REVIEW ARTICLE

Alternatives to subcutaneous injection of amino–amide or amino–ester anesthetics before arterial puncture for blood gas analysis: a systematic review

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Background and objective. Arterial puncture for blood gas analysis is a painful procedure in the emergency department (ED). Local subcutaneous injection of anesthetics containing amino amides or esters is the usual pain-relief technique applied before arterial puncture, but it is little used in some care settings, such as the ED. We aimed to analyze the literature on anesthetic approaches other than the traditional one of local injection of amino-amide or amino-ester compounds for pain relief during arterial puncture and to assess the efficacy of the alternatives.

Methods. A systematic review of the literature was conducted in 6 bibliographic databases. We selected randomized clinical trials (RCTs) published in English or Spanish between 2000 and 2018. The trials compared self-reported pain immediately after arterial puncture for blood gas analysis. Some form of anesthesia other than local injection of an amino–amide or –ester compound was compared to another anesthetic technique, placebo, or no anesthetic.

Results. We found 16 RCTs. Four compared the effect of topical anesthetic creams containing amino amides and/or amino esters, two assessed ultrasound-guided puncture, four used small-caliber needles or special syringes, one used a needle-free high-pressure anesthetic injection system, and five studied cryoanesthesia by application of ice or aerosols.

Conclusion. The only effective alternative approaches to pain relief during arterial puncture for blood gas analysis were the use of very fine-caliber needles, the use of needle–free pressure injectors for subcutaneous delivery of amino amides, and the application of ice for at least 3 minutes.

Keywords: Arterial puncture. Arterial blood gas analysis. Pain. Anesthesia.

Alternativas anestésicas a la inyección de amidas por vía subcutánea en punciones arteriales para gasometría: una revisión sistemática

Introducción y objetivo. La punción arterial para gasometría es una técnica dolorosa. La estrategia anestésica de elección consiste en la inyección local de amidas o esteres por vía subcutánea, pero resulta poco frecuente en algunos ámbitos asistenciales, como los servicios de urgencias. El objetivo de este trabajo es en describir las estrategias anestésicas distintas a la técnica clásica de inyección local de amidas o esteres y evaluar su eficacia en la punción arterial para gasometría.

Método. Se realizó una revisión sistemática de la literatura a través de 6 bases de datos bibliográficas. Fueron seleccionados ensayos clínicos publicados entre 2000 y 2018, en inglés o español, que comparasen el dolor autopercibido por el paciente inmediatamente después de una punción arterial para gasometría en función de si se les aplicó alguna medida anestésica diferente a la inyección subcutánea de amidas o esteres frente a otro procedimiento anestésico local, un placebo o ninguna intervención anestésica.

Resultados. Se localizaron 16 ensayos clínicos aleatorizados: 4 evaluaron la aplicación de anestésicos tópicos compuestos a base de esteres o amidas, 2 la punción ecoguiada, 4 el empleo de agujas de pequeño calibre o jeringuillas especiales, 1 el uso de inyectores a presión sin aguja y 5 la crioanestesia mediante hielo o aerosoles.

Conclusión. Tan sólo el uso de agujas de calibre muy fino, la sustitución de jeringuillas clásicas por inyectores a presión sin aguja para la administración de amidas o esteres subcutáneas o la aplicación previa de hielo durante al menos 3 minutos se mostraron eficaces en la reducción del dolor derivado de la punción arterial para gasometría.

Palabras clave: Punción arterial. Gasometría. Dolor. Anestesia.

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Introduction

Arterial puncture for gasometry is a standard diagnostic procedure in the emergency department (ED). It is an invasive test which provides useful information on gas exchange and acid-base balance but which, besides causing complications, is uncomfortable and painful for patients (in fact, it is considered one of the most common forms of iatrogenic pain induction in hospital EDs)[1]. However, pain related to health interventions is often undervalued and therefore insufficiently prevented and treated[2-4]. The administration of amides by subcutaneous injection a few minutes before the execution of arterial puncture is the anaesthetic strategy of choice. However,

its application during gasometry in the emergency department, despite being considered the standard practice[5], is infrequent during clinical practice[6-9]. This situation may be due to various causes, including lack of time related to the sustained pressure of care in the ED, lack of knowledge or lack of perception by the healthcare professional of the need to prevent pain, the belief that the procedure will hinder the success of the extraction or even that the pain derived from the injection of subcutaneous anaesthesia is equal to or greater than that of the arterial puncture itself[8,10], since the administration of subcutaneous amides has also been found to produce considerable pain[11,12].

