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REVIEW ARTICLE

Peripheral nerve block and rebound pain: literature review



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Abstract

Background and objectives: To investigate, describe, and assess the phenomenon of “rebound pain” as a clinically relevant problem in anesthetic practice.

Content: The phenomenon of “rebound pain” has been demonstrated and described as a very severe pain, which occurs after a peripheral nerve block resolution with the recovery of sensitivity. The incidence of rebound pain is unknown. Usually, it occurs between 12 and 24 hours after surgery and adversely affecting sleep quality. It is not yet possible to establish a mechanism as a definitive cause or trigger factor of rebound pain. Studies suggest that rebound pain is a side effect of peripheral nerve blocks, despite their effectiveness in pain control. Currently, the extent and clinical significance of rebound pain cannot be well determined due to the lack of large prospective studies.

Conclusion: Rebound pain assessment should always be considered in clinical practice, as it is not a rare side effect of peripheral nerve blocks. There are still many challenging questions to be answered about rebound pain, so large prospective studies are needed to address the issue. For prevention, the use of peripheral nerve block techniques that avoid nerve damage and adequate perioperative analgesia associated with patient education on the early administration of analgesics, even during the period of analgesia provided by peripheral nerve block, is recommended. A better understanding of the “rebound pain” phenomenon, its pathophysiology, associated risk factors, and long-term consequences may help in developing more effective preventive strategies.

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PALAVRAS-CHAVE

Bloqueio nervoso;
Nervos periféricos;
Efeito rebote;
Dor pós-operatória

Bloqueio de nervos periféricos e dor rebote: revisão de literatura**Resumo**

Justificativa e objetivos: Investigar, descrever e avaliar o fenômeno da "dor rebote" como um problema clinicamente relevante na prática anestésica.

Conteúdo: O fenômeno da "dor rebote" foi demonstrado e descrito como uma dor muito intensa que ocorre após a resolução do bloqueio de nervo periférico com o retorno da sensibilidade. A incidência de dor rebote é desconhecida. Normalmente ela ocorre entre 12 a 24 horas após a cirurgia e afeta negativamente a qualidade do sono. Ainda não é possível estabelecer um mecanismo como causa definitiva ou fator desencadeante da dor rebote. Estudos sugerem que a dor rebote seja um efeito colateral dos bloqueios de nervos periféricos, apesar destes terem eficácia no controle algico. Atualmente, a extensão e a significância clínica da dor rebote não podem ser bem determinadas, devido à falta de grandes estudos prospectivos.

Conclusão: A avaliação da dor rebote deve ser sempre considerada na prática clínica, pois não é um efeito colateral raro dos bloqueios de nervo periféricos. Ainda existem muitas questões desafiadoras a serem respondidas sobre a dor rebote, portanto fazem-se necessários amplos estudos prospectivos sobre a temática. Para a sua prevenção recomenda-se o uso de técnicas de bloqueio de nervo periférico que evitem a lesão do nervo e uma adequada analgesia perioperatória associada à orientação do paciente sobre a administração precoce de analgésicos mesmo na vigência da analgesia proporcionada pelo bloqueio de nervo periférico. A melhor compreensão do fenômeno "dor rebote", sua fisiopatologia, seus fatores de risco associados e suas consequências em longo prazo poderá ajudar na elaboração de estratégias preventivas mais eficazes.

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Introduction

More than 80% of patients undergoing surgical procedures have acute postoperative pain and approximately 75% of them report moderate to severe pain.¹ The appropriate treatment of acute postoperative pain is associated with better clinical outcomes,² while inadequate pain control may negatively impact patients' postoperative experience.

