



OPEN ACCESS

Key Words

Postoperative pain, butorphanol, pain and anesthesia

Corresponding Author

Sounak Chowdhury,
Department of Anaesthesiology,
Burdwan Medical College,
Bardhaman, West Bengal 713104,
India
swarnamukul@gmail.com

Author Designation

^{1,3,4}Assistant Professor ²Senior Resident ⁵Resident Medical Officer

Received: 21 December 2023 Accepted: 17 January 2024 Published: 23 January 2024

Citation: Swarnamukul Saha, Saikat Das, Tofazzel Haque Sahana, Tirthasis Mondal and Sounak Chowdhury, 2024. Comparison Between Intrathecal Buprenorphine and Butorphenol as Adjuvant to Hyperbaric Levobupivacaine in Spinal Anaesthesia for Infraumbilical Surgeries: Α Comparative Prospective Observational Study of Anaesthetic and Hemodynamic Spectrum. Res. J. Med. Sci., 18: 231-236, doi: 10.59218/makrjms. 2024.2.231.236

Copy Right: MAK HILL Publications

Comparison Between Intrathecal Buprenorphine and Butorphenol as Adjuvant to Hyperbaric Levobupivacaine in Spinal Anaesthesia for Infraumbilical Surgeries: A comparative Prospective Observational Study of Anaesthetic and Hemodynamic Spectrum

¹Swarnamukul Saha, ²Saikat Das, ³Tofazzel Haque Sahana, ⁴Tirthasis Mondal and ⁵Sounak Chowdhury

ABSTRACT

Postoperative pain is becoming a serious concern as it can lead to several physiological and psychological problems. For this reason, early mobilization and surgical release depend on effective pain management. Narcotic analgesics are frequently used in epidural anesthesia. To assess the duration of analgesia following intrathecal butorphenol vs. buprenorphine and hyperbaric levobupivacaine spinal anesthesia. This is an observational prospective cohort research conducted in an institution. Burdwan College and Medical Center is the study area. August 2022-February 2021 is the research period. There were sixty participants in this study. Within Group D Magnesium Sulphate, 3 patients (4.6%) had Bradycardia, 1 patient (1.5%) hypotension, 6 patients (9.2%) experienced nausea, 1 patient (1.5%) shivered and 6 patients (9.2%) vomited. Nalbuphine is in Group N. 3 (4.6%) had bradycardia, 1 (1.5%) hypotension, 8 (12.3%) nausea, 1 (1.5%) shivering and 5 (7.7%) vomiting. Adverse Effects did not exhibit a statistically significant association with group (p=0.9957). Epidurally given butorphanol tartrate and buprenorphine can provide safe and effective postoperative analgesia. On the other hand, epidural buprenorphine significantly reduced pain and enhanced the quality of analgesia with a longer duration of impact than epidural butorphanol tartrate. Thus, we concluded that epidural buprenorphine was a better option than epidural butorphanol for treating postoperative pain.

¹⁻⁵Department of Anaesthesiology, Burdwan Medical College, Bardhaman, West Bengal 713104, India

INTRODUCTION

Postoperative pain is becoming a serious concern as it can lead to several physiological and psychological problems. For this reason, early mobilization and surgical release depend on effective pain management. Narcotic analgesics are commonly used in epidural anesthesia^[1]. Numerous individuals view epidural injection of μ-receptor opioid agonists, such as morphine, as the "gold-standard" single-dose neuraxial opioid due to its prolonged duration of action and effective postoperative analgesic effect. But in addition to pruritus, it has undesirable side effects such nausea, vomiting, urine retention and respiratory depression. Buprenorphine is an opioid that functions as both an agonist and an antagonist at the μ and μ receptors. It is about 30 times more effective than morphine as an analgesic. Buprenorphine's strong affinity for opioid receptors accounts for its prolonged duration of actionButorphanol has partial agonist and antagonist activity at the μ -receptor and partial agonist and competitive antagonist activity at the? Receptor. Adenylate cyclase is intracellularly inhibited, inflow membrane calcium channels close and membrane potassium channels open in response to stimulation of these receptors on CNS neurons. Consequently, the cell membrane potential becomes hyperpolarized and the action potential transmission of the ascending pain pathways is blocked. In order to compare intrathecal buprenorphine and butorphenol's efficacy as adjuvants to hyperbaric levobupivacaine in spinal anesthesia for non-traumatic operations, this study was conducted. The study specifically sought to compare the onset and duration of sensory and motor blockage, as well as the length of effective analgesia during the post-operative period.