However, amide administration by subcutaneous injection may not be the only anaesthetic strategy that can be used to prevent pain and anxiety from arterial blood collection. Other measures have been considered as alternatives when these drugs are not available, there is evidence of a previous history of adverse effects to amides or there is simply no time or no desire to apply punctures other than those to perform blood collection. For this reason, the aim of this work is to describe anaesthetic strategies other than the classic technique of subcutaneous local injection of amides in arterial puncture for blood gasometry in the adult patient and to evaluate their efficacy in reducing pain.

Method

A systematic review was conducted according to the PRISMA regulations. Original articles indexed in Medline databases (through PubMed), Web of Science, Science Direct, EMBASE, CINAHL and CUIDEN were selected. We used the generic search strategy ("pain" AND "arterial puncture") OR (anaesthesia AND "arterial puncture") adapted to the characteristics of each database (Table 1). Searches were limited to humans and publications conducted between January 2000 and January 2018.

Clinical trial articles were selected with at least an abstract available that compared patient self-perceived pain immediately after an arterial puncture for blood gasometry, depending on whether any anaesthetic measure other than the classical technique of subcutaneous injection of amides was applied to them versus another anaesthetic procedure, a placebo or no intervention. Studies referring to arterial catheterisation and those performed on paediatric patients (age under 16) were excluded. Neither were review articles, communications to congresses, clinical case reports or scientific letters, nor works published in languages other than Spanish or English. As a secondary strategy, new articles were manually searched from the bibliographic references cited in the selected studies (inverse search).

Two reviewers selected potentially relevant articles obtained from the search strategy by reading the title or abstract. The full texts of all references screened were then read to check that they met the selection criteria. Disagreements were resolved by consensus.

Table 1. Search strategies implemented

Database	Search Strategy
Medline	((("arterial puncture"[All Fields] AND ("pain"[MeSH Terms] OR "pain"[All Fields])) OR "arterial puncture"[All Fields]) AND ("anaesthesia"[All Fields] OR "anesthesia"[MeSH Terms] OR "anesthesia"[All Fields]) AND (("2000/01/01"[PDAT] : "2018/12/31"[PDAT]) AND "humans"[MeSH Terms])
Web of Science	Tema: ("arterial puncture") AND Tema: (pain) OR Tema: (anaesthesia) AND Tema: ("arterial puncture") AND Tipos de documento: (Article) Período de tiempo: 2000-2018. Índices: SCI-EXPANDED.
Science Direct	docsubtype(FLA) and pub-date > 1999 and pain AND "arterial puncture" OR anaesthesia AND "arterial puncture" AND LIMIT-TO(topics, "patient,needle,pain,arterial puncture") AND LIMIT-TO(contenttype, "JL,BS","Journal").
EMBASE	(((pain and "arterial puncture") or anaesthesia) and "arterial puncture").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word] limit 1 to (human and yr="2000 -Current" and article)
CINAHL	AB arterial puncture AND AB pain OR AB arterial puncture AND AB anaesthesia
CUIDEN	("puncion")AND(("arterial")AND(("dolor")OR(("puncion")AND(("arterial")AND("anestesia")))))

Using the Jadad scale[13] the quality of each study initially included was assessed, and those that did not achieve a score of at least 3 points were withdrawn. The evaluation of the risk of bias of the texts finally selected was done using the system adopted by the Cochrane Collaboration[14]. For the extraction of data from each article, a template designed according to the PICO structure was used. Data were collected referring to the type and number of patients included, the anaesthetic interventions studied and compared and the evaluation of pain referred by the patients (described by means of numerical scales), for each one of them. Both the quality and risk of bias assessment and data extraction were carried out independently between pairs and a third acted as an evaluator, comparing the information collected between the two and agreeing on the contents of the final template.

