



Efficacy of oral Ibuprofen in shoulder pain: a systematic review of randomized controlled trials

Marie Barriere, Laurie Cambourieux

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UNIVERSITÉ CLERMONT AUVERGNE

UFR DE MÉDECINE ET DES PROFESSIONS PARAMÉDICALES

THÈSE D'EXERCICE

pour le

DIPLÔME D'ÉTAT DE DOCTEUR EN MÉDECINE

par

BARRIERE Marie et CAMBOURIEUX Laurie

Présentée et soutenue publiquement le 7 Avril 2022

EFFICACY OF ORAL IBUPROFENE IN SHOULDER PAIN : A SYSTEMATIC REVIEW OF
RANDOMIZED CONTROLLED TRIALS

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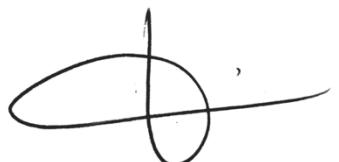


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Listes des abréviations :

BM : Barrière Marie

CL : Cambourieux Laurie

NSAIDs : Non-Steroidal Anti-Inflammatory Drugs

OTC : Over The Counter

PRISMA : Preferred reporting Items for Systematic Reviews and Meta-Analyses

Quick-DASH : Disability of the Arm, Shoulder and Hand

RCT : Randomized Controlled Trials

REB : Rebuild the Evidence Base

SPADI : Shoulder Pain and Disability Index

TJ : Tréfond Jérôme

VAS : Visual Analogue Scale

VRH : Vaillant-Roussel Hélène

WHOQOL-bref : World Health Organization Quality of Life-bref

1 INTRODUCTION

Shoulder pain prevalence in the general population varies from 6.9 to 26 % and increases with the aging population (1,2). It is a common reason for consultation in primary care, ranks third in terms of musculoskeletal symptoms after back and knee pain (3). According to the French observatory of general medicine, 2 % of consultations are related to shoulder pain (4). Shoulder is the most mobile joint and a complex articulation including a wide range of pathologies such as rotator cuff injuries, impingement syndrome, frozen shoulder, osteoarthritis (5). Shoulder is the second most affected joint concerning musculoskeletal disorders in the workplace (6–8). Persistent pain is very common and represents a public health issue by increasing health care needs and work stoppage. In 2000 in the United States, shoulder pain cost \$7 billion (9).

Shoulder pain in a general practitioner consultation leads in more than 50 % to a medication prescription and in 74 % of cases the prescription is an oral NSAIDs (10) in accordance with recommendations (11,12). The recommendations do not specify the superiority of one NSAIDs as shown in a systematic review on rotator-cuff disorders guidelines conducted in 2018 (13). Acetaminophen, NSAIDs and corticosteroid injections were classified as « may be recommended » without any distinction between these three modalities. Ibuprofen is a widely used NSAIDs for antalgic and anti-inflammatory action and belongs to over the counter (OTC) medication. According to a study conducted in 2002 in the USA, 83 % of patients used an antalgic in self-medication and the most used OTC medication was ibuprofen (14). Self-medication market increased to amount to 15 % in 2016 in France, 38 % in Germany, 57 % in England of the global pharmaceutical market (15). As other NSAIDs, ibuprofen can expose to adverse effects as upper gastrointestinal perforation, bleeding, renal and heart failure (16) or to a lower degree can interfere with blood pressure control (17). Few patients are aware of these potential interactions and side effects (14,18,19). In 2019, in France, because of improper use

and fatal side effects, ibuprofen access was modified. No prescription is required but it was placed behind the counter to strengthen the pharmacist's advice.

Considering that shoulder pain is a common musculoskeletal disorder in primary care, a systematic review was carried out to evaluate efficacy and safety of ibuprofen. If data allows it, a meta-analyze could be realized to answer the question of efficacy and safety.

This systematic review is part of the REB project (Rebuild the Evidence Base) which aims to re-evaluate the efficacy and safety of pharmacopeia used in primary care (20).

2 MATERIALS AND METHODS

2.1 MAIN OBJECTIVE

The main objective is to evaluate efficacy of oral ibuprofen in shoulder pain compared to placebo and other oral drugs. Efficacy includes : efficiency on pain, variation in degree of pain, time to reach relief, patient's satisfaction, change in quality of life, change in range of motion and other criteria of interest. Secondary objective was to evaluate the safety profile of oral ibuprofen.

2.2 RESEARCH METHODOLOGY

A systematic review, following the PRISMA statement (Appendix I) (21) was carried out up to May 2021. The protocol details were registered on Prospero (CRD 42021271276) (Appendix III). Articles were collected from the following databases : MEDLINE, EMBASE, Cochrane Library.

Inclusion criteria used were : randomized clinical trials (RCT) comparing oral ibuprofen versus placebo and other oral analgesics in shoulder pain, full text available in English or French, age over 18 years old and both genders. To study the symptom “pain feeling”, shoulder pain was defined as gleno-humeral joint pain but also contracture of the neck. We did not include inflammatory pain caused by auto-immun or auto inflammatory diseases and fractures to target diseases accessible to self-medication.

Articles were found thanks to a research equation composed of Mesh words developed with the help of Pinol Nathalie, the librarian of the University of Clermont-Ferrand (Appendix II). Eligibility was assessed by analyzing title and/or abstract then full text independently by two review authors (CL and BM). Any disagreement between them over the eligibility of particular studies was resolved through discussion with a third reviewer (TJ or VRH).

Information of selected studies were extracted and summed up in a narrative description including details of authors, date of publication, type of intervention, population characteristics, sample size and outcomes. Appropriate effect measures were used to summarize the effects of the study interventions and may include hazard ratios (for dichotomous outcomes) or standardized mean differences (for continuous outcomes).

For the third step, two review authors (CL and BM), independently, assessed the risk of bias in included studies using COCHRANE'S TOLL ROB V2 tool (22,23). This tool is structured into a set of domains of bias, focussing on randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome and the selection of the reported outcome. These risks were rated as low, concern, or high for each type of bias and for each outcome. In function of the RCT, a meta-analysis could be realized.