MATERIALS AND METHODS

Study Area: Burdwan Medical College and Hospital.

Study Design: Institution based observational prospective cohort study.

Study Period: February 2021 to august 2022.

Study Population: Individuals scheduled for surgery meeting the necessary requirements and admitted for lower abdominal surgeries in the general surgery, gynecological, or orthopaedic wards for lower limb surgery.

Sample Size:. 130.

Inclusion Criteria:

 American Society of Anaesthesiology (ASA) physical status 1 and 2

- Age 18 to 60 years both male and female sex
- BMI less 30 kg⁻¹ metre square

Exclusion Criteria:

- ASA physical status 3 and 4
- Patients with untreated bronchial asthma, COPD and obstructed sleep apnea
- Patients with decompensated cardiac disease and hypertension
- Patients with complicated Diabetes Mellitus like nephropathy, neuropathy
- Patient with any neurological disorder
- Patients with known hypersensitivity to the drugs
 Pregnant and lactating mothers
- Patients with history of low back ache 10.
 Pregnancy and lactation

Study Parameters:

- Onset and duration of sensory block
- Onset and duration of motor block
- Duration of postoperative analgesia
- No of rescue analgesics in first 24 hrs in postoperative period
- Heart rate
- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)
- Mean arterial pressure (MAP)
- Oxygen saturation

RESULTS

In Group D Magnesium Sulphate 3 (4.6%) patients had Bradycardia, 1 (1.5%) patient was Hypotension, 6 (9.2%) patients had Nausea, 1 (1.5%) patient was Shivering and 6 (9.2%) patients had Vomiting. In Group N Nalbuphine 3 (4.6%) patients had Bradycardia, 1 (1.5%) patient was Hypotension, 8 (12.3%) patients had Nausea, 1 (1.5%) patient was Shivering and 5 (7.7%) patients had Vomiting. Adverse Effect's relationship to the group was not statistically significant. (p = 0.9957). In Group D Magnesium Sulphate the mean Duration of Surgery (mean±sd) of patients was 98.1692±20.7097 In Group N Nalbuphine the mean Duration of Surgery (mean±sd) of patients was 97.2462±21.0558. The mean duration of surgery was not statistically significant in relation to the group (p = 0.8015). In Group D Magnesium Sulphate, the mean Onset of Sensory Block (mean±sd) of patients was 7.0592±1.2409 In Group N Nalbuphine the Onset of Sensory Block (mean±sd) of patients was 6.1438±1.1330

There was a statistically significant distribution in the mean Onset of Sensory Block with Group (p = <0.0001) In Group D Magnesium Sulphate, the mean Onset of Motor Block (mean \pm sd) of patients was 8.8477 \pm 1.2663. In Group N Nalbuphine the Onset of

Motor Block (mean±sd) of patients was 7.4115 ± 1.1079 The mean Onset of Motor Block distribution within the group was statistically significant (p = <0.0001)

DISCUSSIONS

This investigation was an observational prospective cohort research conducted within an institution. This study was carried out at Burdwan Medical College and Hospital between February 2021 and August 2022. In all, 130 patients were involved in this investigation.

Group D: 65 patients with Magnesium Sulphate **Group N:** 65 patients with Nalbuphine

Rabiee $et~al.^{[2]}$ showed that the mean age of case and control groups was 24.4±5.38 and 26.84±5.42 years, respectively. Diastolic blood pressure exhibited a substantial difference at the 15th and 60th min, however systolic blood pressure did not change significantly until the 45th min (p<0.001) and most of the patients were 21-30 years old [57 (43.8%)] but this was not statistically significant (p = 0.0604). In our study, Age was higher in Group N-Nalbuphine [34.0769±7.9614] compared to Group D Magnesium Sulphate [31.6154±8.9925] but this was not statistically significant (p = 0.1009).

We found that, male population was higher [81 (62.3%)] than the female population [49 (37.7%)]. Male: Female ratio was 1.6:1 but this was not statistically significant (p = 0.8563). Our study showed that, The majority of patients in Group D Magnesium Sulphate had Grade 1 [48 (73.8%)] compared to Group N- Nalbuphine [41 (63.1%)] however, this was statistically noteworthy (p = 0.1864).