Results

Four hundred and ninety-nine references were identified, leaving a total of 317 by eliminating duplicate entries. By expanding the search using the literature reviews of the publications, 2 new records were located that met the inclusion criteria. Of the total number of records selected, 295 were excluded after reading their title or abstract (when available). During the full text reading of them, 8 articles were excluded: three because they were short scientific letters which format did not allow a rigorous evaluation of the applied methodology and another for developing a quasi-experimental design. Finally, 4 articles were eliminated for not reaching the minimum score required in the quality evaluation (Figu-

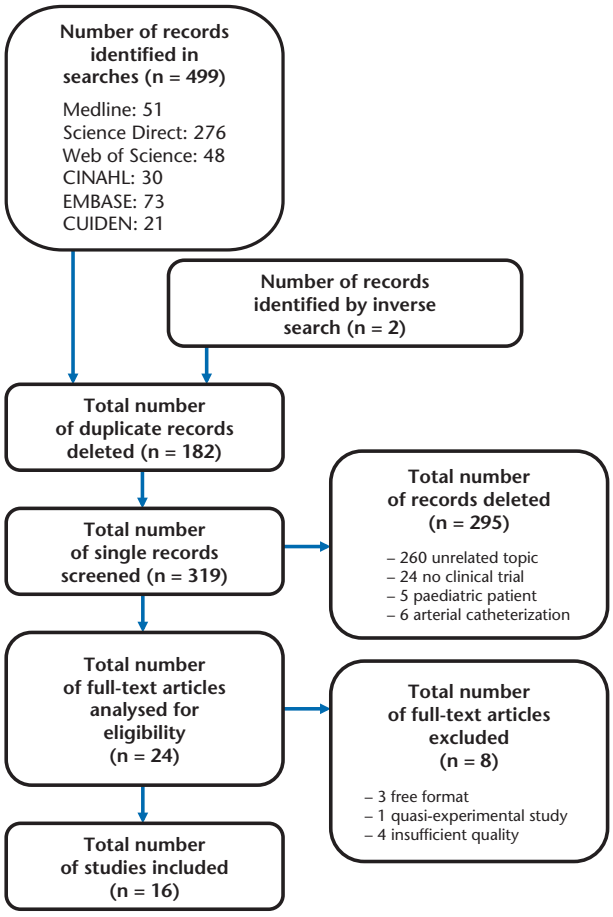

Figure 1. Study selection process.

re 1). The references of the 8 excluded articles can be consulted in Annex 1.

Finally, the study was conducted using 16 publications, all of which were randomised clinical trials aimed at studying the efficacy of anaesthetic techniques other than subcutaneous amide injection in arterial gasometry performed on radial or humeral arteries. Except for one study that was conducted on volunteers, all others were conducted in circumstances that reflected actual clinical practice. They were generally performed with discrete sample sizes, but with procedures that suggested a low risk of bias, most of them in relation to the masking process (Figures 2 and 3).

The strategies evaluated by the trials included in this review were the following: topical anaesthetics based on esters or amides (in cream, gel or ointment form)[15-18], eco-guided puncture[19,20], the use of small calibre[21-23] needles or different types of syringes[24], the use of non-needled injectors to administer amides in the subcutaneous tissue[25] and cryoaesthesia using local ice[26,27] or vaporisation of coolant aerosols[11-28,29]. The main characteristics and results of the included studies are shown in Table 2.

Topical anaesthetics based on esters or amides

Topical anesthetics (gels, pomades or ointments, among others) composed of esters, amides or a combination of both are able to desensitize the skin and shallow tissues in order to perform rapid procedures. They should be applied exclusively topically for at least 30 minutes for optimal anesthetic effects.

Two clinical trials evaluated the effect of EMLA® (Eutetic Mixture of Local Anesthetics) cream, an ointment that mixes lidocaine and prilocaine: one when applied 30 minutes prior to puncture versus placebo[18] and another when applied 60 minutes prior to puncture, compared with placebo and 2% subcutaneous mepivacaine[15]. Tetracaine 4% gel applied 30 and 45 minutes prior to arterial puncture was evaluated by two other placebo-controlled trials[16,17]. None objected that the use of topical anaesthetics based on esters or amides reduced the level of pain compared to placebo or that the anaesthetic effect was similar to or better than that produced by the subcutaneous injection of mepivacaine.

Ecoguided puncture

Ultrasound allows visualization of the blood vessels and other surrounding anatomical structures and facilitates guiding the needle through tissue. Therefore it may seem reasonable to think that it could bring some advantages over the traditional palpation technique and blind puncture of an artery.

