

Incidence of Epidural Hematoma, Infection, and Neurologic Injury in Obstetric Patients with Epidural Analgesia/Anesthesia

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Of the 4 million annual births in the United States, 2.4 million involve epidural analgesia. Serious adverse events are rare but are important in young women. Robust estimates for the risk of harm are not available. Data for superficial and deep infections, hematoma, and transient and permanent neurologic injury were obtained from studies reporting adverse events with obstetric epidural analgesia, and incidence presented as individual risk for a woman, number of events per million women, and percentage incidence. A total of 1.37 million women received an epidural for childbirth, reported in 27 articles. Most information (85% of women) was in larger (> 10,000 women) studies published after 1990, with risk estimates as follows: epidural hematoma, 1 in 168,000; deep epidural infection, 1 in 145,000; persistent neurologic injury, 1 in 240,000; and transient neurologic injury, 1 in 6,700. Earlier and smaller studies produced significantly higher risk estimates for transient neurologic injury plus injury of unknown duration.

IN 2003, there were more than 4 million births in the United States.¶ An increasing number of women choose an epidural, usually a lumbar epidural catheter, to alleviate labor pain. The obstetric anesthesia workforce sur-

vey¹ showed that approximately 60% of women in the United States giving birth in larger hospitals (> 1,500 births a year) have an epidural; this number decreases to 42% in smaller hospitals (100-500 births). Approximately 2.4 million women a year have an epidural for childbirth. In the United Kingdom, the epidural rate is approximately 35%; in Canada, it is 45%#; and in France in 1996, it was 51%,¹ although it is difficult to obtain exact figures.

Although epidural analgesia and anesthesia is generally safe, serious adverse events can occur. Because of the large number of healthy young women having epidurals during labor, even rare adverse events are important, especially if they are serious. Any negative impact on quality of life, together with the economic costs of a serious adverse event, is especially important in this patient group.

The aim of this meta-analysis was to estimate the incidence of rare but serious problems occurring with epidural analgesia in obstetric practice, namely epidural hematoma, epidural infection, and persistent and transient neurologic injuries.

Materials and Methods

We searched PubMed (from 1966), EMBASE (from 1980), and MEDLINE (from 1966) to February 2005, with no restrictions on language or type of study (detailed search strategy in supplementary file 1, available on the ANESTHESIOLOGY Web site at <http://www.anesthesiology.org>). Five journals (ANESTHESIOLOGY, *Anesthesia & Analgesia*, *British Journal of Anesthesia*, *Anesthesia*, and *Acta Anaesthesiologica Scandinavica*) were hand-searched from mid-1999 to 2005. Reference lists were checked for additional studies (fig. 1).

Full paper copies were obtained for all studies not eliminated after reading title and abstract. We then selected those reporting on at least 200 obstetric patients, with numerical data for serious adverse effects such as hematoma, infection, and neurologic injuries. We took definitions of adverse events as described by the authors of the individual studies. For infections, we were interested in both superficial infections (e.g., skin infection around the catheter site) and deep infections (in the epidural space). For neurologic injuries, we were interested in those that were transient (resolved within 1 yr) and persistent (not resolved within 1 yr). Persistence of neurologic deficit was

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¶ Service USDoHH: United States birth rate reaches record low. 2003. Available at: <http://pregnancyabout.com/gi/dynamic/offsitehtm?site=http://www.whsgov/news/press/2003pres/20030625html>. Accessed September 23, 2005.

Information Cliff: A regional profile, Giving Birth in Canada. 2004. Available at: <http://dsp-psd.pwgsc.gc.ca/Collection/H118-25-2004E.pdf>. Accessed October 1, 2005.