Orthopedic procedures are associated with severe postoperative pain³ and an adequate postoperative pain control improves the patient's ability to participate in rehabilitation therapy due to the greater range of motion, which contributes to a better experience perceived by the patient postoperatively.⁴

Peripheral nerve blocks (PNBs) are increasingly used in orthopedic surgery, since the benefits include long-lasting analgesic effects and a high level of safety, as it is well documented in elective foot, knee, and ankle surgeries.⁵ Regional anesthesia, particularly PNB, has the benefits of muscle relaxation and postoperative analgesia, allowing good control of postoperative pain and early hospital discharge.⁶

Although general anesthesia may be used in orthopedic surgeries, the use of regional anesthesia techniques has other additional benefits, such as less airway management, less postoperative nausea and vomiting, less stay in the Post-anesthesia Care Unit (PACU), less need for PACU interventions,^{7,8} and fewer opioid-related side effects such as pruritus and respiratory depression.^{4,9}

Despite the success of regional anesthesia, several studies have demonstrated the occurrence of the phenomenon known as "rebound pain" as soon as the original blockade disappears.^{6,10-12} Although rebound pain occurs in a wide variety of surgeries^{13,14} and the phenomenon is well recognized, all studies have several methodological limitations that make it impossible to determine its clinical significance.

The occurrence of rebound pain may outweigh the benefits of PNBs and represent a clinically relevant problem. A better understanding of the rebound pain profile may allow the identification of at-risk patients and the development of prevention strategies. Given the lack of consistent data in the literature, this article proposes to evaluate the current available literature and the clinical relevance of the rebound pain phenomenon.

Methods

A literature search was performed on PubMed database in December 2017. The search terms used were Rebound AND Pain AND Nerve Block, and 28 results were obtained. Restricting the search to articles published in the last five years yielded 22 results, all of which were written in English. After reading the abstracts of the 22 articles, 19 articles addressing the topic under analysis were selected. In addition to the articles selected from the research, 31 articles referenced in them were also consulted. The analysis included 50 articles that addressed the occurrence of the rebound pain phenomenon in various types of surgeries,

whose procedures were performed both in hospital and outpatient clinic.

Development

Definition

Rebound pain is defined as the quantifiable difference in pain scores when a PNB is working *versus* the acute pain found when the blockade stops working.^{11,15} The rebound pain phenomenon has been demonstrated and described by many authors as a very severe pain that occurs with the return of sensitivity after the PNB resolution.^{6,10–12} Other authors describe it as “a poorly described entity, commonly defined as a dramatic increase in pain once regional anesthesia has dissipated”.¹⁶

Incidence

Due to the scarcity of experimental and clinical studies, the incidence of rebound pain phenomenon is still poorly documented. Nevertheless, its occurrence has been increasingly reported by researchers.

A meta-analysis evaluating the analgesic effect of a single-injection interscalene block for shoulder surgery showed that patients who received interscalene block were more likely to have rebound pain compared with those who did not receive the same blockade.¹⁷ A study with women undergoing breast cancer surgery showed that pectoral nerve block did not improve the quality of recovery score postoperatively when compared to pectoral nerve block with saline solution, and this was attributed to factors such as the occurrence of rebound pain.¹⁸ Regarding outpatient surgeries, a literature review showed that the incidence of rebound pain can reach up to 40% of patients after PNB resolution.¹⁹

Characteristics

Rebound pain presents with a disproportionately higher intensity in relation to the degree of the surgical stimulus.²⁰ It has a rapid onset and a limited duration of about 3–6 hours, occurs soon after PNB cessation, leads to sharp increases in pain scores with high rates of morphine consumption during the rebound period.²¹

Patients often describe rebound pain as a burning sensation that occurs mainly at night and negatively affects sleep quality.^{11,17,22,23}

In a study of patients undergoing surgical fixation of ankle fractures, the patients receiving popliteal block experienced rebound pain within 12–24 hours postoperatively.^{12,24} The occurrence of rebound pain in this same postoperative period was also evidenced in patients undergoing surgical fixation of distal radius fracture who received brachial plexus block.¹⁶

Rebound pain can profoundly impact the patient's recovery experience and if the patient is unaware of this effect he may be subject to a worsening of the unrelieved pain with oral medications.²³ Thus, an increase in opioid consumption and emergency room visits, and a decrease in patient

satisfaction may occur which minimizes the real benefits associated with regional anesthesia and increases the costs of postoperative care.^{17,20,22}

Risk factors

Factors that may be linked to rebound pain include age, type of surgery, surgical site, type of fracture, surgical regimen, type of PNB, nerve injury, local anesthetic concentration, insufficient postoperative analgesia, inadequate orientation of patients on pain control during the postoperative period, presence of preoperative pain, and psychological aspects.