Its use in arterial puncture has been evaluated in EDs in two trials with contradictory results. While in

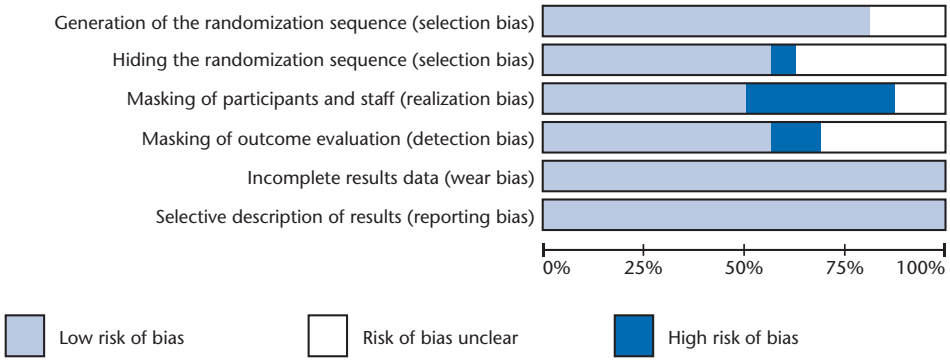

Figure 2. Risk of bias on each criterion presented in percentages of all included studies.

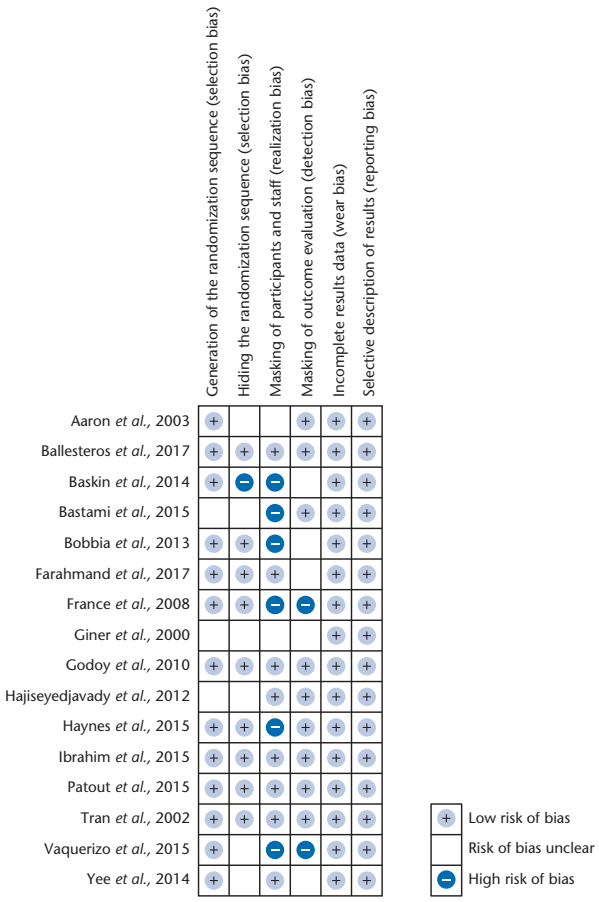

Figure 3. Summary of the risk of bias of the included studies.

one of them the ultrasound-guided arterial puncture resulted in fewer punctures to obtain the arterial blood sample and a significant reduction in pain compared to usual practice[20], the other did not detect variations in pain self-perceived by patients between the two techniques, with the ultrasound-guided puncture being associated with a greater number of punctures necessary until extraction and a greater investment of time in the procedure[19].

Needle punctures of small caliber or with specific syringess

The substitution of standard needles (23G) for the performance of gas measurements by others of smaller calibre has been a strategy to reduce arterial puncture pain evaluated by three clinical trials with different results: while two studies[22,23] found no difference in self-referred pain by patients when 23G or 25G needles were used; another work[21], in which two consecutive punctures were performed with 23G needles and insulin needles (29G) on both radial arteries to healthy volunteers, it did show a significant reduction in pain with smaller diameter needles. Although the presence of post-puncture complications (such as haematomas or paresthesia) was lower in extractions performed with the finest needles[21,23], the rate of haemolysis detected in blood analysis was significantly higher when the puncture was performed with insulin needles[21].

Finally, an investigation compared gasometry performed using a heparinized insulin syringe (26G) and a specific safety syringe (25G), without determining differences in pain level between the two puncture procedures[24].