3 RESULTS

3.1 TRIAL SELECTION

The literature search yielded 928 studies after removal duplicates (Fig.1). 908 were excluded because the title or abstract did not meet inclusion criteria. The causes of exclusion were classified into eight categories. Among the twenty articles remaining, six could not be assessed because the full text was not available in English or in French : three trials were in German, one in Italian, one in Japanese and one in Chinese. Three studies were still in process. After reading the eleven remaining, four RCT were included in the qualitative synthesis for quality assessment and for the realization of the systematic review.

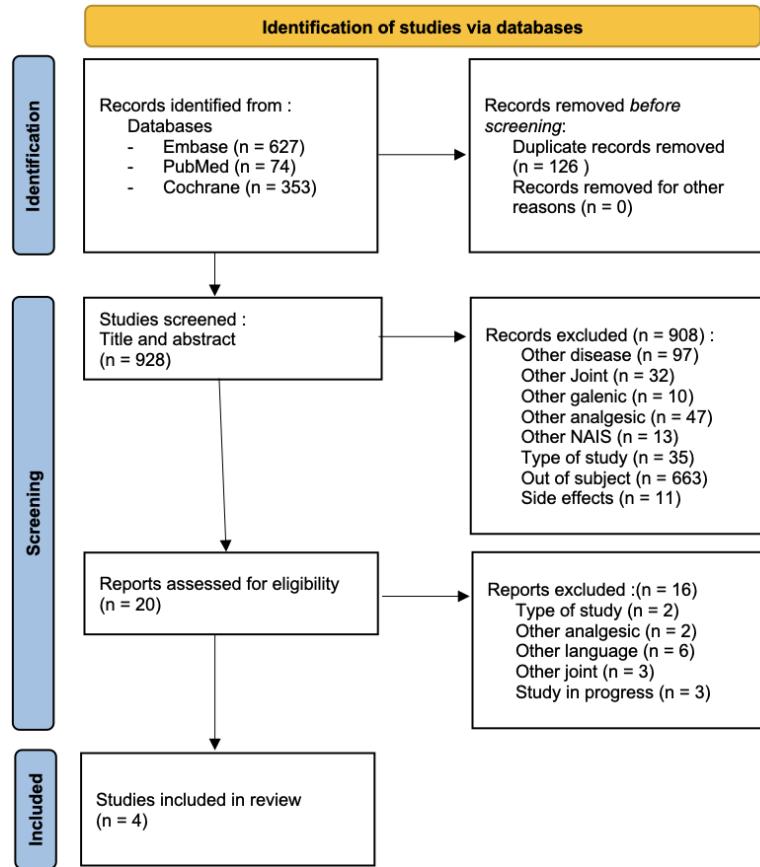


Figure 1. PRISMA 2020 Flow diagram

3.2 STUDIES CHARACTERISTICS

Characteristics of the four trials included in the systematic review are described in table 1. Trials deal with a wide range of pathologies, from rotator cuff shoulder pain, post arthroscopic pain for instability, tendonitis and to periarthritis. Study *Famaey et Ginsberg 1984* (24), besides periarthritis, also explored frozen shoulder, tendonitis and shoulder pain. Each RCT used a different comparative oral molecule : acetaminophen, opioid, ibuprofen and diclofenac. Moreover, time and primary endpoint's evaluation method are specific to each trial. Primary endpoints can be classified into three categories : pain, functional disability and quality of life assessment. For the study *AlRuthia et al. 2019* (22), these three endpoints were evaluated by questionnaires rated from 0 to 100 : Shoulder Pain and disability Index (SPADI), Quick DASH for the function of upper extremity and WHOQOL-BREF for the quality of life. *Thompson et*

al. 2020 (25), evaluated pain by visual analogue scale (VAS) and opioid consumption. Joint function was not represented and quality of life was depicted by patients' satisfaction. Concerning the trial *Friis et al. 1992* (26), the pain was based on the patients' opinion on a five points scale, whereas functional disability was evaluated by doctor's assessment on a three points scale. The article *Famaey et Ginsberg 1984*, did not clearly explain the evaluation method for the different endpoints. They used amplitude rotation and flexion to evaluate articular function. Pain was expressed in degree and the patient's and clinician's feelings were also reported. Quality of life was not represented in these two last articles. Only one RCT, *AlRuthia et al. 2019*, chose to not report side effects (27).

About study protocol the two oldest RCT (24,26), published respectively in 1992 and 1984 were double blinded. Studies *Y. AlRuthia et al* and *Thompson et al.* were more recent but were realized on one or two centers and in an open label.

Table I. Characteristics of the four trials included

First Author, date of publication	Type of study	Articles			Primary endpoint					
		Subject of interest	n= intervention, n= control group	Drug dosage	Age (mean ±SD)	Time and evaluation method	Pain	Function	Quality of life	Side effects
Y. Aruthur et al., 2019	Open-label two center	Shoulder pain to the rotator cuff (RC)	Ibuprofen n=20	Ibuprofen 400-800mg every 6-8h (max 3200mg per day)	39.60 ± 15.93	Three questionnaires before treatment and 6 weeks after therapy	Pain measured by shoulder pain and disability index (SAPDI) (-19.10 ± 29.62; P = 0.01)	Function of the upper extremities (Quick DASH) (-13.41 ± 17.49; P = 0.003)	Quality of life (WHOQOL-BREF)	/
K. Thompson et al., 2021	Single center, non blinded	Postoperative shoulder pain after arthroscopic shoulder for anterior shoulder instability	Acetaminophen n=13	Acetaminophen (500mg PO) every 6-8h can increase to 1000mg PO every 6h	46.15 ± 16.32	No improvement (-15.04 ± 24.91; P = 0.05)	No improvement (-15.04 ± 24.91; P = 0.05)	No significant improvement (8.85 ± 10.67; P = 0.011), environmental health (9.00 ± 12.6; p = 0.025) no significant	Perception of physical (8.85 ± 10.67; P = 0.011), environmental health (9.00 ± 12.6; p = 0.025) psychological and social no significant	/
J. Frails, D. Farmer, B. Toft et al., 1992	7 centers, doubled blind study	Shoulder tendinitis : comparison of two ibuprofen formulation (CI and SRI)	Day 0 CI = Short plasma half-life (n = 74) SRI = Sustained-release formulation (n = 73)	600 mg 4 times a day and 2 placebo tablets twice a day 600 mg twice a day and one placebo tablet 4 times a day	52 (27 - 84)	Day 0: Doctor clinical examination ; Day 21: efficacy measured by patient's opinion, examination, side effects reported by patients	Pain measured by visual analogue scale (VAS)	Patient satisfaction	Incidence of adverse event	/
J. P. Farnday and F. Ginsberg, 1984	Double blind trial	Shoulder pain, Periarthritis, tendinitis and frozen shoulder	Ibuprofen (n = 25) Diclofenac (n = 25)	Ibuprofen 400 mg for 2 weeks Diclofenac 25 mg for 2 weeks	53.6(28.79) 53.1(33.77)	Degree of initial assessment ; Day 7 and 14: assessment treatment efficacy and tolerability	Amplitude of rotation, abduction	Treatment efficacy according to patient and clinician	Treatment tolerability according to both the patient and clinician	/