Rebound pain is probably less problematic in elderly patients, while it is very severe in some patients, particularly younger patients.²¹

The surgical site and type of surgery may influence the occurrence of rebound pain, and studies have shown that certain techniques and surgeries are at greater risk of causing it. Pain severity was greater in shoulder surgery compared to complex knee surgery.¹¹

The use of PNBs for acute fracture surgery has not been thoroughly investigated, and acute fractures have an evolutionary course of postoperative pain that differs from that of elective procedures, which makes PNB less safe in this scenario.¹⁹

Rebound pain is particularly prevalent in patients undergoing outpatient surgery, which is believed to occur as a result of greater difficulty in having adequate pain control outside the hospital setting.¹⁹

The type of PNB used for anesthesia has not been objectively evaluated, but it is believed that neural damage caused by needle insertion and pressure trauma during local anesthetic injection may induce some perineural inflammation.¹⁹ Local anesthetic concentrations can influence rebound pain intensity *in vivo*, but this factor has not been clinically studied.²⁴

The administration of an analgesic drug 1–2 hours before the end of the analgesia provided by PNB may minimize the incidence of rebound pain. The lack of adequate patient education about the need for a pain therapy such as bridging analgesia, even in the absence of pain, may lead to ineffective pain control during the transition period for oral analgesics when the duration of analgesia provided by PNB ceases.¹²

Patients' expectations about PNB may interfere with postoperative pain perception and treatment because a concern for patients with nerve damage may lead to the development of falsely low pain tolerance.²²

Rebound pain mechanisms

The pathophysiological mechanisms of rebound pain are complex and not fully understood. Rebound pain is characterized as a mechanical-surgical pain caused by unopposed nociceptive inputs, which are intensely received by the subject after PNB resolution.¹⁴ Some mechanisms of peripheral nerve injury due to mechanical and chemical effects from PNB in predisposed patients (those with severe preoperative pain and young patients) are still under debate by researchers.¹⁹

Table 1 Rebound pain score. The score should be calculated by subtracting the lowest NS score within 12 hours before PNB resolution from the lowest NS score during the first 12 hours after PNB resolution.

Determine

- PNB performance time

- Initial dose of local anesthetic used

PNB resolution time (patient perspective). Assessed by the following criteria:

- Early need for rescue oral analgesics (context of standardized movement)

- Absence of numbness or heaviness in PNB area

PNB resolution time. Assessed by the following questions asked to patients:

- Does PNB provide pain relief?
- If not, what time did it cease?

PNB, peripheral nerve block; NS, numerical scale from 0 to 10 to measure pain severity in numerical values (0 = no pain and 10 = worst imaginable pain).

The intrinsic proinflammatory properties of local anesthetics, when associated with PNB nerve damage, may cause post-PNB hyperalgesia and neuropathic pain, and these manifestations may present as rebound pain.²⁵

Another theory proposes that while PNB prevents signal transduction, the retained nociceptive signal memories are amplified when the blockage finally wears off.¹⁷

Post-PNB hyperalgesia theories have been tested in rat models with variable and inconclusive results; therefore, the clinical relevance of these findings in rebound pain pathophysiology is still uncertain. Rats undergoing sciatic nerve block with ropivacaine had transient hyperalgesia on thermal (but not mechanical) stimuli as the blockade dissipated (3 hours) compared with placebo, suggesting a potential action on a specific nerve fiber in rebound pain pathophysiology.¹⁴ Transient thermal hyperalgesia was also found in another study with rats after 4 hours of blockade.¹³ Acute opioid-induced hyperalgesia is another hypothesis suggested.²⁶

Rebound pain diagnosis

To better quantify rebound pain, Williams et al. proposed a standardized method of reporting rebound pain scores (Table 1).¹¹

Approaches for rebound pain prevention and treatment

Effective preventive strategies for rebound pain are challenging, as prevention should be done not only by the anesthesiologist, but also by the surgical team. It is necessary to educate the medical staff for effective measures to be taken. The effective prevention of rebound pain should aim at combining pharmacological and non-pharmacological approaches. The use of non-pharmacological approaches, such as informing and educating patients about post-PNB rebound pain and postoperative analgesia,¹⁹ combined with

early administration of analgesics, may allow patients to have a more effective postoperative pain control.¹²