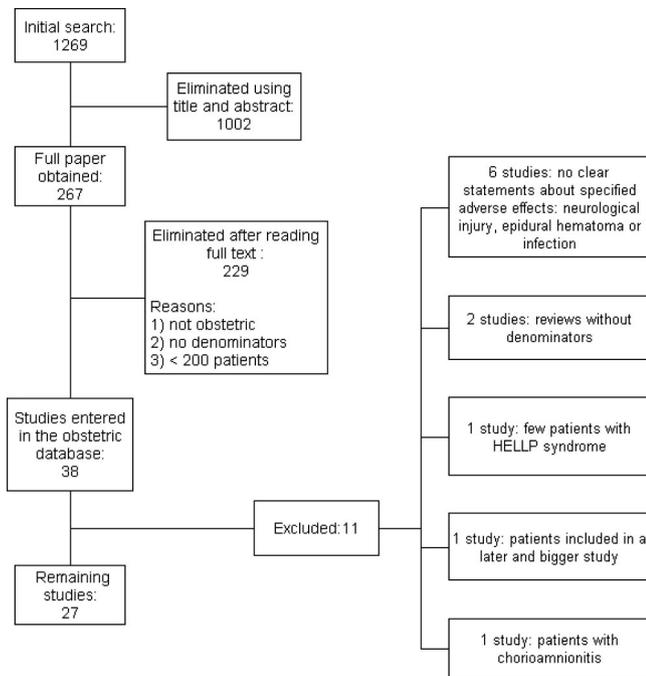


Fig. 1. Flow diagram of selection of studies for inclusion for data analysis. HELLP = hemolysis, elevated liver, low platelet.

likely to be a proxy for seriousness, which we also looked for.

Information about the type of study, patients, intervention, and numbers of patients experiencing individual adverse outcomes was tabulated. We did not use quality-scoring systems. QUOROM (Quality of Reporting of Meta-analyses) guidelines were followed where applicable. For these calculations, a study was included only if it mentioned that an adverse event was present or definitely not present; studies not mentioning the adverse event were omitted from that particular calculation. We planned to perform sensitivity analyses for larger ($> 10,000$ women) *versus* smaller studies and for older (published before 1990) *versus* recent studies. In sensitivity analyses, relative risk was calculated with 95% confidence intervals using a fixed effects model,² with no statistically significant difference assumed when the 95% confidence interval included unity.

It was our previous intent to present the information on rare events in several ways: the risk to an individual woman as odds, the number of events per million women, and percent of women with the complication. In addition, we sought to present information on the annual incidence of these events for several countries, based on number of live births and estimates of epidural rates.

Results

We identified a large number of articles (1,269), with an eventual list of 267 articles relating to epidural com-

plications. Thirty-eight related to obstetrics, of which 11 (references in supplementary file 2, available on the ANESTHESIOLOGY Web site at <http://www.anesthesiology.org>) were excluded (fig. 1). Of the 27 included, only 5 studies (19% of studies, 37% of women) were identified by electronic searches, 2 (7%, 0.1%) were identified by hand searching, and 20 (74%, 63%) were identified by examination of reference lists and reviews.

The 27 articles³⁻²⁹ reported on 1.37 million women having an epidural for childbirth (supplementary file 3 contains details of patients, study design, and detailed results, available on the ANESTHESIOLOGY Web site at <http://www.anesthesiology.org>). Eleven studies^{6,9,13,14,19,22-24,26-28} with 1.31 million women in all each reported on more than 10,000 women (range, 10,995-506,000). Sixteen^{4-6,8,11,12,14,17-19,22-24,26,27,29} with 1.19 million women were published after 1990. The 7 larger post-1990 studies^{6,14,19,22,23,26,27} had 1.16 million women, 85% of the total.

Two randomized trials^{8,11} had information on 3,330 women, 7 prospective cohorts^{4,6,7,14,18,22,24} had information on 58,945 women, 18 retrospective cohorts^{5,9,10,12,13,15-21,23,25-29} had information on 1,304,817 women, and 1 cohort¹⁷ (4,162 women) combined both prospective and retrospective information. One article³ reported prospective and retrospective information separately. Twenty prospective and retrospective cohorts were based either on a population or on a consecutive series without selection, while the remaining 5 cohort studies^{6,9,12,14,18} (10,126 women) made no statement about avoiding selection.

Epidural Hematoma

Eight studies^{5,8,12,19,22,23,25,26} with 1.1 million women reported a total of six epidural hematomas (table 1), with one²⁵ (80,000 women) published before 1990. All six hematomas were reported in three large studies,^{19,23,26} each of at least 200,000 women and reported since 1990. For no case was any clear outcome described. The overall rate of epidural hematoma was 1 in 183,000 women, or 5 per million. Rates in larger post-1990 studies were 1 in 168,000 women, or 6 per million (table 1).

