Editorial Comment

Harald Breivik and Mads U. Werner

Risk for persistent post-delivery pain – increased by pre-pregnancy pain and depression. Similar to persistent post-surgical pain in general?

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Persistent pain after surgery or trauma is a major health problem, also after Caesarian delivery [1]. There are various understandings of how long after an operation a new pain should last before it is more than pain due to a normal, but slow rehabilitation after surgery. Any duration from 6 weeks and up to 12 months has been called persistent post-surgical pain or post-delivery pain [1, 2]. This is one reason for the highly variable outcomes in study-reports of this burdensome clinical and psychosocial problem; another is the lack of information on the severity and burden of post-surgical pain. However, the definition by Mads U. Werner and Ulf E. Kongsgaard [3] is helpful and is now in part adopted by the International Association for the Study of Pain (IASP) and the World Health Organization (WHO) for the diagnosis of secondary pain after surgery or trauma in the 11th version of the International Classification of Diseases, the ICD-11 [4]:

Definitions of clinically significant, pathological, persistent post-surgical pain [3]

The pain develops after a surgical procedure or increases in intensity after the surgical procedure.

The pain should be of at least 3–6 months' duration and significantly affect the quality of life (QOL).

The pain either is a continuation of acute post-surgery pain or develops after an asymptomatic period.

The pain is in the surgical field, projected to the innervation territory of a nerve either situated in the surgical field or is referred to a dermatome (after surgery in deep somatic or visceral tissues).

Other causes of pain should be excluded, e.g., infection or continuing malignancy in cancer surgery.

Traditionally, a healing process is assumed to be completed by three months after surgery or tissue trauma. At this point, the tensile strength of the scar tissue is usually sufficient to avoid dehiscence of the wound, the vasculature, and the visceral tissues. However, the increased sensitivity of injured sensory nerves, and the accompanying increased central nervous system reactions, are normal sensory perturbations in the post-surgical rehabilitation process. In most parturients, the pathophysiological environment reverts to the normal pre-partum level, but in some, the perturbations continue leading to persistent post-partum pain, often with accompanying neuropathic pain components.

The normally increased somatosensory sensations, pain included, from the surgical or the trauma region may continue beyond three months, but they should not be termed abnormal, or pathological, persistent post-surgical pain unless the severity of pain is significant and negatively affects the quality of life [3]. These basic aspects of a normal healing process after injury contribute to the heterogeneous and widely varied results from numerous studies on persistent post-surgical or persistent post-trauma pain [3, 5].

This is well illustrated by studies of “persistent” pain after Caesarean or vaginal deliveries by James Eisenach and co-workers: The high incidence at two months [6] was dramatically reduced 12 months [7] after Caesarean as well as vaginal deliveries. Petter Kainu and co-workers from Finland [8] corroborated this finding of resolution of pain after childbirth, although they reported higher persistent pain after Cesarean delivery (23%) and vaginal delivery (8%) 12 months after childbirth.

Harald Breivik, Division of Emergencies and Critical Care, Department of Pain Management and Research, Oslo University Hospital, Nydalen PB 4950, 0424 Oslo, Norway, Phone: +47 958 65 323, E-mail: harald.breivik@medisin.uio.no

Mads U. Werner, Multidisciplinary Pain Center, Neuroscience Center, Copenhagen University Hospitals, Copenhagen, Denmark, E-mail: mads.u.werner@gmail.com

A modifiable risk factor: severe acute pain after surgery and after childbirth increases the risk of persistent pain

One of the best-documented risk factors for persistent post-surgical pain and persistent pain after traumatic tissue injury is the severity of acute pain soon after the event [1]. This is particularly important because effective and safe management can modify the effects of severe acute post-surgical pain [9–11].

This is also true for acute pain during and soon after childbirth [12–14]. Thus, more severe pain soon after delivery increased the risk of persistent pain in the study from Finland [8]. When documenting pain two months after delivery, James Eisenach and co-workers reported that severity of acute pain soon after delivery, within 36 h of delivery, was associated with more pain at two months after both Caesarean and vaginal deliveries [6]. Persistent vaginal and perineal pain occurs more often when there are severe acute pain and perineal trauma after instrumental vaginal deliveries, causing lacerations requiring surgical vaginal repair [2].

Whenever there is nerve damage following surgery or tissue trauma, the risk for *neuropathic pain* increases [1]. Neuropathic pain components are frequent, occurring between 45 and 80% of patients with persistent post-surgical pain [1, 15]. It is therefore evident that when the surgeons using less invasive, less “traumatic” techniques (keyhole surgery, robotically-assisted surgery), the patients may experience less acute post-surgical neuropathic pain. Laparoscopic and thoracoscopic techniques may be associated with less tissue damage and nerve injury compared with open techniques.

