

Local Anesthetic Resistance: Is there a role for liposomal bupivacaine

Subhradeep Datta MD¹; Adeeb Oweidat, MD¹; Rakesh Sondekoppam MBBS²; Anil Marian MBBS, MD¹; Nada Sadek MD¹

1) Department of Anesthesia, Iowa Healthcare, Iowa City, Iowa, USA
2) Department of Anesthesia, Perioperative and Pain medicine, Stanford, California, USA



Background

Insufficient analgesia from local anesthetics (LA) is often attributed to poor technique, tissue inflammation or patient expectations (1). True resistance to LA is not often considered but there is growing literature to support it (1, 2). The underlying mechanism of true LA resistance is unknown, however certain patient populations may be higher risk including those with Ehler-Danlos syndrome (EDS) (3) and red-heads (2), and chronic opioid users (2). We present a who have reported history of true LA resistance and their experience with Liposomal Bupivacaine.

Material and Methods

This case report does not contain identifiable patient information thus this case report is exempt from IRB review requirements per University of Iowa policy. Patient informed consent was obtained for this presentation

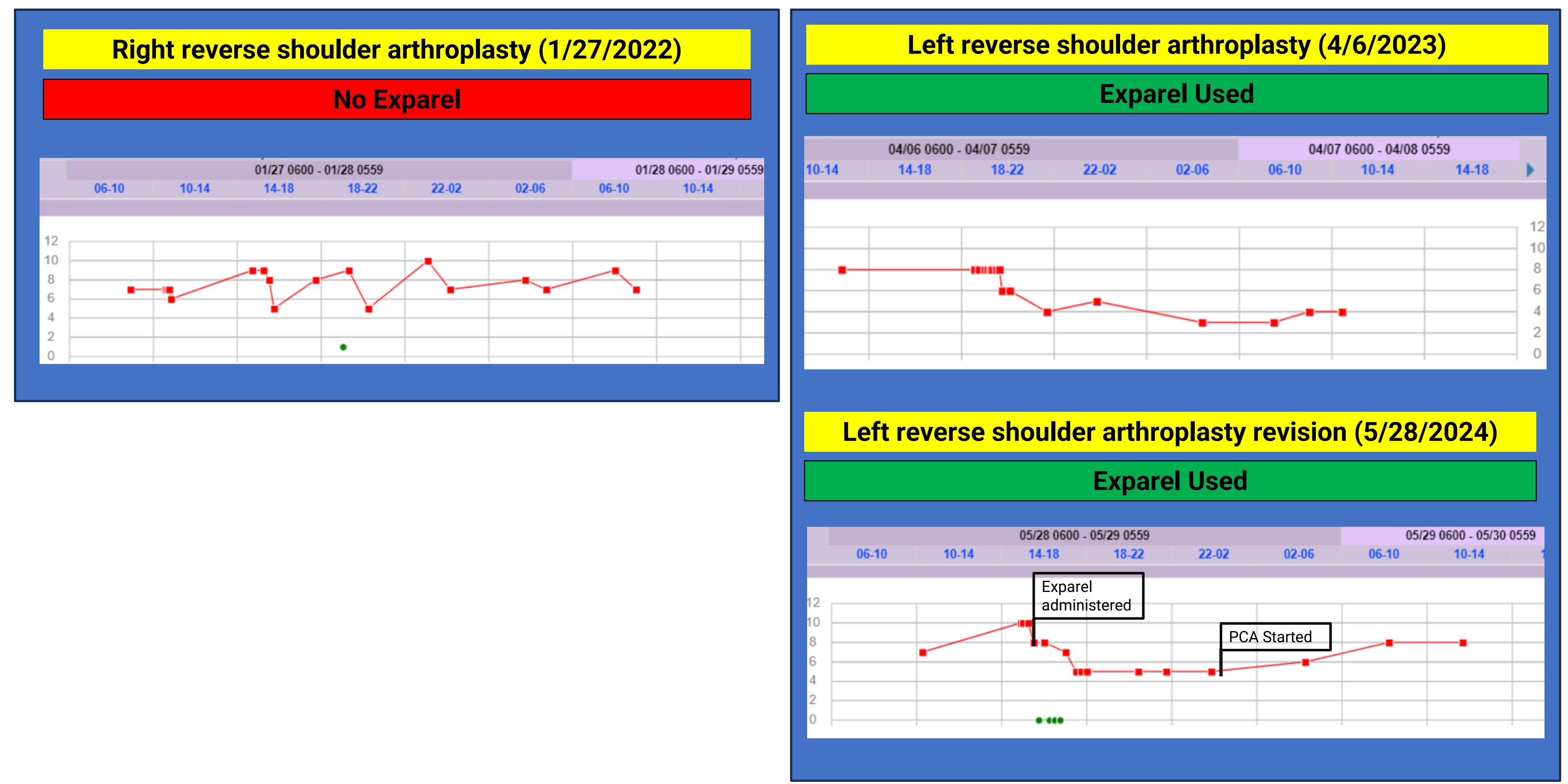
Case

60-year-old female with history of Type III (hypermobile) EDS, chronic opioid use presented for revision total shoulder arthroplasty. Patient reported experiencing resistance to LA in the past. A dry Interscalene (IS) catheter was placed pre-op and was bolused post-op with 10 ml of Ropivacaine 0.5%. VAS score dropped from 10 to 8/10 only and physical exam showed intact pinprick and temperature sensation. Ultrasound visualization of an additional bolus of lidocaine showed proper catheter placement. The next day, she mentioned that “peripheral nerve blocks don’t work for me” the only time she had good relief from a nerve block was when liposomal bupivacaine was used for prior shoulder surgery. 6 months later the patient was admitted for another shoulder surgery. An IS with liposomal bupivacaine achieved adequate analgesia with VAS scores of 2/10 with good patient satisfaction. However, the block lasted only for 16 hours.

