It has been suggested that there has been no major advance in local anaesthetic pharmacology impacting on clinical practice in more than 60 yr since the development of racemic bupivacaine.\(^1\) This is perhaps why there is great interest in the use of adjuvant drugs in combination with local anaesthetics for peripheral regional anaesthesia. This interest is reflected in the large number of studies on this topic published in recent years. Dexamethasone is one of the most promising drugs to increase the efficacy of peripheral regional anaesthesia, and meta-analyses suggest there may be a benefit.\(^2\) However, it should be noted that these meta-analyses did not explore whether dexamethasone administered with the local anaesthetic mixture had a greater effect than i.v. dexamethasone administered concurrently with the peripheral nerve block. This issue of the British Journal of Anaesthesia includes two meta-analyses, in which the use of dexamethasone as a perineural additive to local anaesthetics is compared with the i.v. administration of dexamethasone.\(^5,6\) Both meta-analyses follow standardized protocols generated from international consensus statements. One might have expected the results and conclusions from these two papers to be almost identical and lacking controversy. The fact that this is not the case has implications both for interpretation of these papers, but also emphasizes the limitations of the meta-analyses in general.

Systematic review with meta-analysis (SRMA) is often considered to represent the highest standard of clinical evidence, and has become widespread as a result of the widespread availability of information technology. There are two distinct components: a structured literature search known as a systematic review, and the mathematical treatment of the results to provide an effect size or summary statistic with an estimate of the likely precision, known as meta-analysis. Of the two components, one might envisage that the systematic review is most likely to produce consistent results, but the numbers of included studies and subjects are different (10 vs 11 included articles; 783 vs 914 included subjects) in the SRMAs of Baeriswyl and colleagues\(^5\) and Heesen and colleagues,\(^6\) whilst only eight studies appear in both. The assessment of the risk of bias for two of the studies included in both SRMAs (Kawanishi and colleagues\(^7\) and Rosenfeld and colleagues\(^8\)) suggests subjectivity in these assessments. According to the review by Heesen and colleagues,\(^6\) the publications by Kawanishi and colleagues\(^7\) and Rosenfeld and colleagues\(^8\) have a low risk of bias in all categories, whereas Baeriswyl and colleagues\(^5\) identified a high or unknown risk of selection, performance, detection, and attrition bias for these studies.

Baeriswyl and colleagues\(^5\) and Heesen and colleagues\(^6\) have also adopted different approaches to the statistical heterogeneity they identified. Although statistical software has made it much easier for the novice investigator to deal with statistical heterogeneity, many fail to understand that this does not necessarily deal with the more important issue of heterogeneity between studies in how they were conducted, especially with respect to patient population and the definition, measurement, and recording of research outcomes. Heesen and colleagues\(^6\) chose not to qualify the difference in outcomes they reported despite the high degree of heterogeneity (some authorities recommend not reporting meta-analysis results when high levels of statistical heterogeneity are found), but did summarize the differences in methodology between the studies they
evaluated (e.g. type of block; type, volume, and concentration of local anaesthetic; use of epinephrine-containing local anaesthetic or not; dose of dexamethasone; use of additional general or spinal anaesthesia; type of surgery; and method of determining duration of analgesia). Baeriswyl and colleagues, on the other hand, attempted to explore the cause of the heterogeneity, and found that the statistical heterogeneity could be eliminated by including only those studies where bupivacaine was used. It should be noted, however, that there were only five evaluable studies where bupivacaine was used, and the clinical and methodological variabilities between these (as detailed by Heesen and colleagues) were not apparent in the measure of statistical heterogeneity that they used. Furthermore, in another recently published meta-analysis on the same topic, the authors presented a different subgroup analysis, and concluded that perineural dexamethasone only prolonged the duration of peripheral nerve block when given with epinephrine-containing local anaesthetics. It is interesting that three of the five studies in the bupivacaine subgroup of Baeriswyl and colleagues used bupivacaine with epinephrine.

Despite the recommended methodology for performing SRMAs, it can be seen that there is considerable potential for subjectivity on the part of the authors in selection bias, file-drawer bias, errors in data entry, and the handling of statistical heterogeneity. Perhaps reviewers and editors have become too easily entranced by the structured and apparently quasi-scientific presentation of these reviews, which should be simply viewed as tools to synthesize and present the current body of evidence. Our concern is that journals are publishing too many SRMAs, and this might be at the expense of original clinical trials and experimental research. Clinical trials and experimental research that generate original data are becoming increasingly difficult to do because of bureaucracy and declining governmental research funding, such that young researchers may sense that SRMA is the only realistic route for them to generate peer-review publications. Journal editors may be complicit, as meta-analyses tend to be more highly cited than original research, and are thus more likely to benefit journal citation metrics.

So, what should be the role of SRMA? Technically, all researchers performing experimental and clinical research should be able to perform SRMAs, as this is an excellent way to synthesize current evidence when justifying proposed research in a grant application or ethical approval submission. Similarly, when reporting the results of an original research study or clinical trial, the results of a SRMA could contribute to the rationale for the research. How much new information is being provided by the research could then be assessed by using its results to update the SRMA reported in the Introduction with the new estimates in the Discussion section of the primary research article.

Meanwhile, what should we conclude about the efficacy of perineural vs systemic dexamethasone in combination with local anaesthetic peripheral nerve blocks? Despite both Baeriswyl and colleagues and Heesen and colleagues reporting prolongation of effect of peripheral nerve block when perineural is compared with i.v. dexamethasone (only with bupivacaine in the case of Baeriswyl and colleagues), both authors comment that the effect size is relatively small, and that the overall quality of the original trials is only moderate or low according to the Grades of Recommendation Assessment, Development and Evaluation (GRADE) system. They, therefore, urge caution in the off-label use of perineural dexamethasone. We would go further and suggest that the quality and clinical heterogeneity of published clinical trials preclude any recommendation. Furthermore, rather than suggesting that the current equipoise be interrogated with further clinical trials, perhaps it would be best to establish with greater scientific rigour in the setting of controlled volunteer studies, whether perineural dexamethasone does indeed prolong nociceptive peripheral nerve conduction block in humans.

Authors’ contributions

Design, conceptualisation, and drafting: all authors.

Declaration of interest

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