Needle-free injectors (pressure injectors)

This system is capable of reaching the subcutaneous tissue between 0.2 and 0.4 ml of an anaesthetic solution by infusing the drug through small holes in the tip of the injector, forming a fine jet with sufficient speed and pressure to penetrate the epidermis and be deposited in an area less than 1 cm in diameter.

A single study[25] evaluated the administration of 0.2 ml of 2% lidocaine using a pressure injector model two minutes before radial artery puncture for a blood extraction, as opposed to the use of 2% topical gel lidocaine (applied for two minutes before puncture), finding that application of lidocaine by needle-free injector reduced pain more effectively than lidocaine gel.

Cryoaesthesia using local ice or coolant sprays

Cryoaesthesia is an anaesthetic technique in which local cold is applied in order to numb the peripheral nerves and facilitate minor surgical procedures. There are mainly two ways of doing this: by direct application of ice for a few minutes or by spraying aerosols based on ethyl chloride or a combination of alkanes on the surface of the skin, which produces an immediate tissue cooling of several degrees Celsius below zero. In both cases a local anaesthetic of short duration is achieved.

Two open trials investigated the effects of local ice application 3 to 5 minutes before arterial puncture[26,27], and both found a statistically significant reduction in self-assessed pain when ice was applied. On the other hand, two placebo-controlled trials[28,29] and one open trial[11] evaluated the efficacy of the cryoaesthesia strategy with cooling sprays, and neither detected a significant reduction in pain associated with arterial puncture compared to placebo or the usual technique without anaesthesia of any kind.

Discussion

Pain resulting from arterial puncture for blood gasometry has been self-perceived by ED patients as moderate1. Given that a score of 3 points on an analogue pain scale of 0 to 10 has been agreed as the maximum admissible before starting any analgesic treatment[30], half of the patients have been found to exceed this threshold[1]. This fact testifies to the need not to obviate the adoption of any therapeutic measure to minimise the traumatic impact of extraction. The administration of topical anesthetics composed of esters or amides, ultrasound-guided puncture, the use of fine gauge needles,