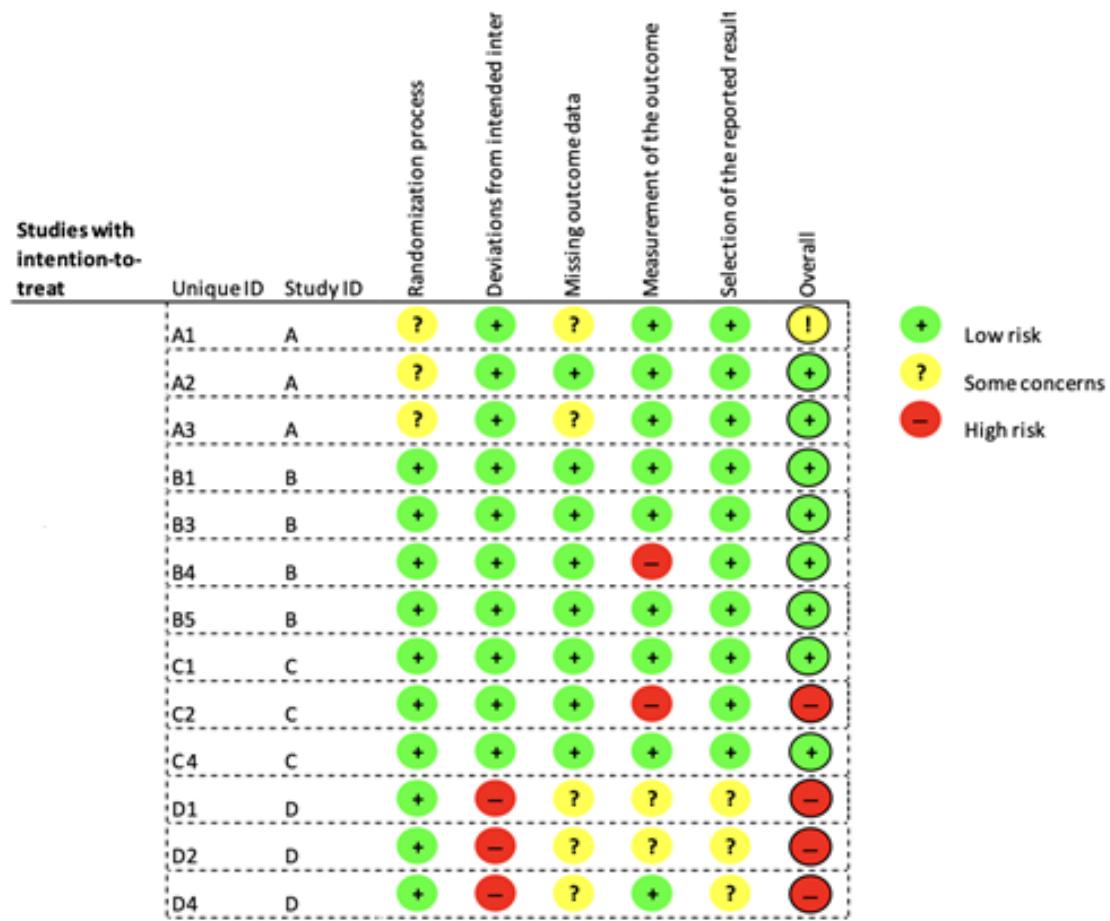
3.3 RISK OF BIAS ANALYSIS

Quality of assessment was focused on internal validity. The risks of bias analysis are summarized in the fig.2. This risk is stratified into three levels : high, some concerns and low.

The study concerning rotator cuff pain *Y. AlRuthia et al* was classified in some concerns because the number of people between the control and intervention group was significantly different.

Study about periarthritis, *Famaey et Ginsberg 1984*, was considered at high risk of bias. Indeed, the primary endpoint and its assessment were not clearly explained so the measuring of the outcome seems to be inappropriate. We had not found any address to contact the authors in order to have more information about the protocol. Missing data were not included in the analysis, the RCT is by the way not in intention to treat. Moreover, some corticosteroid infiltrations were realized and the number of them is different between the two groups. This intervention had not led to supplementary analysis to evaluate its impact on the results.

Two trials, *Thompson et al.* about arthroscopic shoulder instability and *J. Friis et al* tendonitis were judged to bear low risk.



A : AlRuthia and al

B : K. A. Thompson and al

C : J. Friis and al

D : J P Famaey and F Ginsberg

1 : Pain

2 : Functional disability

3 : Quality of life

4 : side effect

5 : medication use

Figure 2. Risk of Bias.