Pharmacological strategies

The supplementation of PNBs with perioperative multimodal analgesia protocols through the combination of analgesic drugs with distinct mechanisms of action is recommended.¹⁷ Drugs such as gabapentin, acetaminophen, ibuprofen, and dextromethorphan may be useful as rescue medications for rebound pain control and the use of these drugs may help maintain analgesia during the transitional period as PNB fades.²⁶

It is recommended to avoid the use of hyperalgesic agents, such as volatile gases and short acting opioids, and to include the use of agents that modulate pain response, such as esmolol.^{27,28}

Use of adjuvants

The use of adjuvants in PNBs seems to play some role in decreasing rebound pain. Blockade efficacy may be enhanced by the addition of adjuvants to local anesthetics. Dexamethasone,²⁹ betamethasone,³⁰ and alpha-2 agonists³¹ have been reported to prolong the effects of brachial plexus block when added to local anesthetics. Non-systemic perineural dexamethasone when added to a clinical dose of bupivacaine may prevent reversible bupivacaine-induced neurotoxicity and rebound hyperalgesia after blockade resolution.³² There are some studies suggesting that the systemic administration of dexamethasone may also prolong the effects of PNB.^{33,34}

Adjuvants not only prolong the duration of local anesthetic action, but it can also modulate PNB to decrease rebound pain through other unknown mechanisms. In blockades combined with general anesthesia aiming at analgesia alone, lower local anesthetic concentrations could be used in combination with perineural adjuvants.²⁴ A recent case series assessing the use of adjuvants in PNB showed that the combination of clonidine, buprenorphine, and dexamethasone with bupivacaine or ropivacaine was associated with reduced rebound pain severity. However, the authors of this study could not determine the optimal dose of adjuvants to achieve this benefit.^{24,35}

Studies performed with radiculopathy patients have shown that the addition of sodium hyaluronate solution and carboxymethylcellulose solution to the conventional cocktail (corticosteroids, 1% lidocaine, 0.5% bupivacaine) in the selective nerve root block led to effective pain control within three days to two weeks,³⁶ and the rebound pain that occurs in these cases within 2–4 weeks after the conventional cocktail injection was reduced when hyaluronate was added to the conventional cocktail.³⁷

Continuous peripheral nerve blocks

Rebound pain may be attenuated by prolonging the blockade duration, either by the continuous local anesthetic infusion technique *via* peripheral catheter or by the single injection technique. Continuous PNBs have an effect on analgesia

due to decreased basal pain and inflammatory markers, in addition to interrupting the formation of neuronal memories associated with surgery.³⁸ In femoral nerve block knee surgery, the numeric rating scale was used to measure pain severity on a scale from 0 to 10 (0 = no pain, 10 = worst pain imaginable). It was observed that in order to reduce rebound pain scores by one unit, an additional 33 hours increase in PNB duration was required.¹¹ The duration of analgesia must be significantly longer than that provided by a typical blockade to achieve a clinically significant reduction in rebound pain.^{11,17} However, rehabilitation planning and patient preferences may limit the application of this technique by not allowing a prolonged period of motor block or decreased sensitivity.

In a meta-analysis, continuous PNBs improved postoperative analgesia and were associated with lower opioid-related complications compared with single-injection PNBs.³⁹ Continuous PNB for pain control in ankle fracture surgery significantly reduced rebound pain and the need for opioid analgesia compared to single-injection PNB.⁴⁰ Continuous interscalene brachial plexus block also reduced postoperative pain and rebound pain.⁴¹

The strategy of using continuous PNBs as a way to reduce the incidence of rebound pain is not yet a consensus in the literature. A prospective clinical trial with patients undergoing distal radius fracture fixation compared single-injection infraclavicular block with continuous infusion block. The use of continuous PNB showed no benefit and did not significantly reduce rebound pain or analgesic use within 8–72 hours postoperatively.²³