Table 2. Summary of the evidence provided by the articles included in the review

Author. Country, year	Participants	Intervention-comparison	Results	Conclusions
Topical anesthetics				
Giner *et al.* Spain, 2000	153 patients who underwent an arterial blood gas.	Placebo-controlled RCTs. Self-perceived pain after arterial puncture was compared after administration of EMLA® (60 minutes) vs placebo (60 minutes) or 0.2 ml subcutaneous mepivacaine. (30 seconds).	Results on a scale of 0-100 points. No significant differences (p = 0.4) between pain scores after EMLA® (X: 2.6; SD: 1.8) and placebo (X: 2.9; SD: 1.8). Differences (p < 0.001) between EMLA® or placebo and mepivacaine (X: 1.6; SD: 1.8).	The use of EMLA® cream does not reduce pain associated with arterial puncture for gasometry.
Tran *et al.* Australia, 2002	81 patients who underwent an arterial blood gas.	Placebo-controlled RCTs. Self-perceived pain was compared after arterial puncture previous to topical administration of tetracaine (amethocaine) 4% (30 minutes) vs. placebo.	Results on a scale of 0-100 points. No significant differences (p = 0.32) between pain scores after tetracaine 4% application (X: 16; SD: 23.3) or placebo (X: 20.7; SD: 18.5).	Topical use of 4% tetracaine does not reduce pain associated with arterial puncture for gasometry.
Aaron *et al.* Canadá, 2003	50 patients who underwent an arterial blood gas.	Placebo-controlled RCTs. Self-perceived pain was compared after arterial puncture previous to topical administration of tetracaine (amethocaine) 4% (45 minutes) vs placebo.	Results on a scale of 0-100 points. No significant differences (p = 0.78) between pain scores after applying tetracaine (X: 26.2; SD: 32.6) or placebo (X: 23.8; SD: 27.4).	Topical use of 4% tetracaine does not reduce pain associated with arterial puncture for gasometry.
Godoy *et al.* Spain, 2010	51 patients who underwent an arterial blood gas.	Placebo-controlled RCTs. Self-perceived pain was compared after arterial puncture previous to administration of EMLA® (30 minutes) vs placebo.	Results on a scale of 0-10 points. No differences significant (p = 0.78) between pain scores after application of EMLA® (X: 2.4) and placebo (X: 3).	The application of EMLA® cream during 30 minutes does not reduce associated pain to the arterial puncture for blood gas.
Eco-Guided				
Bobbia *et al.* France, 2013	72 patients who underwent an arterial blood gas in the ED.	Open RCT. Self-perceived pain was compared after ultrasound arterial puncture vs. standard technique (no eco-guided).	Results on a scale of 0-10 points. No differences (p = 0.743) between pain scores in eco-guided puncture (Me: 3; IQR: 2-5) and non-guided (Me: 3; IQR: 2-5).	Ultrasound-guided arterial puncture does not reduce pain associated with arterial puncture for gasometry.
Vaquerizo *et al.* Spain , 2015	208 patients who received an arterial blood gas in the ED.	Open RCT. Self-perceived pain was compared after ultrasound arterial puncture vs. standard technique (no eco-guided).	Results on a scale of 0-10 points. Differences (p < 0.001) between significant (p < 0.001) pain in ultrasound puncture (X: 3.1; SD: 2.2) and not eco-guided (X: 4.7; SD: 2.6).	Ultrasound-guided arterial puncture reduces pain associated with arterial puncture for gasometry.
Types of needle				
Baskin *et al.* Turkey, 2014	550 patients who underwent an arterial blood gas in the ED.	RCT. Self-perceived pain after arterial puncture was compared with heparinized insulin syringes (26G) and safety device blood gas syringes (25G).	Results on a scale of 0-100 points. No significant difference (p = 0.145) between pain scores after puncture with heparinized insulin syringes (X: 3.5; SD: 2.2) and syringes with safety device (X: 3; SD: 2.4).	Heparinized insulin syringes (26G) and the syringes with the device safety (25G) produce a level of similar pain during arterial puncture for gasometry.
Yee *et al.* Australia, 2014	119 patients who underwent an arterial blood gas in the ED.	RCT. Self-perceived pain was compared after arterial puncture with 23G needle and 25G needle.	Results on a scale of 0-10 points. No significant difference (p = 0.83) between pain scores with 23G needle (X: 3.5; SD: 2.7) and 25G needle (X: 3.4; SD: 2.7).	23G and 25G needles produce the same level of pain during arterial puncture for blood gases.
Ibrahim *et al.* Singapore, 2015	50 healthy volunteers who are were given two arterial punctures for gasometry on both radial arteries.	RCT. Each volunteer was given two punctures, one with an insulin needle (29G) over the radial artery and the other in the contralateral artery with a standard needle (23G). Pain was compared between the two. The order of puncture and the anatomical side were randomized.	Results on a scale of 0-100 points. Significant differences (p < 0.001) between pain with 29G needle (X: 23; SD: 22) vs. 23G needle (X: 39; SD: 24). The rate of hemolysis was higher in extractions with 29G needle (31.3% vs 11.6%; p = 0.035).	Insulin needles (29G) produce less pain than standard needles (23G) in arterial puncture for blood gases, but produce greater haemolysis of the sample.
Patout *et al.* France, 2015	200 patients who underwent an arterial blood gas.	RCT. We compared self-perceived pain after arterial puncture with 23G needle vs 25G needle.	Results on a scale of 0-100 points. No significant differences (p = 0,53) between needle pain scores 23G (Me:6,63; IQR: 0-19) and 25G needle (Me:5.21; IQR: 0-18, 49).	23G and 25G needles produce the same level of pain during arterial puncture for blood gases.
Needle-free injection				
Hajiseyedjavady *et al.* Iran, 2012	42 patients who underwent an arterial blood gas in the ED. .	RCT. Self-perceived pain after arterial puncture was compared after administration of 0.2 ml of 2% lidocaine with needle-free injector (5 minutes before) vs administration of 2% lidocaine in topical gel (5 minutes).	Results on a scale of 0-10 points. Differences (p < 0.001) between significant (p < 0.001) pain with lidocaine 2% by needleless injector (X: 1.29; SD: 0.90) vs. lidocaine 2% topical (X: 4.19); SD: 1.43).	Lidocaine 2% administered by non-needle injector is more effective than topical lidocaine in reducing arterial puncture pain for blood gases.