Departmental experience with this patient over multiple surgeries

Case	Post operative Opioid use		Adjuncts	Regional anesthesia techniques used	Hospital length of stay
Right reverse shoulder arthroplasty (1/27/2022)	PACU: 65 mg OMME	Floor: 85 mg OMME	Tylenol, Aspirin, Ketamine (single dose in PACU), gabapentin	Interscalene catheter placed preoperatively with ropivacaine 0.2 % at 14 cc/h with 0.5% ropivacaine 20cc bolus pre-procedure.	25 hours
Left Reverse shoulder Arthroplasty (4/6/2023)	PACU: 105mg OMME	Floor: 285 mg OMME PCA started on the floor	Ketamine infusion (started intraoperatively, continued until POD 1), Aspirin, Acetaminophen, dexmedetomidine, Gabapentin	Interscalene single shot block Pre-operatively with Liposomal bupivacaine 133mg	22hours 54 minutes
Left Reverse shoulder arthroplasty revision (5/28/2024)	PACU: 102.5mg OMME	Floor: 250 mg OMME PCA started on the floor	Tylenol, Aspirin, Ketamine (single dose in PACU), gabapentin	Interscalene dry catheter done Pre-operatively and bolus with liposomal bupivacaine post-operatively	24 hours

Pain scores for shoulder arthroplasties



Discussion

- Genetic analysis of a family identified mutations in the sodium channel which binds local anesthetic in family members with documented LA resistance (6). Clendenen et al, used immunohistochemistry to specify that these mutant receptors are expressed in peripheral nerves (6).
- Ehlers Danlos syndrome patients show variable and inconsistent level of resistance reported in the literature and seen in clinical practice, making it difficult to point to genetic mutation as the only explanation (1, 2).
- Studies have suggested that changes in EDS patients, the microvascular structure, which vary from one anatomical location to another, may influence the rate of LA uptake by the blood (1, 2, 8).
- In a case series looking at EDS patients receiving peripheral nerve blocks with plain LA, all those patients with uncontrolled pain had type III hypermobile EDS (7).
- Our patient had greatly improved pain scores with liposomal bupivacaine but did require opioids and other adjunctive analgesics 12 to 16 hours after the Exparel diminished.
- Exparel appears to have improved analgesia for patients with Ehlers Danlos syndrome albeit with a shorter duration of action compared to other patients.

Conclusion

Although the mechanism of action is not clearly understood, our case demonstrated a potential benefit of utilizing liposomal bupivacaine for peripheral nerve blocks in patients with Type III EDS who exhibit history of LA resistance. More studies are needed.

References

1. Resistance to local anaesthetics: a literature review Marti, Florian et al. British Journal of Anaesthesia, Volume 129, Issue 2, e43 - e45
2. Hötschl F, Lirk P, Marti F. Failure of local anesthesia : Technical shortcoming or true resistance? Anaesthesiologie. 2023 Oct;72(10):723-725. English. doi: 10.1007/s00101-023-01295-z. Epub 2023 Jun 6. PMID: 37280377
3. Schubart JR, Schaefer E, Janicki P, Adhikary SD, Schilling A, Hakim AJ, Bascom R, Francomano CA, Raj SR. Resistance to local anesthesia in people with the Ehlers-Danlos Syndromes presenting for dental surgery. J Dent Anesth Pain Med. 2019 Oct;19(5):261-270. doi: 10.17245/jdamp.2019.19.5.261. Epub 2019 Oct 30. PMID: 31723666; PMCID: PMC6834718.
4. Yan Z, Chen Z, Ma C. Liposomal bupivacaine versus interscalene nerve block for pain control after shoulder arthroplasty: A meta-analysis. Medicine (Baltimore). 2017 Jul;96(27):e7226. doi: 10.1016/j.jclineane.2016.01.005. Epub 2016 Apr 6. PMID: 27555128.
5. Neice AE, Stubblefield EE, Woodworth GE, Aziz MF. Peripheral nerve block in patients with Ehlers-Danlos syndrome, hypermobility type: a case series. J Clin Anesth. 2016 Sep;33:26-30. doi: 10.1016/j.jclineane.2016.01.005. Epub 2016 Apr 6. PMID: 27555128.
6. Clendenen N, Cannon AD, Porter S, Robards CB, Parker AS, Clendenen SR. Whole-exome sequencing of a family with local anesthetic resistance. Minerva Anesthesiol. 2016 Oct;82(10):1089-1097. Epub 2016 May 31. PMID: 27243970.
7. Neice AE, Stubblefield EE, Woodworth GE, Aziz MF. Peripheral nerve block in patients with Ehlers-Danlos syndrome, hypermobility type: a case series. J Clin Anesth. 2016 Sep;33:26-30. doi: 10.1016/j.jclineane.2016.01.005. Epub 2016 Apr 6. PMID: 27555128.
8. Oliver DW, Balan KK, Burrows NP, Hall PN. Dispersal of radioisotope labelled solution following deep dermal injection in Ehlers-Danlos syndrome. Br J Plast Surg. 2000 Jun;53(4):308-12. doi: 10.1054/bjps.2000.3338. PMID: 10876255