Epidural Infection

Only two studies^{4,16} (1,294 women) reported on superficial infection stating no events. Eleven cases of deep epidural infection were reported in 13 studies^{4-6,9,10,14,16,17,19,22,23,26,27} with 1.2 million women (table 1). For none of these events was there clear description of the clinical consequences. The overall rate of deep infection was 1 in 110,000 women, or 9 per million. Rates in larger post-1990 studies were 1 in 145,000 women, or 7 per million.

Table 1. Event Rates for Complications

Outcome	Data Source	Number of			Percent	Individual Risk, 1 in	Per Million Number
		Studies	Patients	Events			
Epidural hematoma	All studies	8	1,100,299	6	0.00055	183,383	5
	Larger, more recent studies	4	1,010,346	6	0.00059	168,391	6
Deep epidural infection	All studies	13	1,208,698	11	0.00091	109,882	9
	Larger, more recent studies	7	1,161,218	8	0.00069	145,152	7
Persistent neurologic injury	All studies	9	770,938	3	0.00039	256,979	4
	Larger, more recent studies	2	711,000	3	0.00042	237,000	4
Transient neurologic injury	All studies	15	987,218	254	0.02573	3,887	257
	Larger, more recent studies	3	902,484	163	0.01800	5,537	180
Transient + unknown injury	All studies	21	1,250,718	288	0.02303	4,343	230
	Larger, more recent studies	7	1,150,223	172	0.01500	6,690	150

Larger studies had more than 10,000 women, and more recent studies were published during or after 1990.

Persistent Neurologic Injury

Nine studies with 770,000 women^{3,5,11,13,19,20,24,26,28} reported three cases of persistent neurologic injury (table 1). None of these was clearly related to epidural hematoma or epidural infection. The overall rate of persistent neurologic injury was 1 in 257,000 women, or 4 per million. Rates in larger post-1990 studies were 1 in 237,000 women, or 4 per million.

Transient Neurologic Injury

Fifteen studies^{3,7,9-11,15,16,20,21,23,24,26-29} with 987,000 women reported 254 cases of transient neurologic injury lasting less than 1 yr (table 1). Definitions of neurologic damage were not always clear; in almost all cases, only symptoms were described, without any link between the injury and either epidural or childbirth. The overall rate of transient neurologic injury was 1 in 3,900 women, or 257 per million. Rates in larger post-1990 studies were 1 in 5,537, or 180 per million.

Transient Neurologic Injury plus Injury of Unknown Duration

Six studies^{6,9,14,18,19,22} with 290,000 women reported 34 neurologic injuries of unspecified duration. Because it is probable that these were transient, we analyzed them together with known transient injuries (table 1). Combining the information on 1,250,000 women in 20 studies, the overall rate of transient neurologic injury or injury of unknown duration was 1 in 4,300 women, or 230 per million. Rates in larger post-1990 studies were 1 in 6,700 women, or 150 per million. Using only these newer, larger studies with 92% of all the women studied produced a significantly lower estimate for the event rate than all data combined, with a relative risk of 0.65 (0.54-0.78).

Sensitivity Analysis

We performed sensitivity analysis only for transient neurologic injury or injury of unknown duration because this had the largest number of events. In individual

studies, rates of transient neurologic injury or injury of unknown duration were as low as 1 per million and as high as 1,000 per million (fig. 2). Predictably, most of the variability was in the small studies, and the largest were close to the overall average. Eleven smaller studies (< 10,000 women)^{3,7,10,11,15,16,18,20,21,24,29} recorded 111 events in 48,059 women, or 2,300 per million. Nine larger studies (> 10,000 women)^{6,9,14,19,22,23,26-28} recorded 177 events in 1,202,659 women, or 150 per million. Larger studies gave a significantly lower rate of transient neurologic injuries plus injuries of unknown duration than did smaller studies, with a relative risk of 0.06 (95% confidence interval, 0.05-0.08), a 15-fold difference.