Pre-surgery pain and pre-surgery anxiety and depression increase the risk of persistent post-surgical pain

It is well-established that patients who experience chronic pain before surgical treatment have an increased risk of developing a persistent pain condition after the procedure [1]. The same is true for persistent pain after traumatic injuries [5], as well as after childbirth [8]. Preoperative

psychological morbidity, especially severe anxiety, and depressed mood are also well-documented risk factors of persistent post-surgical pain [1]. Severe anxiety before a surgical procedure is important to recognize, particularly in the form of *catastrophizing* thoughts and anticipation of detrimental outcomes [1]. These could be modifiable risk factors if the responsible surgeon and anaesthesiologist are able, in a cognitive and empathetic fashion, to inform the hyper-vigilant, anxious patient about the safety procedures and normal course of surgery and postoperative rehabilitation [13].

Since chronic pain-conditions are prevalent in the population (12–30%, mean 20% [16]), a large proportion of surgeries are likely to be performed in patients with a pre-surgically sensitized pain system. The likelihood of developing persistent post-surgical pain, therefore, may be increased in about 20% of the adult population [16]. Still, a focus on chronic pre-surgical pain should instigate the surgeon and the anaesthesiologist to carefully re-evaluate the indication for the surgical intervention, as well as pay close attention to other more modifiable risk factors, especially severe acute pain during and early after the operation.

As for surgeries in general, a history of pain and a history of depression *before* pregnancy are risk factors for persistent post-delivery pain

In the Eisenach studies in the USA [6, 7] as well as the Finnish study [8], a history of pain *before* pregnancy as well as severe pain *during* and *soon after* delivery were significant predictors of persistent pain after childbirth. These findings agree with most types of surgery where highly predictive risk factors for persistent post-surgical pain are chronic pain before surgery and severe acute pain soon after surgery [1]. Severe psychological problems before surgery are also reasonably well documented risk factors [1].

Recently, Leiv Arne Rosseland, Silje Endresen Reme, and their co-workers published, in the *Scandinavian Journal of Pain* [17], a high-powered study (n=2,217) on persistent post-delivery pain and post-partum depression two months after delivery. They confirmed that pain before pregnancy (OR 3.70; 95% CI 2.71–5.04) and a history of depression before pregnancy (OR 2.31; 95% CI 1.85–2.88)

were statistically significant predictors of persistent pain two months after childbirth [17].

Negative overall birth-experience is a risk factor for development of post-partum depression

Importantly, Leiv Arne Rosseland and his co-workers designed a numerical rating score (NRS 0–10), where the parturients within 48 h after delivery answered the question “What was your experience of the birth?” (0 = “very good” to 10 = “extremely bad”). They documented significant association between the negative qualities of the overall birth-experience and depression two months after delivery [17].

Pain and depression two months after delivery must be important determinants for the quality of life of the mother, as well as for the development and consolidation of the mother-child bonding. It is important that Eisenach and co-workers documented that 12 months after delivery, only a minority of the mothers still experienced pain [7]. Unfortunately, Eisenach and co-workers at the follow-up at six and 12 months contacted only parturients with pain at two months. This means that we are not able to recognize a phenotype switch from ‘no pain’ at two months to ‘pain’ at 12 months in the total cohort. This *phenotype switch* has been documented after groin hernia repair, lung cancer surgery, and breast cancer surgery [18, 19] and may well be an issue after childbirth. Thus, Kainu and co-workers [8], who followed their entire cohort for 12 months after childbirth, reported much higher percentages than Eisenach and coworkers [7] of pain after Cesarean section (23%) and after vaginal delivery (8%) at 12 months post-partum.

Leiv Arne Rosseland and co-workers emphasized that the *overall* birth-experience depends on how well the parturient is taken care of, e.g., is the parturient left alone for long periods in the delivery room? The delivery situation is, obviously, anxiety-provoking, particularly in primiparas, and it is not unlikely that catastrophizing thoughts sometimes are harbored. Do the midwives and obstetricians always manage to communicate well with the parturient about the progress and likely outcome of the labour?

Pain during the early hours after giving birth is likely to be related to the qualities of the overall birth-experience, although Rosseland and co-workers only observed a weak (but statistically significant) association between pain during labour and a negative overall birth experience [17].

Prevention of persistent post-surgical pain – principles that may apply to persistent post-delivery pain as well

Do not operate when there is no valid indication for surgery

A gruesome story of long-lasting pain after an unnecessary cosmetic surgery is breast augmentation surgery [20]; is there ever an indication for implanting prostheses to make perfectly normal breasts looking larger?

