually follows by cardiac arrest.[2] Without any alarming central nervous system symptoms sudden occurrence of cardiac arrest have been reported.[3] This toxic capability of bupivacaine lead to further research with bupivacaine which led to discovering of the levo isomer of bupivacaine having better effectiveness in local anesthesia without cardiac toxicity. The isomers of bupivacaine includes dextrobupivacaine and levobupivacaine, the difference in effectiveness and other properties of these two isomers of bupivacaine was first reported by Aberg and Luduena in 1972.[4,5] Based on the chirality which is the rotation of the optical light these isomers are denoted with R (+) and S (-). R (+) refers to the

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clockwise rotation of the light by the isomer and S (-) refers to the anticlockwise rotation. In comparison levobupivacaine was found to have longer duration with dextrobupivacaine. Initially all these positive effects of levobupivacaine were useful only for theoretical purpose, once technology for chiral synthesis in extracting a single isomer came into practice the use of levobupivacaine became useful in anesthetic management. Levobupivacaine is S (-) enantiomer of bupivacaine, it benefits over bupivacaine by having reduced toxicity in causing cardiac and central nervous system adverse effects. Levobupivacaine was initially introduced for epidural anesthesia for obstetric surgeries such as caesarean section and other lower abdominal surgeries like herniopalasty, sphincterotomy, fistulectomy, hemorrhoidectomy, wound debridement, etc. Levobupivacaine has gained its place as spinal anesthetic agent along the years. Bupivacaine is commonly used as intrathecal anesthetic agent for many abdominal surgeries. The clinical comparison for the intrathecal anesthetic effectiveness of levobupivacaine Vs bupivacaine is very less. Taking that into consideration we tried to compare the efficacy of intrathecal levobupivacaine and intrathecal bupivacaine in patient undergoing lower abdominal surgeries in a tertiary care hospital in southern Indian setting.

2. Methodology

This is a prospective randomized control trial which was conducted for a period of three months (October 2022 – December 2022) in Government Employment State of Insurance Hospital in ayanavaram, Chennai, Tamil Nadu. The aim of the study is to evaluate the effect of intrathecal 0.5% levobupivacaine heavy and 0.5% bupivacaine heavy in lower abdominal surgeries. This study has to objectives primary and secondary objectives. The primary objective is to o access the onset and duration intrathecal 0.5% bupivacaine heavy versus 0.5% levobupivacaine heavy and the secondary objective is comparing efficacy, hemodynamic stability of the drug. After receiving written informed from each participant the study was conducted on patients posted for spinal anesthesia undergoing lower abdominal surgeries such as caesarean section, hysterectomy, hernia, orthopedics surgeries, plastic surgeries, etc. Patients of both sex between the age of 25-60 years with ASA PS 1 and 2 (American Society of Anesthetists Physical Status) who were posted for lower abdominal surgeries were included. Patients with Bleeding disorders, Coagulation abnormality, Hypersensitivity towards local anesthetic drugs, Neurological deficits, morbid obesity (more the 150% of the ideal weight or more than 130 kgs) were excluded.[6]

A total of 60 participants were recruited and they were randomly divided into two groups group A and group B, 30 participants were randomly allotted to each group. Patients in group A Received 3.5ml of 0.5% levobupivacaine and patients in group B Received 3.5ml of 0.5% bupivacaine.

Pre-anesthetic checkup was done for the participants one day before surgery. A general physical examination assessment of airway and local examination of the lumbar spine were done. Relevant investigation (Complete blood count, renal function tests, coagulation Profile, electrocardiogram, viral serology, chest X-ray) were done for the participants. Study participants were asked to restrict solids for six hours before surgery and fluids for two hours before surgery.

