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## L26/P-896 Electrical versus chemical oocyte activation in assisted reproduction: A systematic review of clinical effectiveness, safety, and neonatal outcomes following fertilisation failure

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**Study question:** Does electrical oocyte activation (EOA) offer a comparable alternative to calcium ionophores in terms of fertilisation, pregnancy rates, and offspring safety?

**Summary answer:** EOA demonstrates clinical equivalence to calcium ionophores, providing a safe and effective non-chemical methodology for overcoming oocyte activation deficiency while mitigating regulatory and chemical concerns.

**What is known already:** Total fertilisation failure (TFF) in ICSI cycles, often attributed to oocyte activation deficiency, remains a significant clinical challenge. Artificial oocyte activation (AOA) using calcium ionophores like ionomycin has established efficacy in improving fertilisation and embryo development. Despite reassuring safety data from over a decade of child follow-up, concerns regarding chemical exposure and varying international regulatory restrictions persist. Electrical oocyte activation (EOA) presents a physical alternative that simulates physiological calcium oscillations. However, comparative evidence synthesising the efficacy and safety of EOA against established chemical methods remains limited, necessitating a comprehensive systematic review.

**Study design, size, duration:** A systematic review followed PRISMA guidelines, searching PubMed and Embase through August 2025. The study included 27 reports ($n > 4,700$ cycles) comprising 19 studies on calcium ionophores and 8 on EOA. Eligible studies were RCTs and cohorts reporting AOA in cycles complicated by TFF, globozoospermia, or PLCζ deficiency. Risk of bias was evaluated using Cochrane RoB2 and Newcastle-Ottawa tools, focusing on fertilisation, pregnancy, and neonatal health as primary outcomes.

**Participants/materials, setting, methods:** The analysis compared clinical outcomes from patients undergoing ICSI-AOA using either chemical ionophores (ionomycin, A23187) or electrical pulses (EOA). Data extraction prioritised fertilisation rates, blastulation, and long-term offspring health. EOA protocols were assessed for their ability to induce activation without chemical media. Statistical significance was verified through study-specific p-values, with a focus on the relative efficacy of EOA in diverse clinical settings including low-fertilisation cases and specific male factor pathologies.

**Main results and the role of chance:** Chemical activation using ionomycin and A23187 consistently enhanced fertilisation by 20–40% relative to controls, with clinical pregnancy rates reaching 57%. Robust follow-up data from over 600 children across ten years indicated no significant increase in congenital anomalies. EOA demonstrated significant clinical promise, achieving fertilisation rates between 70% and 80%, compared to 50–55% in non-activated control groups ($p < 0.05$).

Embryo development and pregnancy outcomes following EOA were broadly comparable to ionophore-based cycles. Specifically, EOA protocols utilising delayed activation provided incremental benefits in blastocyst quality. Offspring data for EOA, while more limited in volume than ionophore cohorts, reported no adverse neonatal outcomes. These findings suggest that electrical stimulation provides a potent, non-chemical alternative to achieve oocyte triggers. The data indicate that EOA performance is not merely an adjunct but a primary activation strategy that matches the fertilisation potential of ionomycin. While individual study variability was noted, the collective evidence reinforces EOA as a robust methodology for laboratories seeking to avoid chemical additives while maintaining high success rates in cases of suspected oocyte activation deficiency.

**Limitations, reasons for caution:** The review is limited by the heterogeneity of AOA protocols and the relatively smaller number of EOA studies compared to ionophores. While current neonatal data are encouraging, the longitudinal evidence for EOA offspring is less extensive than that for calcium ionophores, requiring continued monitoring of long-term health.

**Wider implications of the findings:** EOA provides a robust, non-chemical alternative that sidesteps the increasing regulatory hurdles and toxicological ambiguities associated with ionophore use. As protocols are refined, EOA is positioned to replace chemical activation as the primary clinical strategy, particularly in regions where ionophores remain unapproved or strictly controlled.

**Trial registration number:** No