3.4. MAIN AND SECONDARY OUTCOMES

RCT, Y. AlRuthia et al, compared acetaminophen versus ibuprofen in shoulder pain related to rotator cuff with the help of three questionnaires evaluating pain, functional disability and quality of life. It concluded with a significant improvement in the severity of pain evaluated by the SPADI (-19.10 ± 29.62 ; $P=0.01$) and in functional disability evaluated by the Quick-DASH (-17.30 ± 20.54 ; $P=0.002$) and not in the acetaminophen group. However, in the acetaminophen group, there is a significant improvement in physical (8.85 ± 10.67 ; $P=0.011$) and

environmental (9.00 ± 12.68 ; $P=0.025$) health domain in quality of life. Side effects were not recorded.

The RCT, *Thompson et al*, focused on post arthroscopic pain in instability shoulder. In this trial ibuprofen was associated with opioid and compared to opioid only use. Pain was evaluated by a visual analogue scale. After one week of follow-up, there is no significant difference in postoperative analgesia between NSAIDs and opioid only group. The opioid consumption is significantly lower in NSAID group (11.7 versus 7.9 tablets in NSAID group $P=0.05$) after one week of treatment. 35 % of patients reported adverse effects in opioid only group versus 17 % in the other one. Adverse effects recorded were nausea, vomiting and constipation.

The RCT, *J. Friis et al*, worked on tendonitis comparing conventional tablets ibuprofen (600 mg four times a day) with sustained release tablets ibuprofen (1200 mg two times a day). Three weeks of follow-up was conducted and pain was evaluated by the patient with a five points scale. Complete pain relief was significantly higher in conventional tablets (7 % vs 21 % ; $P=0.020$). For these two different formulations, no difference was found in the number of improvements, in physician's assessment and frequency of side effects.

The RCT, *Thompson et al*, compared ibuprofen and diclofenac in periarthritis of the shoulder. At day 0, 7 and 14, pain was measured in degree, efficacy treatment by patient's and clinician's own assessment and functional disability by degrees of amplitude of abduction and rotation. A significant improvement occurred in each group (no data, $P<0.001$) for the five variables. No difference was noted between the two molecules for these variables and for the adverse effects who were in majority gastro-intestinal in nature.

4 DISCUSSION

We conducted a systematic review on the efficacy of oral ibuprofen in shoulder pain, the third common musculoskeletal complaint after low back and knee pain (3).

Four articles were found. The RCT, *Y. AlRuthia et al*, is interesting on two points. This trial worked on ibuprofen and acetaminophen, an antalgic drug widely prescribed and used in self-medication (14). According to the authors, the primary endpoints are measured with standardized scales but were too complicated leading to the exclusion of many people because of misunderstanding. Unfortunately, this exclusion created an imbalance in the size of the two groups, so ibuprofen was not compared with acetaminophen because of a significant difference. Nevertheless, in the ibuprofen group, ibuprofen seems to be efficient on pain and functional disability. This improvement was not found in the acetaminophen group, but the quality of life appears to be better probably because of a better tolerability even if side effects were not reported.

The trial *Thompson et al* differs from the others because it studies postoperative pain. The conclusion is interesting concerning pain management and self-medication because patients were authorized to take another antalgic. The trial showed that NSAIDs could limit opioid consumption. In RCT *J. Friis et al* adverse effects and number of improvements are similar in the groups of conventional and sustained-release ibuprofen tablets but the study was conducted per protocol. For the last one, *Thompson et al*, diclofenac and ibuprofen seem to be identical but there is too much missing data to conclude. The risk of bias is important because the number of corticosteroid injections were not similar in each group and this difference was not considered in statistical analysis.

Strength and limits :

To our knowledge this review is the first one evaluating efficacy of oral ibuprofen on shoulder pain. To be closed to practice, it was important to start the study from the symptom “pain” instead of a pathology because that is real life. A patient centered approach is wanted by the patient (28) and thesis in general medicine try to answer to this request (29). We wanted to explore patient feeling, if the pain or the functionality was relieved whatever was the diagnostic. Although a high prevalence in general practice, few articles were found. Several reasons can explain this lack of articles. Selection criteria were strict to guarantee the quality of the study. We focus only on one NSAIDs compared to gold standard or placebo which limited the review.

Six articles were excluded because of the language : three in German, one in Italian, one in Chinese and one in Japanese published between 1973 and 1995. The Japanese RCT could have been interesting, it was a double-blind trial about ibuprofen efficacy on neck-shoulder arm and scapula-humeral periarthritis. This RCT, may have allowed us to conduct a meta-analysis. This is also the case for the Chinese RCT dealing with arthroscopic postoperative pain and efficacy of different NSAIDs. Also, some articles can be missing. The grey literature was not taken into account and a publication bias is possible.

Concerning our four articles included in our review, the methodological quality was variable and population size was limited. For instance, two studies working only on one or two centers. The randomized controlled trials were very heterogeneous. Shoulder pain included many diseases, complicating the comparison of the articles. The comparative drugs were not identical in each study and placebo was never used. Moreover, time and evaluation criteria (pain and functional disabilities) were very different and do not permit conducting a meta-analysis.

Comparison with literature :

In 2015, a meta-analysis in shoulder pain was realized comparing steroid injections versus NSAIDs, more specifically diclofenac and naproxen tablets (30). A significant functional improvement in favour of corticosteroid injection was found. Concerning the pain, no difference was found between these different treatments. Another meta-analysis also suggested the efficacy of corticosteroid injection in rotator cuff tendonitis (31). However, these two meta-analyses and several reviews (32,33) highlighted the need to conduct more quality studies in front of the poor quality of the literature on this domain. Difficult to access in primary care, corticosteroid injections appear to be the most efficient. This well known efficacy could be a limitation to conduct RCT about oral drug.

There is a wide range of NSAIDs used in shoulder or osteo-articular pain. Ibuprofen is not the most prescribed, making it probably less interesting to study and specially following COX 2 selective NSAIDs apparition (34).

In contrast with other joints like knee, hip and low back, the shoulder pain seems to be the least studied. A meta-analysis tried to evaluate the different NSAIDs in hip and knee pain (35). Diclofenac was the most effective, but the risk of bias was high. However, another systematic review did not find any difference between them (36). These results emphasize the need to carry out high quality research to improve prescription about rheumatology in primary care.