Oral premedication ranitidine 50mg and ondansetron 4mg were given orally in the early morning with sips of water. Outcome for the study is based on sensory and motor blockade time for rescue analgesia, hemodynamic parameters, complication. Hypotension is defined as decrease in systolic pressure >= 20% from the base line. Managed with IV fluids vasopressors. Bradycardia is defined as heart rate (HR) < 60 beats/min, treated with IV atropine 0.6 mg. Nausea vomiting if any, and were treated with ondansetron 4 mg. Sensory block assessed with pin prick every minute after intrathecal injection till 10mins, then every 15mins till the level regressed to T10. Motor blockade assessed using modified bromage scale. The modified bromage scale has four-point scoring system which includes score from 0-3 were score 0 is no paralysis, score 1 is inability to rare the leg against the gravity but can flex the knee, score 2 is inability to flex the knee but can flex ankle, score 3 is inability to flex the ankle. Effectiveness of anesthesia, motor blockade, and sensory blockade was determined as satisfactory, not

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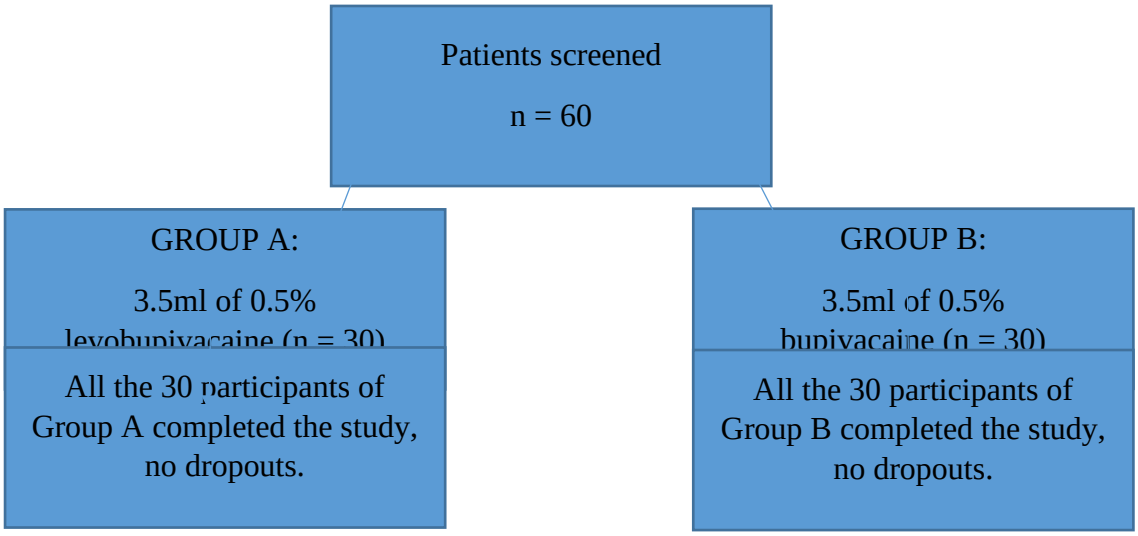
satisfactory and excellent. Once motor and sensory blockade had regressed fully, patients were advised for mobilization.

3. Statistical Analysis

The collected data were analyzed with IBM SPSS Statistics for Windows, Version 29.0. (Armonk, NY: IBM Corp).To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in Independent groups the Independent sample t-test was used. To find the significance in qualitative categorical data Chi-Square test was used. In all the above statistical tools the probability value .05 is considered as significant level.

4. Results

A total of 60 participants with ASA PS 1 and ASA PS 2 after pre-anesthetic check-up who were posted for intrathecal anesthesia undergoing lower abdominal surgeries were included in the study. These 60 participants were divided into two groups – group A and group B with 30 participants in each group. There were no drop outs from the study in both group A and group B, all the 60 participants completed the study. Figure.1 shows the participant flow chart of the study.



Age group among both the study groups ranged between 35 – 55 years. The inclusion criteria for age in this study is between 25-60 years of age. The mean ± standard deviation (SD) for group A is 44 ± 10.8 years and for group B is 45.2 ± 12.8 years, when statistically compared there was no statistical significance between age groups of group A and group B.