(Continues)

Tabla 2. Summary of the evidence provided by the articles included in the review (Continuation)

Author. Country, year	Participants	Intervention-comparison	Results	Conclusions
Crioanesthesia				
France *et al.* United Kingdom, 2008	54 patients underwent arterial blood gases in the emergency department.	Open RCT. Self-perceived pain was compared after arterial puncture prior administration of chloride of ethyl vs 0.5 ml subcutaneous lidocaine 2% (2 minutes before) or the standard technique (without anesthesia).	Results on a scale of 0-100 points. No differences between pain scores after applying ethyl chloride (X: 23.9; 95% CI: 12.4-35.5) or standard technique (X: 23.4; 95% CI: 11.7-35). There were significant differences between ethyl chloride or placebo and lidocaine (X: 10.2, 95% CI: 4.8-16.3).	The application of ethyl chloride does not reduce the pain associated with arterial puncture for blood gases.
Haynes *et al.* USA, 2015	82 patients underwent arterial blood gas.	Open RCT. Self-perceived pain was compared after arterial puncture prior application of ice (3 minutes) vs. standard technique (no ice).	Results on a scale of 0-100 points. Differences (p = 0.01) between scores of pain after applying ice (X: 13.8; SD: 16.9) or common technique (X: 25; SD: 23).	The application of ice reduces the pain associated with arterial puncture for blood gases.
Bastami *et al.* Iran, 2015	61 patients underwent arterial blood gas in the ED.	Open RCT. Self-perceived pain was compared after arterial puncture prior application of ice (5 minutes) vs. standard technique (no ice).	Results on a scale of 0-10 points. Differences (p < 0.001) between significant (p < 0.001) pain with ice (X: 3.1; SD: 1.7) and not ice (X: 4.6; SD: 1.6).	The application of ice reduces the pain associated with arterial puncture for blood gases.
Ballesteros *et al.* Spain, 2017	126 patients underwent arterial blood gas in the ED.	Placebo-controlled RCT. Self-perceived pain was compared after arterial puncture prior application of ethyl chloride vs. placebo.	Results on a scale of 0-10 points. No differences (p = 0.72) between scores of pain after applying ethyl chloride (Me = 2; IQR 1-4.5) or placebo (Me = 2; IQR 1-5).	The application of ethyl chloride does not reduce the pain associated with arterial puncture for blood gasometry.
Farahmand *et al.* Iran, 2017	80 patients underwent arterial blood gas in the ED.	Placebo-controlled RCT. Self-perceived pain was compared after arterial puncture prior application of refrigerant spray (composed of alkanes) vs. placebo (water spray).	Results in pain scale 0-10 points. No significant differences (p = 0.94) between pain scores after applying coolant spray (X: 4.8; SD: 1.8) and placebo (X: 4.9; SD: 1.8).	The application of coolant spray does not reduce the pain associated with arterial puncture for blood gases.

SD: standard deviation; RCT: randomised clinical trial; 95% CI: 95% confidence interval; Me: median; IQR: interquartile range; X: mean.

the use of pressure injectors without needles or the application of local cold are alternative techniques to the administration of amides by subcutaneous injection that have been evaluated as strategies for the reduction of arterial puncture pain for blood gasometry in adult patients. However, with the exception of the use of fine needles or needleless injectors or the local application of ice, no other strategy has resulted in a reduction in puncture pain compared to the usual technique. It should be noted that in this review no therapeutic equivalence studies have been located between the three options that have been shown to be effective and the standard technique of subcutaneous administration of amides. Finally, it should also be borne in mind that only the first two techniques seem appropriate for use in the ED, taking into account the need for time or materials for their implementation.

Topical anaesthetics based on esters or amides applied in the form of creams, gels or ointments have been proven with some success in reducing pain from venipuncture or venous channelling in paediatric patients[31], but appear to be ineffective in arterial punctures when administered pre-puncture for no more than one hour (there are no quality studies evaluating topical application for more than 60 minutes). The anatomical plane in which the radial artery is located, deeper than that of the veins, could justify this difference. Some authors have suggested that skin characteristics may determine the effectiveness of this strategy. For example, the thinner epidermis present in the elderly might maximize the effects of topical gel anesthetics[18], although this hypothesis has not been demonstrated to date by any clinical trial.