Finally, the main purpose of the systematic review was to study a common drug prescribed in primary care for shoulder pain. Despite the high prevalence, very few articles were found, our review does not permit us to conduct a meta-analysis. These results are in accordance with other systematic reviews with a similar purpose to study the pharmacopeia of the general physician (37,38). The prescription in primary care is not based on solid evidence of efficacy. In the literature studies about shoulder pain, focused mainly on corticosteroid injections, often a

second line treatment in general physician practices. Most scientific studies are not adapted for primary care. There is a real need to study more rigorously treatments used in this practice, especially those accessible in self-medication as ibuprofen to better patient care in accordance with an evidence-based prescription. In scientific literature, “old treatments” although frequently prescribed, are forsaken in favor of new treatments and consequently not really adapted to general physician practice even if they represent half of all doctors. It could be interesting to study different NSAIDs and to focus on only one shoulder injury. A crossing-over trial could be adapted comparing two NSAIDs.

5 CONCLUSION

This systematic review explored the efficacy of oral ibuprofen in shoulder pain. The guidelines recommend NSAIDs or acetaminophen for the management of shoulder pain without superiority of one of them. The few RCT found were very heterogeneous, therefore, a meta-analysis could not be conducted. This review highlights the interest to explore more rigorously the efficacy of the drugs of pain shoulder pharmacopeia in general medicine to improve evidence based medicine practice.

Le doyen de l'UFR de médecine

Le président du Jury

Pr P VIGUION ,
D.Y.

Pierre CLAVELOU
Doyen-Directeur



6 BIBLIOGRAPHIC REFERENCES

1. Bot S, van der Waal JM, Terwee C, van der Windt DAWM, Schellevis F, Bouter L, et al. Incidence and prevalence of complaints of the neck and upper extremity in general practice. Ann Rheum Dis. janv 2005;64(1):118-23.
2. Luime JJ, Koes BW, Hendriksen IJM, Burdorf A, Verhagen AP, Miedema HS, et al. Prevalence and incidence of shoulder pain in the general population; a systematic review. Scand J Rheumatol. 2004;33(2):73-81.
3. Urwin M, Symmons D, Allison T, Brammah T, Busby H, Roxby M, et al. Estimating the burden of musculoskeletal disorders in the community: the comparative prevalence of symptoms at different anatomical sites, and the relation to social deprivation. Ann Rheum Dis. nov 1998;57(11):649-55.
4. OMG - Top 50 des RC [Internet]. 2021 [cité 10 déc 2021]. Disponible sur: <http://omg.sfm.org/content/donnees/top25.php>
5. Ramponi DR. Shoulder Pain. Adv Emerg Nurs J. avr 2011;33(2):114-26.
6. TMS : définition et impact [Internet]. 2022 [cité 13 mars 2022]. Disponible sur: <https://www.ameli.fr/entreprise/sante-travail/risques/troubles-musculosquelettiques-tms/tms-definition-impact>
7. TMS_3.pdf [Internet]. [cité 22 mars 2022]. Disponible sur: https://travail-emploi.gouv.fr/IMG/pdf/TMS_3.pdf
8. Roquelaure Y, Ha C, Leclerc A, Touranchet A, Mariot C, Imbernon E, et al. Troubles musculo-squelettiques en France : données du réseau pilote de surveillance épidémiologique dans les entreprises des Pays de la Loire en 2002 et 2003. Santé Société Solidar.

2006;5(2):35-43.

9. Andersson GBJ. The burden of musculoskeletal diseases in the United States prevalence, societal and economic cost. Rosemont, IL: American Acad. of Orthopaedic Surgeons; 2008.
10. Dorrestijn O, Greving K, van der Veen WJ, van der Meer K, Diercks RL, Winters JC, et al. Patients with shoulder complaints in general practice: consumption of medical care. *Rheumatology*. 1 févr 2011;50(2):389-95.
11. Petri M, Dobrow R, Neiman R, Whiting-O'keefe Q, Seaman WE. Randomized, double-blind, placebo-controlled study of the treatment of the painful shoulder. *Arthritis Rheum*. 1987;30(9):1040-5.
12. Mariasiewiez T. Prise en charge diagnostique et thérapeutique des tendinopathies de la coiffe des rotateurs, en médecine générale, en Seine-Maritime. :187.
13. Doiron-Cadrin P, Lafrance S, Saulnier M, Cournoyer É, Roy J-S, Dyer J-O, et al. Shoulder Rotator Cuff Disorders: A Systematic Review of Clinical Practice Guidelines and Semantic Analyses of Recommendations. *Arch Phys Med Rehabil*. juill 2020;101(7):1233-42.
14. Wilcox CM, Cryer B, Triadafilopoulos G. Patterns of use and public perception of over-the-counter pain relievers: focus on nonsteroidal antiinflammatory drugs. *J Rheumatol*. nov 2005;32(11):2218-24.
15. 2020-02-03-Baromètre-Afipa-du-Selfcare-2019-VERSION-FINALE.pdf [Internet]. [cité 22 mars 2022]. Disponible sur: <https://neres.fr/wp-content/uploads/2020/02/2020-02-03-Barom%C3%A8tre-Afipa-du-Selfcare-2019-VERSION-FINALE.pdf>
16. Hernández-Díaz S, García-Rodríguez LA. Epidemiologic assessment of the safety of

conventional nonsteroidal anti-inflammatory drugs. Am J Med. févr 2001;110(3):20-7.