Gender distribution between the two study groups were equal in between group A and group B, however a small female predominance in group B was seen. Table.1shows the gender distribution between the two groups.

			Groups		Total
			Group A	Group B	
GENDER	Female	Count	15	17	32
		%	50.0%	56.7%	53.3%
	Male	Count	15	13	28
		%	50.0%	43.3%	46.7%

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Total	Count	30	30	60
	%	100.0%	100.0%	100.0%

Table.1: Gender distribution.

Both systolic and diastolic blood pressure were assessed and recorded for both group A and group B from baseline i.e. 0 minutes till the level of anesthetic blockade regressed to T10 which was 210 minutes or three and a half hours. The mean systolic blood pressure (SBP) between the levobupivacaine group and bupivacaine group was found to be highly statistically significant for the first 1 hour from the injection except for the baseline values which didn't show statistical significance. Table.2 and figure.2 shows the statistical difference between the systolic blood pressure of each group from baseline,10 minutes and every 15 minutes from baseline till 210 minutes.

SBP	Groups	N	Mean	SD	t-value	p-value
Base line	Group A	30	124.3	4.5	0.063	0.950 #
	Group B	30	124.4	3.6		
10 Mins	Group A	30	110.2	2.8	15.136	0.0005 **
	Group B	30	100.6	2.1		
20 Mins	Group A	30	112.8	3.4	10.133	0.0005 **
	Group B	30	105.4	2.1		
35 Mins	Group A	30	115.8	3.8	6.365	0.0005 **
	Group B	30	110.9	1.8		
50 Mins	Group A	30	120.7	3.9	5.146	0.0005 **
	Group B	30	116.4	2.5		
65 Mins	Group A	30	122.9	4.1	3.504	0.0005 **
	Group B	30	120.0	2.0		
80 Mins	Group A	30	121.2	4.7	1.327	0.190 #
	Group B	30	122.6	3.4		
95 Mins	Group A	30	123.3	3.9	1.468	0.147 #
	Group B	30	124.7	3.1		
110 Mins	Group A	30	123.0	4.0	2.804	0.0005 **
	Group B	30	125.4	2.5		
125 Mins	Group A	30	122.0	4.2	5.026	0.0005 **
	Group B	30	126.3	2.2		
140 Mins	Group A	30	122.0	4.0	4.859	0.0005 **
	Group B	30	126.2	2.4		
165 Mins	Group A	30	123.6	4.1	3.642	0.0005 **
	Group B	30	126.6	2.0		
180 Mins	Group A	30	124.2	3.4	2.777	0.0005 **
	Group B	30	126.3	2.5		
195 Mins	Group A	30	124.2	3.1	0.603	0.549 #
	Group B	30	123.7	2.8		
210 Mins	Group A	30	124.1	3.5	0.118	0.906 #

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	Group B	30	124.0	3.0		
** Highly Statistical Significance at p < 0.01 ,* Significant at p < 0.05 and # No Statistical Significance at p > 0.05						