Gupta et al. [3] found that, This study compared and assessed intrathecal dexmedetomidine and intrathecal buprenorphine as adjuvants to 0.5% hyperbaric bupivacaine for lower abdominal procedures, with a focus on subarachnoid blocking, hemodynamic stability and side effects. We observed that, A somewhat higher percentage of patients in Group D-Magnesium Sulfate-did not experience any adverse effects. [48 (73.8%)] compared to Group N-Nalbuphine [47 (72.3%)] however, this was not statistically significant (p = 0.9957).

Kaushal *et al.*^[4] found in After 90 min the maximal height of sensory block was reached by the patients in both groups. The mean heart rate and blood pressure of the buprenorphine and nallbuphine groups differed significantly. We found that, In Group D Magnesium Sulphate, height was higher. [159.5385±7.2974] compared to Group N Nalbuphine [159.3231±7.3103] however, there was no statistical significance (p = 0.8668). In our study, Weight was greater in the magnesium sulfate group (Group D). [66.6462±8.1210]

compared to Group N Nalbuphine [66.6000 ± 8.1390] however, there was no statistical significance (p = 0.9742). We found that, Surgery took longer in Group D (Magnesium Sulphate). [98.1692 ± 20.7097] compared to Group N Nalbuphine [97.2462 ± 21.0558] however, there was no statistical significance (p = 0.8015).

Dhawale *et al.*^[5] showed that The BF group experienced the earliest onset of sensory block (2.87 min), p<0.05. Goyal *et al.*^[6] observed that the time of onset of sensory block was 6.57±1.794 minutes in group IB, 2.30±1.343 minutes in group HB, and 4.57±1.960 minutes in group IL and This difference was very statistically significant (p<0.001).

In our study, Sensory Block Onset was greater in Group D (Magnesium Sulfate) [7.0592 ± 1.2409] compared to Group N Nalbuphine [6.1438 ± 1.1330] however, this was statistically noteworthy (p<0.0001). We found that, More of the motor block was in Group D, which is magnesium sulfate [8.8477 ± 1.2663] compared to Group N Nalbuphine [7.4115 ± 1.1079] however, this was statistically noteworthy (p<0.0001). In our study The Sensory Block Duration was longer in Group N Nalbuphine [224.0769 ± 35.9015] compared to Group D Magnesium Sulphate [222.1692 ± 21.3231] Nevertheless, this was not statistically significant with Group (p = 0.7132).

Nirmal *et al.*^[7] observed that in group RN, the duration of sensory analgesia and motor block was extended (p<0.001). We found that, the motor block duration was longer in Group D (Magnesium Sulphate) [179.7846 \pm 18.3085] compared to Group N Nalbuphine [168.6308 \pm 41.2366] however, this was statistically noteworthy (p = 0.0484).

Attri et al. [8] showed that in group LF the length of the sensory and motor block was noticeably longer (270.98±28.60 and 188.52±9.81 min) as compared to group L (197.58±11.20 and 152.76±9.79 min). In group LF the overall length of analgesia was also extended (265.16±26.18 min) as compared to group L (168.16±11.08 min). In our study, Analgesia lasted in Group D Magnesium Sulfate [257.8923±25.3433] compared to Group N Nalbuphine [265.4154±34.8590] however, there was no statistical significance (p = 0.1618). We found that, Group D Magnesium Sulphate had higher HR0 a [86.2615 ±10.2352] compared to Group N - Nalbuphine [84.3846±9.8198] however, there was no statistical significance (p = 0.2880). In our study, In Group D Magnesium HR5 Sulphate, was greater [81.7231±10.3509] compared to Group N Nalbuphine [80.4462±9.1173] however, there was no statistical significance (p = 0.4568). We found that, HR 10 was in Group Magnesium more D Sulphate [82.6923±7.0952] compared to Group N Nalbuphine [81.1385±5.9500] but this not statistically significant