Combined peripheral nerve blocks

Ultrasound-guided axillary nerve block combined with suprascapular nerve block reduced the rebound pain phenomenon after arthroscopic rotator cuff repair.⁴² The use of combined ultrasound-guided brachial plexus block and suprascapular nerve block reduced postoperative pain more effectively than single-injection block within 36 hours after arthroscopic cuff repair, in addition to decreasing the rebound pain phenomenon.⁴³

Other techniques

Comparing patients undergoing total knee arthroplasty (TKA) who received a continuous femoral nerve block and a single-injection sciatic nerve block or periarticular infiltrate and a postoperative continuous intra-articular infusion, the periarticular injections combined with an intra-articular catheter provided better pain control, no rebound pain, and decreased risk of motor block-related complications.⁴⁴ In another study of TKA, the combination of intraoperative periarticular injection with preoperative femoral nerve block provided better pain management within the first 24 hours after surgery.⁴⁵

In primary shoulder arthroplasty, the patients treated with intraoperative soft tissue infiltration with injectable bupivacaine liposomal suspension required an equivalent amount of postoperative analgesics compared with patients treated with interscalene brachial plexus block, despite

higher pain scores after 8 h in the group of patients who received PNB.⁴⁶

Non-pharmacological strategies

Initial pain assessment and psychological follow-up of high-risk patients may be beneficial.¹⁵ Patient education and guidance may be the most useful short-term strategy and can be done during the preoperative assessment in which patients receive clarifications about PNB and rebound pain. Patients may be instructed regarding early analgesic use before regional anesthesia decline to maintain pain control, stay ahead of pain, while the PNB analgesia is still present. This strategy may allow patients to have more effective postoperative pain control.¹⁶

Clinical implications

PNB is likely to be effective, but rebound pain cannot be neglected as a side effect despite the appropriate use of a multimodal analgesic regimen. The long-term consequences of rebound pain in terms of functional recovery and persistent pain have not been thoroughly demonstrated and investigated in elective and emergency surgeries. However, according to the few published studies, the phenomenon does not appear to influence long-term patient recovery, both in terms of function¹⁶ and pain.¹⁷

Evidence suggests that the incidence of rebound pain may outweigh the benefits of PNBs in preventive analgesia, considering acute postoperative pain as an important risk factor for the development of persistent postoperative pain.⁴⁷ Thus, rebound pain may represent a clinically relevant problem and increase the use of health resources.

Studies report that despite the occurrence of rebound pain, patient satisfaction scores were high with the use of PNB, both as an anesthetic technique and in postoperative pain control.²¹ A result also found in a review of outpatient surgery, in which regional anesthesia was associated with higher patient satisfaction compared with general anesthesia.⁴⁸ Many patients may have experienced a sense of relief by avoiding general anesthesia and this may have increased the satisfaction with PNB, as many patients fear general anesthesia.⁴⁹ On the other hand, patients may simply have considered the benefits of being awake during the procedure, absence of nausea, and many painless hours as “worth it” even if they experienced rebound pain for a few hours.²¹

Conclusion

Rebound pain is an entity of unknown etiology that interferes with the quality of the patient’s postoperative recovery. Assessment of rebound pain should always be considered in clinical practice as it is not a rare side effect of PNBs.

For rebound pain prevention, we recommend the use of PNB techniques that prevent nerve damage and adequate perioperative analgesia associated with patient education about the early use of analgesics even in the presence of analgesia provided by PNB.

Despite the effort to better understand the rebound pain phenomenon and to identify at-risk patients, its management and prevention remain inappropriate.

The findings on this rebound pain phenomenon in the current literature are still scarce and the studies analyzed present several limitations regarding pain score measurements and data on postoperative analgesic medications, which hinders the analysis of the clinical implications of this event.

Extensive prospective studies and further studies aimed at better understanding the pathophysiology, prevalence, associated risk factors, and preventive methods are recommended. Currently, Sort et al. conducted a randomized study comparing PNBs with spinal anesthesia for ankle fracture surgery regarding postoperative pain profiles and quality of recovery. The secondary outcomes of this study include rebound pain.⁵⁰

Conflicts of interest

The authors declare no conflicts of interest.

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