Table.2: comparison of SBP between the two groups

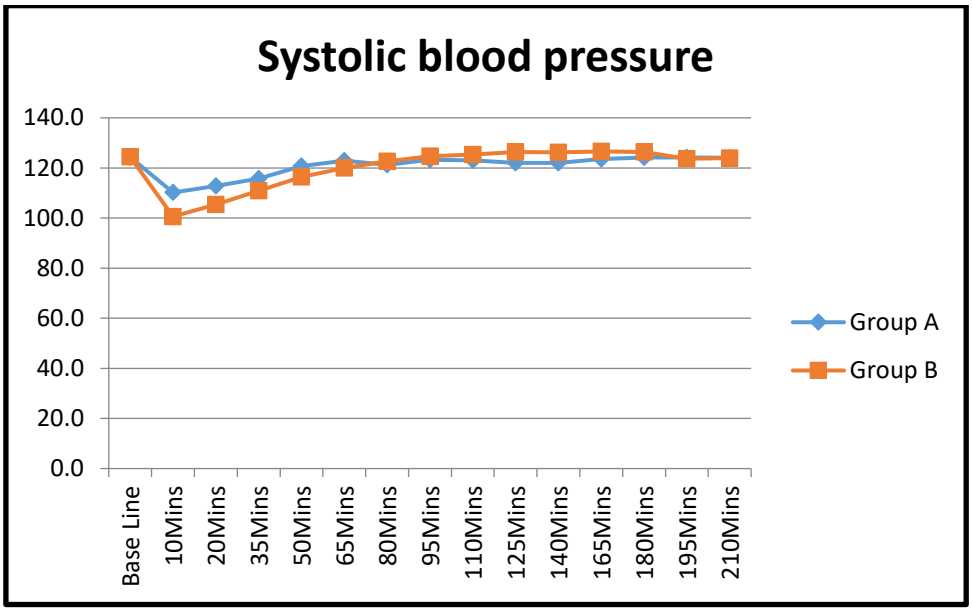

Figure.2

The mean diastolic blood pressure (DBP) were statistically significant at baseline and 10 minutes and showed high statistic significance in all the other recordings of 15 minute interval till the first hour from the injection. Table.3 and figure.3 shows the statistical difference between the systolic blood pressure of each group from baseline, 10 minutes and every 15 minutes from baseline till 210 minutes. The values for the first 1 hour is taken into consideration for comparing the efficacy because it is the effective period of both the drugs.

DBP	Groups	N	Mean	SD	t-value	p-value
Base line	Group A	30	79.7	6.5	2.575	0.013 *
	Group B	30	83.1	2.8		
10 Mins	Group A	30	69.9	4.6	2.339	0.023 *
	Group B	30	72.1	2.1		
20 Mins	Group A	30	72.4	3.4	5.902	0.0005 **
	Group B	30	76.5	1.7		
35 Mins	Group A	30	73.3	4.3	6.094	0.0005 **
	Group B	30	78.3	1.4		
50 Mins	Group A	30	79.8	4.5	3.261	0.0005 **
	Group B	30	82.8	2.0		
65 Mins	Group A	30	82.5	4.6	2.859	0.0005 **
	Group B	30	85.3	2.4		
80 Mins	Group A	30	82.6	4.7	3.274	0.0005 **
	Group B	30	85.6	1.8		

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95 Mins	Group A	30	81.4	5.6	2.144	0.036 *
	Group B	30	83.9	3.4		
110 Mins	Group A	30	80.7	5.5	2.259	0.028 *
	Group B	30	83.5	4.0		
125 Mins	Group A	30	79.7	6.0	5.036	0.0005 **
	Group B	30	85.6	2.4		
140 Mins	Group A	30	78.3	5.1	5.674	0.0005 **
	Group B	30	84.0	1.8		
165 Mins	Group A	30	78.4	5.2	6.437	0.0005 **
	Group B	30	85.0	2.1		
180 Mins	Group A	30	79.2	4.7	7.494	0.0005 **
	Group B	30	86.2	2.0		
195 Mins	Group A	30	79.5	4.6	4.802	0.0005 **
	Group B	30	84.1	2.5		
210 Mins	Group A	30	79.9	4.5	5.212	0.0005 **
	Group B	30	84.8	2.5		
** Highly Statistical Significance at p < 0.01 and * Significant at p < 0.05						

Table.3: comparison of DBP between the two groups.