Table 1: Association between adverse effects group

Group Adverse Effects Group D-magnesium sulphate Group N-nalbuphine Total Bradycardia 6 50.0 50.0 100.0 Row% Col% 4.6 4.6 4.6 Hypotension 50.0 100.0 Row% 50.0 Col % 1.5 1.5 1.5 Nausea 14 6 8 42.9 100.0 57.1 Row% Col% 9.2 10.8 12.3 Nil 48 47 95 50.5 100.0 Row% 49.5 Col% 73.8 72.3 73.1 Shivering 100.0 50.0 50.0 Row% 8.5 Col% 1.5 1.5 Vomiting 6 11 54.5 100.0 Row% 45.5 Col% 9.2 7.7 8.5 Total 65 65 130 50.0 Row% 50.0 100.0 Col% 100.0 100.0 100.0

Chi-square value: .3871; df: 5 p-value: 0.9957

Table 02: Distribution Of mean duration of surgery group

Number	Mean	SD	Minimum	Maximum	Median	p-value	T-statistic
Duration of surgery							
Group D-magnesium sulphate	65	98.1692	20.7097	60.0000	150.0000	100.0000	
							0.2520
Group N-Nalbuphine	65	97.2462	21.0558	60.0000	150.0000	100.0000	

Table 3: Distribution of mean onset of se	ensory block group							
Onset of sensory block	Number	Mean	SD	Minimum	Maximum	Median	p-value	T-statistic
Group D-magnesium sulphate	65	7.0592	1.2409	5.0000	10.0000	7.0000	< 0.0001	4.3920
Group N-Nalhuphine	65	6 1438	1 1330	4 0000	9 0000	6 0000		

Table 4: Distribution of mean onset of r	motor block group							
Onset of motor block	Number	Mean	SD	Minimum	Maximum	Median	p-value	T-statistic
Group D-magnesium Sulphate	65	8.8477	1.2663	7.0000	12.0000	9.0000	< 0.0001	6.8817
Group N. palbuphing	6E	7 /11 [1 1070	E 0000	10 0000	7 2500		

(p = 0.1785). In our study, HR20 was higher in Group D Magnesium Sulphate [81.8769 \pm 6.4699] compared to Group N Nalbuphine [80.1846 \pm 5.9105] but this was not statistically significant (p = 0.1220). We found that, HR30 was more in Group D Magnesium Sulphate [82.2769 \pm 9.4265] compared to Group N Nalbuphine [81.9077 \pm 4.5884] but this was not statistically significant (p = 0.7769). In our study, HR 45 was higher in Group D Magnesium Sulphate [83.2462 \pm 6.3567] compared to Group N Nalbuphine [81.0154 \pm 6.6438] but this was not statistically significant (p = 0.0526). We found that, HR60 was more in Group D Magnesium Sulphate [83.6923 \pm 5.0557] compared to Group N Nalbuphine [82.3846 \pm 4.4885] but this was not statistically significant (p = 0.1214) $^{[9-11]}$.

In our study, HR90 was higher in Group D Magnesium Sulphate [82.5538±4.3733] compared to Group N Nalbuphine [82.2462±5.2053] but this was not statistically significant (p = 0.7158). We found that, SBPO was more in Group N Nalbuphine [130.9077±8.4553] compared to Group D Magnesium Sulphate [129.4923±9.3293] but this was not statistically significant (p = 0.3665). In our study, SBP

10 was higher in Group D Magnesium Sulphate [125.4615 \pm 8.2312] compared to Group N Nalbuphine [122.6615 \pm 7.3724] but this was statistically significant (p = 0.0431)^[12-19].

We found that, SBP20 was more in Group D Magnesium Sulphate [126.1231 ± 6.4699] compared to Group N Nalbuphine [122.0615 ± 8.3589] but this was statistically significant (p=0.0024). In our study, SBP30 was higher in Group N Nalbuphine [126.4462 ± 6.4760] compared to Group D Magnesium Sulphate [124.5231 ± 5.7666] but this was not statistically significant (p=0.0761). We found that, SBP 45 was more in Group D Magnesium Sulphate [126.3385 ± 7.6695] compared to Group N Nalbuphine [124.5385 ± 5.9505] but this was not statistically significant (p=0.1374).

In our study, SBP60 was higher in Group N Nalbuphine [126.3231±4.5795] compared to Group D Magnesium Sulphate [125.1538±6.6385] but this was not statistically significant (p = 0.2446). We found that, DBP 0 of Surgery was more in Group D Magnesium Sulphate [82.9385±7.1324] compared to Group N Nalbuphine [76.2000±6.9174] but this was statistically

significant (p<0.0001). In our study, DBP 10 was higher in Group D Magnesium Sulphate [81.3538±6.8862] compared to Group N Nalbuphine [73.9538±6.1427] but this was statistically significant (p<0.0001).

