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**POOLED ANALYSIS OF RANDOMIZED TRIALS OF EPIDURAL VS. OPIOID ANALGESIA ON THE RISK OF CESAREAN SECTION**

*Segal, S.[1] Su, M.[2]* 1. Brigham and Women's Hospital, Harvard Medical School, Boston, MA; 2. Harvard School of Public Health, Boston, MA

Ten trials have randomized laboring women to epidural analgesia or parenteral opioids to analyze the effect of regional anesthesia on the risk of cesarean section. Unfortunately, protocol noncompliance has been a consistent methodological shortcoming. Although intent-to-treat analysis is technically the correct way to analyze such trials, power is markedly reduced when 1/3 of the subjects fail to receive their assigned treatment. We attempted to compensate for the low effective power of the individual studies by performing a pooled analysis, in which the subjects from the various trials were combined as if they had all participated in a single multicenter study. We utilized the method of Friedenreich (1) to combine the results of all published studies, supplementing the results with additional data provided by the authors when possible. The results were tested for homogeneity across studies with the Breslow-Day test. The odds ratio (OR) and 95% confidence interval (CI) for the risk of cesarean section were calculated by the Mantel-Haenszel (M-H) chi-square test and confirmed with logistic regression in which the individual study was treated as a fixed-effect covariate. Power was calculated for the pooled results by both standard formulas on the total pooled sample as well as a more conservative method applied to the M-H test. The results showed the component studies to be homogeneous, allowing a pooled analysis of the data. The simple OR for the effect of epidural analgesia on C/S from pooling the data for all 10 studies was 0.9839. The M-H estimate of OR was virtually identical, 0.9841 with 95% confidence interval (0.8116, 1.193). Logistic regression with an indicator variable for "study" also found similar results, with an OR of 0.984 (0.811, 1.193). Together these three estimates indicate no increased risk of C/S in patients randomized to epidural analgesia. The power of the pooled sample was nearly 90% to detect an OR of at least 1.4 and 99% to detect an OR of 1.6 (difference of 37.5 and 50% in C/S rates, respectively). We conclude that when analyzed as a large pooled sample (N=5611), it is possible to conclude with a high degree of certainty that epidural analgesia does not increase the risk of cesarean section. This finding should help answer the remaining criticism of these randomized trials, namely that protocol noncompliance renders them difficult to interpret. Our study adds to the evidence provided by individual trials and meta-analyses, by compensating for protocol noncompliance and increasing effective power.

*1. Friedenreich CM. Methods for pooled analyses of epidemiologic studies. Epidemiology. 1993;4:295-302.*

## P-52

**EFFECT OF LOW DOSE MOBILE VERSUS HIGH DOSE EPIDURAL TECHNIQUES ON THE PROGRESS OF LABOR:A META-ANALYSIS**

*Angle, P. Halpern, S.; Morgan, A. Anesthesia, Sunnybrook & Womens College HSC, Toronto, ON, Canada*

Epidural analgesia has been associated with a higher incidence of instrumental delivery compared with intravenous opioids(1).This meta-analysis examined the impact of low vs high dose neuraxial analgesia on mode of delivery with the primary outcome being the odds of instrumental delivery.Secondary outcomes included:maternal hypotension;pruritus;nausea;and neonatal APGAR scores <7 at 5minutes.We identified relevant RCTs using independent searches of computerized databases(PreMEDLINE,MEDLINE-,HealthSTAR,EMBASE,Cochrane Library,Dissertation Abstracts on Disk)from 1980-December 4,2001 using all languages and limited to human only.MeSH/text terms used included:epidural;analgesia;obstetric;labor; combined spinal epidural;mobile and bupivacaine.References of retrieved articles,relevant book chapters,high impact journals,abstracts of major conferences,and publications of authors of major articles were searched. Selected researchers were contacted to locate unpublished studies."Low dose mobile"(LD)was defined a priori to mean any low dose initiation(CSE(of any type) or epidural loaded with a solution containing bupivacaine <0.125%)) followed by a LD maintenance solution containing bupivacaine <0.125%. "High dose"(HD-)was defined as initiation and maintenance of analgesia with a solution including bupivacaine >/=0.125%. We included all RCTs comparing LD vs HD labor analgesia,mode of delivery and use of bupivacaine as the sole local anesthetic.Study quality was assessed with a 5 point validated scale. 2 reviewers independently assessed study relevance-,quality and performed data extraction.Agreement was assessed using an unweighted Cohen's kappa and differences resolved by re-review of the article and consensus. Four trials(2-5)enrolling 2092 patients were found.Statistical heterogeneity was not significant.Pooled Odds Ratios(OR)for categorical data and 95%confidence intervals(CI)were calculated using a random-effects model.Results are in the table.The odds of instrumental delivery was significantly reduced in the low dose group-,coinciding with increased odds of spontaneous vaginal delivery in this group and no difference in risk of cesarean section.The LD group was more likely to have pruritus.No differences were found in hypotension,nausea or neonatal APGAR scores.

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| Outcome | Low Dose n/N | High Dose n/N | OR(95%CI) | p value |
|---|---|---|---|---|
| Instrum. delivery | 371/1344 | 268/748 | 0.69(0.53,0.92 | 0.01* |
| SVD | 665/1344 | 323/748 | 1.3(1.1,1.6) | 0.003* |
| C/Section | 308/1344 | 157/748 | 1.1(0.86,1.3) | 0.51 |
| Pruritus | 261/589 | 23/342 | 10.39 (6.6,16.4) | 0.00* |
| Nausea | 17/589 | 10/342 | 1.2(0.52,2.9) | 0.65 |
| Decreased BP | 20/589 | 11/340 | 1.63(0.75,3.6) | 0.22 |
| 5min Apgar <7 | 2/1303 | 5/708 | 1.83(0.72,4.6) | 0.20 |