Nine studies published before 1990^{3,7,9,10,15,16,20,21,28} reported 72 events in 88,182 women, 820 per million. Eleven studies published after 1990^{6,11,14,18,19,22-24,26,27,29} reported 217 events in 1,173,531 women, 190 per million. Post-1990 studies gave a significantly lower rate of transient neurologic injuries plus injuries of unknown

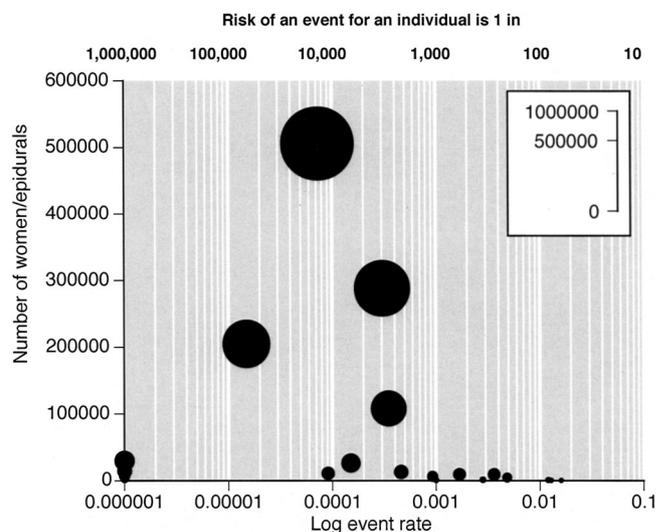


Fig. 2. Risk of temporary neurologic outcome, or a neurologic outcome of unknown duration in individual studies (size of circle is proportional to size of study, inset scale).

duration than did earlier studies, with a relative risk of 0.23 (0.17–0.30), a fourfold difference.

Discussion

Pregnant women are usually young and healthy, and the expectation is that modern childbirth is relatively safe for mother and baby. Any intervention in childbirth, for example, to provide good analgesia, should carry minimal risk. Rare but serious adverse events are important in this circumstance.

To calculate the incidence of rare adverse events requires large numbers of patients. Rare adverse events are more likely to be identified in large observational studies than in small randomized trials. These observational studies should report on a whole obstetric population to eliminate selection bias.

This analysis sought studies reporting adverse events of various sorts associated with the use of epidural analgesia in obstetrics. It found 27 studies with 1.4 million women, compared with a previous review containing 11 studies and 681,000 women.³⁰ Almost all of the studies were prospective or retrospective cohorts, with only 10,000 of 1.4 million women (0.07%) in 5 studies that were not identified clearly as unselected population cohorts or randomized trials. Almost all of the information (85% of women studied) was in the larger post-1990 studies. For transient neurologic injury plus neurologic injury of unknown duration, there were sufficient numbers of events for sensitivity analyses. Smaller studies (< 10,000 women) compared with larger ones, and older studies (before 1990) compared with newer ones, overestimated adverse events by 15- and 4-fold, respectively.

Only 6 epidural hematomas, 11 deep epidural infections, and 3 persistent neurologic injuries were reported. This is inadequate to produce a robust estimate of event rates; 95% confidence intervals were 1–11 per million for epidural hematoma, 2–12 per million for deep epidural infection, and 0–8 per million for persistent neurologic injury. More events, perhaps 25–50, would be needed to narrow these confidence intervals, implying studying 6 million to 12 million women for a robust estimate for persistent neurologic injury. Since our searches in February 2005, one further prospective study of cesarean delivery³¹ found no cases of epidural hematoma or infection among 15,443 women having an epidural.

The risk associated with these adverse outcomes was calculated and presented in different ways (table 1). The use of several different ways of conveying information about rare adverse events is important, because we know that individuals overestimate risk when presented verbally by up to 400-fold.³²

These event rates can be used to estimate the likely burden for a whole country, depending on the number of live births and the use of epidural analgesia in obstet-

rics. We obtained estimates for number of births and epidural rates for the United States, Canada, United Kingdom, France, and Switzerland. Using realistic figures for epidural rates, and the overall rates of adverse events, the impact was as high as nine cases of persistent neurologic injury in the United States per year, to one every 10 yr in Switzerland (table 2). Such calculations may be of use in developing guidance or critical incident reporting rules. For rare events, even the largest hospital would be unlikely to see one in a decade.

Transient neurologic injuries resolving within 1 yr were more common. Although few of these could clearly be linked unequivocally with the epidural, they occurred in 1 in 4,300 women. This rate could be inflated by small studies, because larger studies had lower event rates (fig. 2).