17. Ibuprofen Interferes with the Efficacy of Antihypertensive Drugs: A Randomized, Double-Blind, Placebo-Controlled Trial of Ibuprofen Compared with Acetaminophen: Annals of Internal Medicine: Vol 107, No 5 [Internet]. 2021 [cité 7 déc 2021]. Disponible sur: <https://www.acpjournals.org/doi/10.7326/0003-4819-107-5-628>
18. Ibuprofène et grossesse : un français sur deux ignore sa toxicité [Internet]. OFMA. 2022 [cité 18 mars 2022]. Disponible sur: <http://www.ofma.fr/sondage-ibuprofene-douleur-grossesse-femme/>
19. Matoulková P, Dosedel M, Růžková B, Kubena A. Information and awareness concerning ibuprofen as an ingredient in over the counter analgesics: a questionnaire-based survey of residents of retirement communities. Acta Pol Pharm. avr 2013;70(2):333-8.
20. Boussageon R, Huas C, Rat C, Pouchain D, Renard V, Supper I, et al. Reconstruire l’Evidence Based pour une décision médicale partagée. Evaluation de l’efficacité et de la sécurité des médicaments fondée sur une revue systématique des essais cliniques randomisés et des méta-analyses. exercer. 1 janv 2017;90-4.
21. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. The BMJ. 29 mars 2021;372:n71.
22. Higgins JP, Sterne JA, Savovic J, Page MJ, Hróbjartsson A, Boutron I, et al. A revised tool for assessing risk of bias in randomized trials. Cochrane Database Syst Rev. 2016;10(Suppl 1):29-31.
23. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a

revised tool for assessing risk of bias in randomised trials. BMJ. 28 août 2019;366:14898.

24. Famaey JP, Ginsberg F. Treatment of periarthritis of the shoulder: a comparison of ibuprofen and diclofenac. J Int Med Res. 1984;12(4):238-43.
25. Thompson KA, Klein D, Alaia MJ, Strauss EJ, Jazrawi LM, Campbell KA. Opioid Use Is Reduced in Patients Treated with NSAIDs After Arthroscopic Bankart Repair: A Randomized Controlled Study. Arthrosc Sports Med Rehabil. févr 2021;3(1):e15-22.
26. Friis J, Jarner D, Toft B, Christensen K, Christophersen J, Ibfeldt HH, et al. Comparison of two ibuprofen formulations in the treatment of shoulder tendonitis. Clin Rheumatol. mars 1992;11(1):105-8.
27. AlRuthia Y, Alghadeer S, Balkhi B, Almalag HM, Alsobayel H, Alodaibi F, et al. Efficacy of acetaminophen versus ibuprofen for the management of rotator cuff-related shoulder pain: Randomized open-label study. Saudi Pharm J SPJ Off Publ Saudi Pharm Soc. sept 2019;27(6):882-8.
28. Little P, Everitt H, Williamson I, Warner G, Moore M, Gould C, et al. Preferences of patients for patient centred approach to consultation in primary care: observational study. BMJ. 24 févr 2001;322(7284):468-72.
29. Carrier H, Agrifoglio G, Genin G, Lecorff J, Montredon C, Casanova L, et al. Médecine générale, une discipline centrée patient, une recherche centrée médecin : un paradoxe ? A propos des thèses d'exercice General practice, a patient-centered discipline, a physician-centered research : a paradox ? About doctoral theses. 1 oct 2019;
30. Sun Y, Chen J, Li H, Jiang J, Chen S. Steroid Injection and Nonsteroidal Anti-inflammatory Agents for Shoulder Pain. Medicine (Baltimore). 18 déc 2015;94(50):e2216.

31. Arroll B, Goodyear-Smith F. Corticosteroid injections for painful shoulder: a meta-analysis. *Br J Gen Pract.* 1 mars 2005;55(512):224-8.
32. van der Heijden GJ, van der Windt DA, Kleijnen J, Koes BW, Bouter LM. Steroid injections for shoulder disorders: a systematic review of randomized clinical trials. *Br J Gen Pract J R Coll Gen Pract.* mai 1996;46(406):309-16.
33. Green S, Buchbinder R, Glazier R, Forbes A. Systematic review of randomised controlled trials of interventions for painful shoulder: selection criteria, outcome assessment, and efficacy. *BMJ.* 31 janv 1998;316(7128):354-60.
34. McGettigan P, Henry D. Use of Non-Steroidal Anti-Inflammatory Drugs That Elevate Cardiovascular Risk: An Examination of Sales and Essential Medicines Lists in Low-, Middle-, and High-Income Countries. Turnbull FM, éditeur. *PLoS Med.* 12 févr 2013;10(2):e1001388.
35. Costa BR da, Reichenbach S, Keller N, Nartey L, Wandel S, Jüni P, et al. Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis. *The Lancet.* 8 juill 2017;390(10090):e21-33.
36. Chou R, McDonagh MS, Nakamoto E, Griffin J. Analgesics for Osteoarthritis: An Update of the 2006 Comparative Effectiveness Review [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2011 [cité 18 mars 2022]. (AHRQ Comparative Effectiveness Reviews). Disponible sur: <http://www.ncbi.nlm.nih.gov/books/NBK65646/>
37. Blanchard C, Pouchain D, Vanderkam P, Perault-Pochat M-C, Boussageon R, Vaillant-Roussel H. Efficacy of phloroglucinol for treatment of abdominal pain: a systematic review of literature and meta-analysis of randomised controlled trials versus placebo. *Eur J Clin Pharmacol.* mai 2018;74(5):541-8.

38. Vanderkam P, Blanchard C, Naudet F, Pouchain D, Vaillant Roussel H, Perault-Pochat MC, et al. Efficacy of acetylleucine in vertigo and dizziness: a systematic review of randomised controlled trials. Eur J Clin Pharmacol. mai 2019;75(5):603-7.