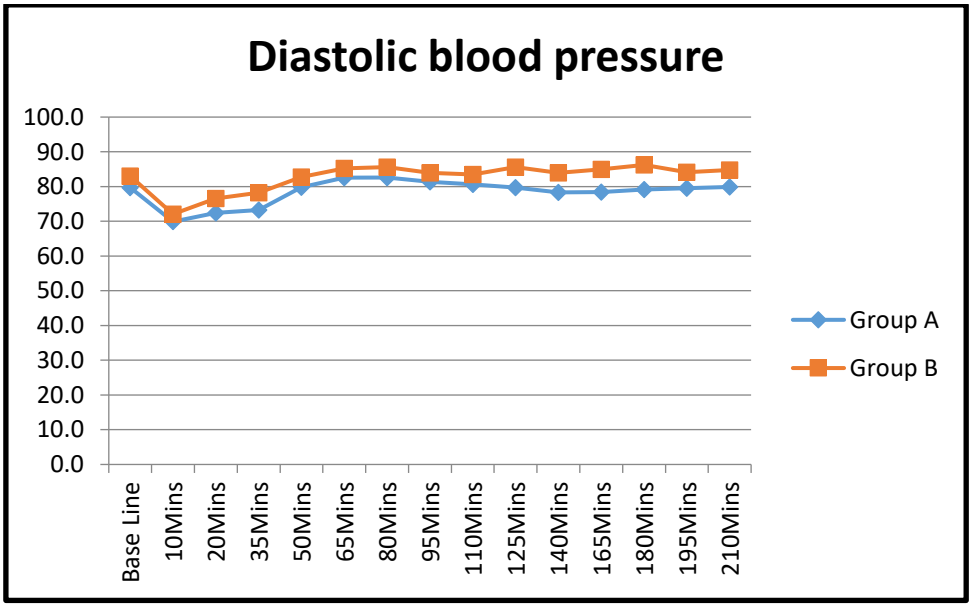

Figure.3

Mean time of onset of sensory blockade of levobupivacaine group was 6.3 minutes, while the racemic bupivacaine group was 4.5 minutes. Group B has faster regression of sensory blockade when compared to group A. Duration of sensory analgesia, group A had a longer duration of sensory analgesia when compared to group B.

Group A had a slower onset time of motor blockade as compared to group B, group A has shorter duration of motor blockade as compared to group B, which is statistically a significant difference, comparing the fall of blood pressure (hypotension) between the two groups with "P" value < 0.01 during initial 10 minutes of onset of the blockade.

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5. Discussion

Levobupivacaine is relatively a newer long acting local anesthetic drug with less cardio toxicity, when compared to racemic bupivacaine.[6]

Bupivacaine is the most commonly used drug for the central nuraxial blockade, a racemic mixture of equal amounts of optical isomers of levobupivacaine and dextrobupivacaine which is known as S(-) and or R (+) enantiomers.[7]

There were no statistically significant difference in patients demographic parameters and clinical characteristics. Our study showed a safe hemodynamic profile, with less number of patients had hypotension and hemodynamic instability. The mean pulse pressure is normal in levobupivacaine group A and it is evident that there is low volume in group B (racemic bupivacaine group) as the mean pulse pressure is increased, this is likely responsible to cause hypotension. This shows there is a better hemodynamic profile with levobupivacaine than racemic bupivacaine.

Levobupivacaine showed shorter duration and degree of motor blockade when compared with the racemic bupivacaine. Duration of sensory blockade was longer and more consistent in levobupivacaine than the racemic bupivacaine. The spread of local anesthesia depends on the factor such as the speed of injection and the simple diffusion.[8]

In a similar study by Glaser *et al*, the results indicated that both levobupivacaine and bupivacaine were equally effective as spinal anesthetic drug in accounts of onset of action, time period of motor blockade and sensory blockade. They also reported that levobupivacaine showed a sustained pattern in sensory and motor blocking ability as an anesthetic drug.[9]

In another similar study by Gautier *et al*, were they compared the effects of intrathecal ropivacaine, levobupivacaine, and bupivacaine for Caesarean section the results came out to be effective in bupivacaine more than ropivacaine followed by levobupivacaine . The results of this study was not similar to my study.