We found that, DBP20 was more in Group D Magnesium Sulphate [79.6769 \pm 6.9734] compared to Group N Nalbuphine [78.8615 \pm 4.1903] but this was not statistically significant (p = 0.4206). In our study, DBP 30 was higher in Group D Magnesium Sulphate [78.2923 \pm 4.1823] compared to Group N Nalbuphine [78.1692 \pm 4.0061] but this with Group was not statistically significant (p = 0.8642). We found that, DBP 45 was more in Group N Nalbuphine [77.1538 \pm 4.3454] compared to Group D - Magnesium Sulphate [75.3692 \pm 5.2873] but this was statistically significant (p= 0.0375).

In our study, DBP60 was higher in Group N Nalbuphine $[74.4769\pm2.5987]$ compared to Group D Magnesium $[73.5692\pm4.8669]$ but this was not statistically significant (p=0.1871). We found that, MAP0 was more in Group D Magnesium Sulphate $[98.4564\pm6.3181]$ compared to Group N Nalbuphine $[94.4359\pm5.4750]$ but this was statistically significant (p=0.0002). In our study, MAP10 was higher in Group D Magnesium Sulphate $[96.0564\pm5.5373]$ compared to Group N Nalbuphine $[90.1897\pm4.9746]$ but this was statistically significant (p<0.0001).

We found that, MAP 20 was more in Group D Magnesium Sulphate [95.1590 \pm 5.1751] compared to Group N Nalbuphine [93.2615 \pm 4.4412] but this was statistically significant (p = 0.0266). In our study, MAP 30 was higher in Group N Nalbuphine [94.3436 \pm 3.6846] compared to Group D Magnesium [93.6205 \pm 3.3577] but this was not statistically significant (p = 0.2444). We found that, MAP 45 was more in Group N Nalbuphine [92.9487 \pm 3.4051] compared to Group D Magnesium Sulphate [92.3590 \pm 3.9993] but this was not statistically significant (p = 0.3670).

In our study, MAP60 was higher in Group N Nalbuphine [91.7590 \pm 2.5080] compared to Group D Magnesium Sulphate [90.7641 \pm 3.3576] but this was not statistically significant (p = 0.0579). We found that, SP0 20 was more in Group D Magnesium Sulphate [99.8923 \pm 3590] compared to Group N Nalbuphine [99.8769 \pm 3753] but this not statistically significant (p = 0.8116). In our study, SPO2 20 was higher in Group D Magnesium Sulphate [99.7231 \pm .5997] compared to Group N Nalbuphine [99.7538 \pm .5599] but this was not statistically significant (p = 0.7629).

We found that, SPO 2 30 was more in Group N Nalbuphine [99.8154 \pm .4291] compared to Group D Magnesium Sulphate [99.8000 \pm .4402] but this was not statistically significant (p = 0.8404). In our study, SPO2 45 was higher in Group N Nalbuphine [99.8923 \pm .3590] compared to Group D Magnesium Sulphate

[99.8000 \pm .4743] but this was not statistically significant (p = 0.2132). We found that, SPO2 60 was less in Group D Magnesium Sulphate [99.7538 \pm .5599] compared to Group N Nalbuphine [99.8154 \pm .4641] but this was not statistically significant (p = .4641)

We found that, equal number of patient had SPO2 90 but this was not statistically significant (p= 1.0000) Ravindran $et\ al.$ [9] found that the VAS score and the need for rescue analgesics were considerably lower in the buprenorphine groups. No major side effects were observed. In our study, Group D-Magnesium Sulfate had a higher Vas Score throughout the first hour [.8769 \pm .3311] compared to Group N-Nalbuphine [.8308 \pm .3779] however, there was no statistical significanc. (p = 0.4603). We found that, 1 hr Vas Score was higher in Group D Magnesium Sulfate [.8769 \pm .3311] compared to Group N Nalbuphine [.8308 \pm .3779] yet (p = 0.4603), this did not seem to be statistically significant.

