Title: DO SEIZURES OCCUR DURING CLINICAL INDUCTION WITH
             OPIATES?

Authors: N. T. Smith, M.D., R.G. Bickford, M.D., T. J. Sanford, Jr., M.D.,
             H. Dec-Silver, R.N., C.R.T.T., and T. A. Blasco, M.D.

Affiliation: Departments of Anesthesiology and Neurology, University of California, San
             Diego, Veterans Administration Medical Center, San Diego, CA 92161

Introduction. Numerous case reports have appeared suggesting that induction with fentanyl (F) or sufentanil (S) can be accompanied by seizure activity (1-6). Unfortunately, there has not been enough information in these reports to substantiate these claims, mainly because the EEG has rarely been recorded, and when it has been it has not demonstrated seizures (7). We retrospectively analyzed the tape recorded EEGs of 127 patients for evidence of opiate-induced seizures and correlated the records with movements that could be interpreted as seizures.

Methods. Our data were derived from six projects. Each project received approval from our Human Research Committees; each patient gave written informed consent. 20 patients received F, 20 S, and 87 alfentanil (A). Bilateral EEGs were recorded from each patient. The administration of F or S was relatively slow, while that of A was relatively rapid (1 min for an induction dose of 150 µg/kg [n=18] or 175 µg/kg [n=69]). The patients receiving A were either given no pretreatment, or one of a number of agents selected to reduce rigidity. In 69 patients we recorded a surface EMG over each of the following muscle groups: deltoid, right and left biceps, forearm flexors, intercostal, rectus abdominus, vastus medialis, and gastrocnemius. All cardiovascular, EEG, and EMG signals were recorded on FM tape recorders at 3-3/4 ips. From the tapes, both EEG leads plus the ECG were played back onto a Beckman EEG recorder, which ran at speeds of 30 or 60 mm/sec. The playbacks began 5 min before induction and continued until incision with the patients receiving F or S, and for 15 min after induction with the patients receiving A. The resulting records were examined independently by three readers, who searched particularly for epileptiform activity, including sharp-waves and spikes. In addition to the playback onto tape, one of the investigators monitored the entire set of tapes, 355 hours in all, on an oscilloscope. The phenomenon called rigidity was divided into three groups: none, mild, and intense. "Mild" rigidity was defined as clinically obvious rigidity during which the lungs were relatively easy to ventilate, while during "intense" rigidity the lungs were difficult or impossible to ventilate.

Results. Of the 127 patients, 93 manifested mild to intense muscle activity, as determined clinically and, when recorded, by the EMG. Rigidity occurred in 7 of the 20 patients receiving F, 7 of the 20 receiving S and 79 of the 87 receiving A. 46 episodes of rigidity were classified as "intense" (4, 2, and 40 with F, S and A, respectively). A total of 2,227 min (13,360 pages) of EEGs were analyzed for F and S, and 1,943 min (11,658 pages) for A. Before anesthesia, the EEG usually contained marked sharp-wave activity, which was accompanied by similar EMG activity, both fluctuating with movement or relaxation. After induction, the high-amplitude slow waves characteristic of deep-opiate anesthesia appeared. If rigidity occurred, sharp-wave muscle activity was superimposed on the slow waves. The sharp waves disappeared after the injection of a neuromuscular blocking agent at a rate consistent with the speed of action of that agent, and with the disappearance of spontaneous EMG activity. In no instance, with any of the opiates, did we detect epileptiform EEG activity, (sharp-waves, spikes, spike-waves, or frank seizures) after neuromuscular blockade. All random or periodic sharp-waves occurring after the establishment of the neuromuscular blockade could be related to the ECG; infusion pumps; electrode or cable movement; electrical interference, including pacemakers, or nerve stimulators; or head movement. Clinically,

rigidity was often explosive in onset, occurring almost simultaneously with the loss of response to voice, with the subjects' assuming postures typified as follows: flexion of the upper extremities at the fingers, wrists, and elbows; extension at the toes, ankles, knees, and hips; rigid immobility of the head with atlanto-occipital flexion of the chin onto the chest; severe rigidity of the abdominal and chest wall musculature frequently with athetoid movements of the extremities, as well as vertical nystagmus. These signs were accentuated with any stimulus, including sound or touch. There was no EEG evidence of a postictal state in any patient, as occurs after seizures induced by inhaled, local, or opiate anesthetics.

Discussion. The EEG at no time showed evidence of frank seizure activity, even during intense muscle activity. In contrast, the EEG of true seizures is very characteristic even during gross muscle movement. Since we have been unable to detect EEGs characteristic of seizures in patients with ostensible motor seizure activity, we suggest that the following criteria be used for case reports purporting to describe seizures during anesthesia. These include a complete description of 1.The patient's medical history, including negatives, where appropriate. 2.The patient's chronic preoperative medications, including antipsychotic medications and street drugs. 3. A history of chemical dependency, including alcoholic, with a description of the amount consumed, and the date of the last consumption. 4. The patient's emotional state upon entering the operating room, including the presence or absence of hyperventilation. 5.The presence or absence of fever. 6. The alleged seizure phenomenon, including rate of drug adminstration, time of onset in relation to the injection of the drug(s), speed of onset, parts of the body involved, duration and any indication of a postictal state. 7. Any cardiovascular changes accompanying the "seizures". 8. Postoperative neurological assessment and EEGs, including hyperventilation and stroboscopic stimulation. The criteria also include technically sound recordings of the EEG, with a permanent record if at all possible, and a series of illustrations to help the reader perform an independent interpretation. A recording of the ECG should accompany any illustrations of the EEG to establish that sharp-waves on the latter are not electrocardiographic in origin. Ideally, an independent EMG recording should also accompany the EEG.

References.
1. Rao TLK, Mummaneni N, El-Etr AA: Convulsions: An unusual response to intravenous fentanyl administration. Correspondence. Anesth Analg 61:1020-1021, 1982.
2. Rao TLK, El-Etr AA: Fentanyl and convulsions. Correspondence. Anesth Analg 62:855-862, 1983.
3. Safwat AM, Daniel D: Grand mal seizure after fentanyl administration. Correspondence. Anesthesiology 59-78, 1983.
4. Hoien AO: Another case of grand mal seizure after fentanyl administration. Correspondence. Anesthesiology 60:387-388, 1984.
5. Baraka A, Haroun S: Grand mal seizures following fentanyl-lidocaine. Correspondence. Anesthesiology 62:205, 1985.
6. Molbegott LP, Flashburg MH, Karasic L, Karlin BL: Probable seizures after sufentanil. Anesth Analg 66:91-93, 1987.
7. Murkin JM, Moldenhauer CC, Hug CC, Jr., Epstein CM: Absence of seizures during induction of anesthesia with high-dose fentanyl. Anesth Analg 63:489-494, 1984.