6. Summary

This study titled "Comparison of efficacy of Intrathecal 0.5% levobupivacaine heavy versus 0.5% bupivacaine heavy in patients for lower abdominal surgeries," was conducted with the aim to compare the effects of levobupivacaine and racemic bupivacaine as intrathecal injection in lower abdominal surgeries. This prospective study was initiated and conducted in a tertiary care hospital in Chennai, Tamil Nadu, India. The study participants were explained about the consent and written informed consent were obtained from each participant before the commencement of the study. The study was conducted in department of anaesthesiology in Employment State of Insurance Hospital in ayanavaram, Chennai, Tamil Nadu, India for a period of three months from October 2022 – December 2022. The study sample size was 60. The study participants were equally divided into two groups with 30 participants per group. Patients with ASA PS1 and PS2 posted for various lower abdominal surgeries were included in the study. Patients who satisfied the eligibility criteria were injected with both the study drugs (levobupivacaine and racemic bupivacaine) prior to the surgery. Recruitment was carried out until 30 patients in both study drug groups were reached. The study participants were examined, and proper history was taken at the first visit of the study participants. Patients were kept nil per oral for a day before the surgery. Adverse reactions were monitored and no other adverse effects were recorded.

In the present study levobupivacaine was found to be a better effective drug than racemic as an anesthetic intrathecal injection for lower abdominal surgeries. Levobupivacaine showed slower onset of action and produced sustained anesthetic effect with no pulse pressure drop. Further exploration with this topic is required to understand the effectiveness of levobupivacaine and racemic as an intrathecal anesthetic agent.

7. Conclusion

Levobupivacaine an isomer of racemic bupivacaine was found to be hemodynamically better than racemic bupivacaine itself as a spinal anesthetic agent, it had a slower onset of action and a faster regression of action which is beneficial. Since all the parameters of comparison were better in levobupivacaine group we conclude with saying that

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levobupivacaine is effective as an anesthetic drug as an intrathecal administration for lower abdominal surgeries. Further research in this comparison is required with larger population in different socioeconomic status, different ethnic and geographical backgrounds were needed for better understanding of the drugs and better patient care.

References

[1] Reynolds F, Taylor G. Plasma concentrations of bupivacaine during continuous epidural analgesia in labor: the effect of adrenaline. British Journal of Anesthesia 1971; 43: 436 - 40.

[2] Covino BG, Vassallo HG. In: Local Anesthetics: Mechanisms of Action and Clinical Use. New York: Grune and Stratton, 1976.

[3] Albright GA. Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. Anesthesiology 1979; 51: 285-7.

[4] Aberg G. Toxicological and local anaesthetic effects of optically active isomers of two local anaesthetic compounds. Acta Pharmacologica et Toxicologica 1972; 31: 273-86.

[5] Luduena FP, Bogado EF, Tullar BF. Optical Isomers of Mepivacaine and Bupivacaine. Archives of International Pharmacodynamics 1972; 200: 359-69.

[6] Glaser C, Marhofer P, Zimpfer G, Heinz MT, Sitzwohl C, Kapral S, Schindler I. Levobupivacaine versus racemic bupivacaine for spinal anesthesia. Anesthesia & Analgesia. 2002 Jan 1;94(1):194-8.

[7] Leone S, Di Cianni S, Casati A, Fanelli G. Pharmacology, toxicology, and clinical use of new long acting local anesthetics, ropivacaine and levobupivacaine. Acta Biomed. 2008 Aug 1;79(2):92-105.

[8] Lirk P, Picardi S, Hollmann MW. Local anaesthetics: 10 essentials. European Journal of Anaesthesiology| EJA. 2014 Nov 1;31(11):575-85.

[9] Meechan JG. Supplementary routes to local anaesthesia. International endodontic journal. 2002 Nov;35(11):885-96.

[10] Gautier P, De Kock M, Huberty L, Demir T, Izydorczic M, Vanderick B. Comparison of the effects of intrathecal ropivacaine, levobupivacaine, and bupivacaine for Caesarean section. British Journal of Anaesthesia. 2003 Nov 1;91(5):684-9.