In our study, Within Group D-Magnesium Sulphate, Vas 2nd Hrs was greater. [$1.9846\pm.4143$] compared to Group N-Nalbuphine [$1.8308\pm.3779$] However, this was statistically significant (p = 0.0287) with Group.

CONCLUSION

Epidurally given butorphanol tartrate and buprenorphine can provide safe and effective postoperative analgesia. On the other hand, epidural buprenorphine significantly reduced pain and enhanced the quality of analgesia with a longer duration of impact than epidural butorphanol tartrate. Thus, we concluded that epidural buprenorphine was a better option than epidural butorphanol for treating postoperative pain.

REFERENCES

- Moore, K.,L. and A.F Dalley, 2015. Aradiginiz Tüm Tip Kitaplari. Nobel. Tip. Kitabevleri., Vol. 1136.
- 2. William, M.,R. and L.M. Newell, 2005. Aradiginiz Tüm Tip Kitaplari. 39th Edn., Elsevier Churchill Livingstone, London, UK, Pages: 746.
- 3. J. Bone. Joint. Surg. B., 1997. Variation of the groove in the axis vertebra for the vertebral artery. J. Bone. Joint. Surg. Br., 79: 820-823.
- 4. Korres, D.S., 2013. Fractures of the odontoid process. In: The axis vertebra., Korres, D.S., (Ed.)., Berlin, Verlag, pp: 45-59.
- 5. Akobo, S., E. Rizk, M. Loukas, J.R. Chapman, R.J. Oskouian and R.S. Tubbs, 2015. The odontoid process: A comprehensive review of its anatomy, embryology, and variations. Child's. Nervous. Syst., 31: 2025-2034.
- Cramer, G.D., 2014. The Cervical Region. In: Clinical Anatomy of the Spine, Spinal Cord and Ans., Cramer, G., D and S.A. Darby, (Eds.)., St. Louis, Mosby, pp: 135-209.

- 7. Böhler, J., 1982. Anterior stabilization for acute fractures and non-unions of the dens. J. Bone. Joint. Surg. Am., 64: 18-27.
- 8. Bednar, D.,A. and J. Parikh, 1995. Management of type II odontoid process fractures in geriatric patients; a prospective study of sequential cohorts with attention to survivorship. J. Spinal. Disord., 1: 166-169.
- 9. Henry, A.,D.J. Bohly, 1999. Fixation of odontoid fractures by an anterior screw. J. Bone. Joint. Surg. Br., 81: 472-477.
- Cloché, T. and J.M. Vital, 2016. Chirurgie des traumatismes récents du rachis cer vical. EMC-Techniques chirurgicales. Orthop. Traumatol., 11: 1-28.
- 11. Doherty, B.J. and M.H. Heggeness, 1995. Quantitative anatomy of the second cervical vertebra. Spine., 20: 513-517.
- 12. Sengul, G. and H.H. Kodiglu, 2006. Morphometric anatomy of atlas and axis vertebra. Turk. neur. surg., 16: 69-76.
- 13. Xu, R., M.C. Nadaud, N.A. Ebraheim and R.A. Yeasting, 1995. Morphology of the second cervical vertebra and the posterior projection of the c2 pedicle axis. Spine., 20: 259-263.
- 14. Naderi, S. and C. Arman, 2006. Morphometric analysis of the C2 body and the odontoid process. Turk. Neur. surg., 16: 14-18.

- 15. Gosavi, S. and V. Swamy, 2012. Morphometric anatomy of the axis vertebra. Eur. J. Anat., 16: 98-103.
- 16. Singla, M., 2015. Morphometric analysis of axis and its clinical significance -an anatomical study of Indian human axis vertebrae. j. Clin diagno res., 9⋅4-9
- 17. EC, T., 2017. Morphometric analysis of human second cervical vertebrae (axis). J. Spine., 6: 1-7.
- 18. Yousuf, S.M., S. Gulzar, M.S. Itoo and M.A. Khan, 2023. Morphometeric study of dens and its clinical importance. Int. J. Res. Med. Sci., 11: 1268-1271.
- Daher, M.T., S. Daher, M.H. Nogueira-Barbosa and H.L.A. Defino, 2011. Computed tomographic evaluation of odontoid process: Implications for anterior screw fixation of odontoid fractures in an adult population. Eur. Spine J., 20: 1908-1914.