Leiv Arne Rosseland and co-workers confirmed that Cesarean delivery is a risk factor for persistent pain after birth [17], as did Kainu and co-workers in Finland [8]. Cesarean deliveries also increase risk of post-partum depression [21]. Cesarean deliveries account for 32% of all deliveries in the USA,¹ and 15–20% in the Nordic countries.² Reducing the number of elective caesarean deliveries may possibly be feasible by emphasizing the higher risk of persistent post-delivery pain and depression for the pregnant women wishing Cesarean delivery?

Reduce acute pain during and after a surgical procedure

Multiple beneficial effects from *epidural analgesia during and after* thoracic and abdominal operations are well documented [10, 11], among them the reduced risk of persistent post-surgical pain [9, 22, 23], most effectively when *optimal* epidural analgesia is used *during* surgery as well as in the otherwise most painful period *after* surgery [10, 11]. *Optimal* epidural analgesia should be emphasized because there are multiple ways of conducting and managing epidural analgesia, and not all are “optimal” [11]. Why should this not be true for optimal labour-epidurals as well?

Unfortunately, the only significant risk factors, in addition to pain and depression before pregnancy, that Leiv Arne Rosseland and co-workers documented as significantly associated with pain two months after delivery, were Cesarean delivery *and* epidural analgesia

¹ <https://www.cesareanrates.org/#:~:text=Percentage%20of%20Repeat%20Cesarean%20Births%20vs.&text=Of%20the%20nearly%204%20million,with%20a%20previous%20C%2Dsection>

² https://www.sundhed.dk/content/cms/66/4666_aarsrapport-dkf-2017-2018-hovedrapport-samt-bilag-12.pdf

during delivery [17]. However, the only detail of the labour-epidural practice reported is that the mean cervical dilatation was 6.5 cm when initiating the labour-epidurals.

Delaying the epidural analgesia until this magnitude of cervical dilatation is achieved could be considered a relic of the past, of the early labour-epidural praxis more than 20–30 years ago when too concentrated and too large doses of local anaesthetics were used, causing motor-weakness or paralyzed abdominal and pelvic muscles. The motor-blockade increased the duration of labour, augmenting the likelihood and risks of instrumental vaginal deliveries and non-elective Caesarean sections. Therefore, the accepted praxis at that time was never to start an epidural too early, not before cervical dilatation was at least 4 cm.

When opioid receptors in the spinal cord dorsal horn were discovered, and we thereafter added tiny doses of lipophilic opioids (fentanyl or sufentanil) that pass through the dura and arachnoid into the spinal liquor and spinal cord, only low concentrations and small doses of local anaesthetics were needed for high efficacy labour-epidurals. Muscular weakness and motor-blockade have since not been a problem, and it is now widely agreed that a labour-epidural should start as soon as it is needed for relief of unbearable labour pain during the opening, first stage of labour [12–14].

With this type of optimal labour-epidurals, there is no prolongation of labour and no increased risk of vaginal instrumental deliveries or non-elective Caesarean deliveries. In scientific literature after 2005, this old problem has disappeared [24].

In thoraco-abdominal surgical procedures, an optimal postoperative analgesia requires an extension of the epidural analgesia [11]. Correspondingly, it may be an important point that the labour-epidural analgesia should continue *after* the delivery, at least through the third stage of labour, during and after the expulsion of the placenta – “the after-birth.” During this stage of labour, pain from uterine contractions and pain from vaginal and perineal tissue damage are frequently severe [2] and likely can be a negative factor for the overall birth experience, especially if the parturient is interviewed about the “total birth experience” soon after.

Pharmacological means of reducing the risk of persistent post-surgical and post-partum pain.

Multimodal pharmacological analgesia is recommended to relieve acute pain and to reduce the need for opioids, mitigating their well-known adverse effects. Unfortunately, our

hopes for mitigating the risk of persistent pain after surgery with pharmacologic means have not come true: This is true for the gabapentinoids, possibly also for ketamine, and glucocorticoids [25].

Conclusions

Severe persistent post-surgical pain and persistent post-traumatic pain are recognized as major health problems [1, 4]. Management of this type of persistent pain is often difficult because of nerve injury, and neuropathic pain components are so very frequent [1, 15].

Therefore, we must be aware of risk factors, reduce these whenever possible, treat acute postoperative pain well, and refer these patients early in the course to pain clinics for management by experienced multi-professional teams that are able to evaluate and manage these unfortunate patients with persistent complex pain conditions [1, 26]. This is also true for parturients who have developed persistent pain after childbirth.

If not a “basic human right,” optimal labour-epidurals should be made freely available, preferably as in Sweden, where the health care providers are required by law to offer labour-epidural analgesia whenever a parturient needs effective and safe pain relief [27]. This is especially true for parturients who have a history of chronic pain and/or depression *before pregnancy*, so well documented by Leiv Arne Rosseland and his co-workers [17]. Optimal labour-epidural analgesia may reduce the risk of persistent pain after delivery. It will *not* increase the risk of persistent pain after delivery.

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