ANNEX I. PRISMA 2020 CHECKLIST: EVIDENCE-BASED MINIMUM SET OF ITEMS FOR REPORTING IN SYSTEMATIC REVIEWS AND META-ANALYSES

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	

Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	
Study characteristics	17	Cite each included study and present its characteristics.	
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	
	23b	Discuss any limitations of the evidence included in the review.	
	23c	Discuss any limitations of the review processes used.	
	23d	Discuss implications of the results for practice, policy, and future research.	
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	
Competing interests	26	Declare any competing interests of review authors.	
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

ANNEX II. MESH WORD EQUATION

"ibuprofen"[MeSH Terms] OR "nuprin"[Text Word] OR "advil"[Text Word] OR "trauma-dolgit gel"[Text Word] OR "trauma-dolgit gel"[Text Word] OR "ip-82"[Text Word] OR "brufen"[Text Word] OR "motrin"[Text Word] OR "alpha methyl 4 2 methylpropyl benzeneacetic acid"[Text Word] OR "ibumetin"[Text Word] OR "ibuprofen"[Text Word] OR "ip82"[Text Word] OR "rufen"[Text Word] OR "nurofen"[Text Word]

AND

"shoulder"[MeSH Terms] OR "Shoulder Injuries"[MeSH Terms] OR "shoulder pain"[MeSH Terms] OR "shoulders"[Text Word] OR "shoulder"[Text Word] OR "slap tear"[Text Word] OR "tear slap"[Text Word] OR "tears slap"[Text Word] OR "superior labrum from anterior to posterior injuries"[Text Word] OR "slap tears"[Text Word] OR "rotator cuff"[MeSH Terms] OR "teres minor"[Text Word] OR "supraspinatus"[Text Word] OR "subscapularis"[Text Word] OR "rotator cuff"[Text Word] OR "rotator cuffs"[Text Word] OR "infraspinatus"[Text Word] OR "cuff rotator"[Text Word] OR "cuff tear arthropathy"[Text Word] OR "bursitis"[MeSH Terms] OR "bursitis"[Text Word] OR "bursal synovitis"[Text Word] OR "inflammation of bursa"[Text Word] OR "capsulitis"[Text Word] OR "bursitides"[Text Word] OR "shoulder dislocation"[MeSH Terms] OR "subluxation glenohumeral"[Text Word] OR "glenohumeral subluxations"[Text Word] OR "dislocation glenohumeral"[Text Word] OR "dislocations glenohumeral"[Text Word] OR "dislocation glenoid"[Text Word] OR "dislocation glenohumeral joint"[Text Word] OR "dislocation glenohumeral joint"[Text Word] OR "glenohumeral subluxation"[Text Word] OR "glenohumeral dislocation"[Text Word] OR "glenohumeral dislocations"[Text Word] OR "glenohumeral dislocation"[Text Word] OR "subglenoid dislocation"[Text Word] OR "dislocations glenohumeral"[Text Word] OR "shoulder joint"[MeSH Terms] OR "joint glenohumeral"[Text Word] OR "glenohumeral joints"[Text Word] OR "joints glenohumeral"[Text Word] OR "labrum glenoid"[Text Word] OR "glenohumeral joint"[Text Word] OR "glenoid labrum"[Text Word] OR "Rotator Cuff Injuries"[MeSH Terms] OR "labral tears glenoid"[Text Word] OR "glenoid labral tears"[Text Word] OR "glenoid labral tear"[Text Word] OR "tears glenoid labral"[Text Word] OR "shoulder impingement syndrome"[MeSH Terms] OR "internal impingement syndromes"[Text Word] OR "internal impingement syndrome"[Text Word] OR "syndrome subacromial impingement"[Text Word] OR "posterosuperior glenoid impingement"[Text Word] OR "outlet impingement"[Text Word] OR "subacromial impingement syndrome"[Text Word] OR "impingement posterosuperior glenoid"[Text Word] OR "coracohumeral impingement"[Text Word] OR "impingement syndrome subacromial"[Text Word] OR "coracoid impingement syndrome"[Text Word] OR "outlet impingement syndrome"[Text Word] OR "subacromial impingement"[Text Word] OR "torticollis"[MeSH Terms] OR "torticollis"[Text Word] OR "contracture of neck"[Text Word] OR "head tilt"[Text Word] OR "head tilted"[Text Word] OR "tilted head"[Text Word] OR "loxia"[Text Word] OR "dystonia cervical"[Text Word] OR "cervical dystonia"[Text Word] OR "head tilting"[Text Word] OR "cervical dystonias"[Text Word] OR "neck torsion"[Text Word] OR "wryneck"[Text Word] OR "wry neck"[Text Word] OR "superficial back muscles"[MeSH Terms] OR "rhomboideus major"[Text Word] OR "superficial back muscles"[Text Word] OR "rhomboid minor"[Text Word] OR "rhomboideus major muscle"[Text Word] OR "levator scapulae"[Text Word] OR "rhomboid major"[Text Word] OR "levator scapulae muscle"[Text Word] OR "rhomboid minors"[Text Word] OR "muscle trapezius"[Text Word] OR "latissimus dorsi"[Text Word] OR "scapulae levator"[Text Word] OR "rhomboideus minor"[Text Word] OR "rhomboid minor muscle"[Text Word] OR "rhomboid major muscle"[Text Word] OR "trapezius"[Text Word] OR "trapezius muscle"[Text Word] OR "muscles trapezius"[Text Word] OR "latissimus dorsi muscle"[Text Word] OR "rhomboideus minor muscle"[Text Word] OR "superficial back muscle"[Text Word] OR "rhomboid majors"[Text Word] OR "trapezius muscles"[Text Word]

ANNEX III. PROSPERO

Review question

Efficacy and safety of oral ibuprofen in shoulder pain in adults.

Searches The sources will be free access databases: Embase, Cochrane Library, PubMed/MEDLINE, and clinical trials? All studies in English and in French will be used.

Types of study to be included

Randomized controlled trials

Condition or domain being studied

Shoulder pain covers gleno humeral joint and neck contracture. Are excluded inflammatory pain caused by auto immun or auto inflammatory disease, [cancer pain](#), ([pain related to diagnosis or therapeutic procedure?](#)) and fractures [or dislocation](#)?