Although the use of ultrasound to obtain blood samples for arterial gasometry has proven to be a useful and safe technique in radial artery catheterisation[32], the use of ultrasound to obtain blood samples for arterial gasometry has presented contradictory results in the two articles in which it has been investigated. So, as with the use of ultrasound for the catheterisation of central venous access[33], with the information currently available it is not possible to make any strong recommendation in this regard. Since ultrasound is a technique highly dependent on the operator, experience and expertise in the procedure could be very relevant to the results related to the pain produced during the puncture. Therefore, the training of the sonographer should be a variable to be controlled in future trials that address this research question.

Contrary to what has been observed in venous canalizations[1], the needle size seems to be important in the generation of painful stimuli in arterial gasometry, but the systematic use of very fine needles could also make the execution of the technique difficult, since small calibre needles have not been conceived for blood extractions, which could increase the risk of obstruction of the needle or haemolysis of the sample and, therefore, the need to repeat the procedure. This hypothesis has only been evaluated in one study[21], showing greater haemolysis in insulin needle extractions, suggesting that

blood extraction using this technique should be performed exclusively for the determination of pCO_2 or pO_2 and never for hematimetry or biochemistry studies.

The use of high-pressure needleless injectors is a procedure that is not currently widespread in Spain, although some promising experiences have been reported[34,35]. In this review a single study has been identified that used this painless technique for the administration of anesthetics based on usual amides, using a very discrete sample size. In spite of the interesting results, the experience is insufficient to make a strong recommendation, although its characteristics (painless, cheap and fast) suggest a clear line of future research.

Cryoaesthesia using coolant aerosols is a technique that has also proved effective in the treatment of peripheral venous catheterisation pain[36], but its effects do not appear to be applicable to the arterial puncture technique. In this case, the difference in the effect induced by cold depending on the agent applied is striking. Thus, it has been possible to observe how cryotherapy using ice is effective, but not when it is performed by vaporization of ethyl chloride. This disparity of results has been explained by the hypothesis that the action of cold gas is more superficial, being therefore less effective and lasting than the direct application of ice[37].

Several factors seem to be involved in minimizing arterial puncture pain. It has been pointed out that gastric measurements qualified as technically simple to be performed by nurses[28] are not very painful, so the experience and expertise of the extractor seems to be a determining condition in the production of iatrogenic pain[18]. Moreover, some authors have considered that arterial gasometry would not require prior anaesthesia if extracted by experienced nurses[38], where there are high guarantees of success in a first attempt. On the other hand, the role that sociocultural, racial or gender characteristics play in arterial puncture pain has not been clearly identified and should be the subject of future studies.

In summary, existing alternatives to subcutaneous amides are currently scarce and, unfortunately, uninteresting, especially in the critical patient or in the context of the ED. Subcutaneous injection of amides (lidocaine or mepivacaine) at the puncture site should continue to be considered a standard of action, as it has been shown to be effective in reducing pain during the arterial blood extraction technique[11,39], although some authors have questioned its anaesthetic effects[40].

The most representative limitations of this work are those derived from the methodology of systematic reviews (fundamentally the possibility of selection and publication biases) and the exclusion of publications in languages other than those selected. The measures adopted to limit the possibility of not finding potentially selectable studies focused on involving two researchers in the process of searching and selecting articles through various bibliographic databases and on employing an unrestrictive search strategy. Finally, no meta-analysis could be performed on any group of trials, given the great heterogeneity of the methodologies used and the scarcity of publications on the subject. Despite the existing limitations, we can conclude that the use of very fine calibre needles, the substitution of classic syringes by pressure injectors without needles for the administration of subcutaneous amides or the application of ice for at least 3 minutes prior to puncture could be effective strategies for the reduction of iatrogenic pain derived from arterial puncture for blood gasometry in adults.

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Annex 1. List of publications finally excluded, grouped by cause of exclusion

As they are short scientific letters or communications to congresses

Micu E, Guillot C, Badier M, Delpierre S, Régis JM, Roussel P. Pain induced by radial artery puncture is not reduced by lidocaine-prilocaine patch. Respiratory Medicine Extra. 2006;2:52-3.

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For insufficient methodological quality (Score < 3 on the Jadad scale)

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García M, Arellano C, Luján MD, Sánchez MC, Alonso JM, García M. Punción arterial y crema EMLA. ¿Alivio eficaz del dolor? Atención Farmacéutica 2005;7:20-4.

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