Neurologic deficits after childbirth may have many causes, and all of these rare adverse events could occur spontaneously or because of childbirth.^{3,21,33–38} Lack of evidence of causation is a weakness of this study, because in almost no case was there a definite link between the adverse event and the epidural. Usubiaga³⁹ reported several cases in which epidurals were unjustifiably linked to harm in nonobstetric cases. Murray⁴⁰ reported 95 cases with neurologic damage in obstetrics with and without epidurals. He found that 85% of cases of neurologic damage occurred with forceps delivery. Doblar and Schumacher⁴¹ report one case of spontaneous epidural hematoma, as well as six other reports of spontaneous epidural hematoma during pregnancy, all with some neurologic symptoms. Male and Martin⁴² and Kitching and Rice⁴³ reported spontaneous puerperal spinal epidural abscesses without epidural anesthesia.

There are other potential weaknesses. Searching for observational studies is not as simple as for randomized trials. Lemeshow *et al.*⁴⁴ found that searching in only one database yielded only 60–80% of relevant observational studies, and here, searching several electronic databases with a comprehensive search strategy yielded only 5 of 27 studies (18%). Most of the studies were found from reference lists and review articles. Whether this is a special case cannot be known, but the finding has implications for adverse event research. Serious adverse events may also be underreported. Cultural, social, and legal considerations, especially relating to epidurals and childbirth, might also restrict reporting in the medical literature.

This analysis used transient, less than 1 yr, and permanent, more than 1 yr, to categorize neurologic damage. Although time is clearly important, the seriousness of the damage, on a spectrum of pathology from skin numbness through to paraplegia, should also be borne in mind. We were unable to report on seriousness.

Several questions could not be answered by this review. We found no information about risk factors for adverse events, or information linking events such as

Table 2. Calculations for Different Countries

Outcome	United States	Canada	United Kingdom	France	Switzerland
Births per year	4,019,280	330,000	646,000	761,464	72,905
Epidural rate, % births	59	45	35	51	40
Number of injuries per country per year					
Epidural hematoma	13	1	1	2	0.2
Deep epidural infection	22	1	2	4	0.3
Persistent neurologic injury	9	1	1	2	0.1
Transient neurologic injury	603	50	98	114	11

For individual countries, information is from:

United States:

Service USDoHH: U.S. birth rate reaches record low. Available at: http://pregnancyabout.com/gi/dynamic/offsitehtm?site=http://www.hhs.gov/news/press/2005oct01_1, 2005.

Declercq E, Sakala C, Corry M, Applebaum S, Risher P: Listening to mothers: Report of the First National U.S. Survey of Women's Childbearing Experiences. Available at: www.maternitywise.org/pdfs/LtMreportpdf.2002.3pres/20030625html. Accessed October 1, 2005.

Canada:

Information CifH: A regional profile, Giving Birth in Canada. 2005. Available at: <http://dsp-psd.pwgsc.gc.ca/Collection/H118-22-2004E.pdf>. Accessed October 1, 2005.

United Kingdom:

UNICEF: UNICEF Website UK. 2003. Available at: http://www.unicef.org/infobycountry/uk_statistics.html. Accessed October 1, 2005.

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France:

France in facts and figures. 2005. Available at: http://www.insee.fr/en/ffc/chifcle_fiche.asp?ref_id=NATTEF02133&tab_id=237. Accessed October 1, 2005.

*Clergue et al.*¹

Switzerland:

Bundesamt für Statistik. Statistik Schweiz: Birth rate Switzerland 2002. 2004. Available at: http://www.bfs.admin.ch/bfs/portal/de/index/themen/bevoelkerung/stand_u_struktur/blank/kennzahlen0/natuerliche_bevoelkerungsbewegung/gebuerden.html. Accessed October 1, 2005.

Markus Schneider, M.D., personal communication by electronic mail, June 2005. Basel approximately 43%; Geneva about 80%. 40% is assumed.

epidural hematoma or infection to neurologic injury. The types of study sought were unlikely to provide this information, which is more likely to be found in case reports. There was also no information about the clinical consequences of these adverse events, although in studies not restricted to obstetric populations, complete recovery was achieved in only 40% of 561 cases of spinal hematoma,⁴⁵ and a good outcome occurred in 26 of 40 patients with an epidural abscess.⁴⁶

Finally, our results relate only to childbirth. Different results might be expected in older patients with epidurals for a short period for surgical procedures, or patients with long-term epidurals for chronic pain relief. Clinicians should be aware of the possibility of serious complications of epidural analgesia in obstetrics, however rare. We provide best available estimates for some serious adverse events.

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