Participants/population

Inclusion criteria: ages over 18, both gender

Exclusion criteria: children, [patients diagnosed](#) Auto immun or auto inflammatory disease or [cancer or fractures/dislocation](#)

Intervention(s), exposure(s)

Comparison of oral ibuprofen with Placebo and [other analgesic](#)

Main outcome(s)

Efficacy:

Change in degree of pain,

[Time to pain relief](#)

Satisfaction

Change in quality of life

Change in functional articular amplitude

And other outcomes of interest

Tolerance : type, frequency of side effect

Analysis of subgroups or subsets

[Efficacy of ibuprofen in shoulder pain](#)

Data extraction (selection and coding)

Titles and/or abstracts of studies retrieved using the search strategy will be screened independently by two review authors to identify studies that potentially meet the inclusion criteria outlined above. The full text of these potentially eligible studies will be retrieved and independently assessed for eligibility by two review team members (CL and BM). Any disagreement between them over the eligibility of particular studies will be resolved through discussion with a third reviewer (TJ or HVR). Extracted information will include: study setting; study population and participant demographics and baseline characteristics; details of the intervention and control conditions; study methodology; recruitment and study completion rates; outcomes International prospective register of systematic reviews and times of measurement; indicators of acceptability to users; suggested mechanisms of intervention action; information for assessment of the risk of bias. Two review authors (CL and BM) will extract data independently, discrepancies will be identified and resolved through discussion (with a third author where necessary, TJ or HVR). Missing data will be requested from study authors.

Risk of bias (quality) assessment

Two review authors (CL and BM) will independently assess the risk of bias in included studies using Cochrane's tool by considering the following characteristics:

- Selection bias: sequence generation and allocation concealment
- Performance bias: blinding of participants and personnel.
- Detection bias: blinding of outcome assessment
- Attrition bias: incomplete outcome data.
- Reporting bias: selective reporting
- Other potential biases

Strategy for data synthesis

A narrative description of the included studies will detail the type of intervention, population characteristics and outcomes. Appropriate effect measures will be used to summarise the effects of the study interventions and may include risk ratios (for dichotomous outcomes) or standardised mean differences (for continuous outcomes). If the data allow, we intend to conduct a meta-analysis. This meta-analysis will take into consideration an assessment of heterogeneity and the need for sensitivity analyses. We will use the GRADE system to classify the quality of evidence in one of four levels—high, moderate, low, and very low. Analysis of subgroups or subsets No investigation of subgroups is planned.

SERMENT D'HIPPOCRATE

Au moment d'être admis(e) à exercer la médecine, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité.

Mon premier souci sera de rétablir, de préserver ou de promouvoir la santé dans tous ses éléments, physiques et mentaux, individuels et sociaux.

Je respecterai toutes les personnes, leur autonomie et leur volonté, sans aucune discrimination selon leur état ou leurs convictions. J'interviendrai pour les protéger si elles sont affaiblies, vulnérables ou menacées dans leur intégrité ou leur dignité. Même sous la contrainte, je ne ferai pas usage de mes connaissances contre les lois de l'humanité.

J'informerai les patients des décisions envisagées, de leurs raisons et de leurs conséquences. Je ne tromperai jamais leur confiance et n'exploiterai pas le pouvoir hérité des circonstances pour forcer les consciences.

Je donnerai mes soins à l'indigent et à quiconque me les demandera. Je ne me laisserai pas influencer par la soif du gain ou la recherche de la gloire.

Admis(e) dans l'intimité des personnes, je tairai les secrets qui me seront confiés. Reçu(e) à l'intérieur des maisons, je respecterai les secrets des foyers et ma conduite ne servira pas à corrompre les mœurs.

Je ferai tout pour soulager les souffrances. Je ne prolongerai pas abusivement les agonies. Je ne provoquerai jamais la mort délibérément.

Je préserverai l'indépendance nécessaire à l'accomplissement de ma mission. Je n'entreprendrai rien qui dépasse mes compétences. Je les entretiendrai et les perfectionnerai pour assurer au mieux les services qui me seront demandés.

J'apporterai mon aide à mes confrères ainsi qu'à leurs familles dans l'adversité.

Que les hommes et mes confrères m'accordent leur estime si je suis fidèle à mes promesses ; que je sois déshonoré(e) et méprisé(e) si j'y manque.

SERMENT D'HIPPOCRATE

En présence des Maitres de cette FACULTE et de mes chers CONDISCIPLES, je promets et je jure d'être fidèle aux lois de l'Honneur et de la Probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuits à l'indigent et je n'exigerai jamais un salaire au-dessus de mon travail. Admis dans l'intérieur des maisons, mes yeux ne verront pas ce qui s'y passe, ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les mœurs ni à favoriser le crime.

Respectueux et reconnaissant envers mes MAÎTRES, je rendrai à leurs enfants l'instruction que j'ai reçu de leurs pères.

Que les HOMMES m'accordent leur estime si je suis fidèle à mes promesses. Que je sois couvert d'OPPROBRE et méprisé de mes confrères si j'y manque.

Efficacy of oral Ibuprofen in shoulder pain : a systematic review of randomized controlled trials

Abstract :

BACKGROUND : Shoulder pain is a common reason for consultation in primary care and leads in 74 % of cases to an oral NSAIDs prescription. Ibuprofen is a widely used NSAID and is also accessible to self medication, which raises questions about its benefits/risks of its use.

PURPOSE : Assess efficacy of oral Ibuprofen in shoulder pain.

METHODS : A systematic review was carried out up to August 2021. It selected randomized controlled trials (RCT) comparing the efficacy of oral Ibuprofen with placebo or other antalgic drugs in shoulder pain. Efficacy including : efficiency on pain, variation in degree of pain, time to reach relief, patient's satisfaction, change in quality of life, change in range of motion. Were not included studies concerning inflammatory pain caused by auto-immun or auto inflammatory diseases and fractures.

RESULTS : Four RCT were included and analyzed for risk of bias. Outcomes measurement, pathologies and antalgic drugs interventions were too heterogeneous to conduct a meta-analysis. One RCT found that Ibuprofen leads to pain and functional disability improvement versus Acetaminophen in rotator cuff pain with a moderate risk of bias. Another one found no significant difference between Ibuprofen and Diclofenac in shoulder periarthritis with a high risk of bias. Lastly, a RCT with low risk of bias, did not find any difference in improvement between conventional and sustained release ibuprofen tablets.

CONCLUSION : Although Ibuprofen is widely prescribed in primary care, there is no solid evidence of its efficacy on shoulder pain.

Keywords :

- Shoulder pain
- Ibuprofen
- NSAIDs
- Randomized controlled trial
- Evidence-based health care