The intracorporeal use of 2-octyl cyanoacrylate resin to control air leaks after lung resection

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Abstract

Objective: To describe the outcome of patients who had 2-octyl cyanoacrylate used as an adjunct to control air leaks after lung resection by application directly onto the visceral pleura. Methods: A retrospective review of these patients from 2007 to 2009 from a single surgeon’s practice. Results: Seven challenging patients had 2-octyl cyanoacrylate used to control difficult air leaks after lung resection. The indications included lack of standard sealants in patients with emphysematous lung that would not hold suture and vast air leaks after decortication or extensive nonanatomic resections in patients that would not tolerate the loss of tidal volume. All air leaks sealed immediately and none of the patients left the operating theater with an air leak, including three patients who underwent difficult decortications for empyema. All patients recovered uneventfully, except one patient who died from acute respiratory distress syndrome. His postmortem examination revealed that the resin remained intact on the lung without signs of degradation after being in an intracorporeal environment for weeks. There were no complications nor toxicity directly related to the 2-octyl cyanoacrylate resin. Conclusions: 2-Octyl cyanoacrylate is extremely effective in immediately controlling air leaks, with the results being seen instantly. It dries quickly, does not wash off the lung, and remains intact on the visceral pleura for several weeks. 2-Octyl cyanoacrylate deserves additional testing as an adjunct to control air leaks after lung resection.

Keywords: Air leaks; Sealant; Bronchopleural fistula; 2-Octyl cyanoacrylate; Glue

1. Introduction

Cyanoacrylates are fast-acting adhesive polymers with great strength [1]. Many variants exist including 2-methyl cyanoacrylate, 2-ethyl cyanoacrylate (Super Glue®, Krazy Glue®), and n-butyl cyanoacrylate used in veterinary glues (Vetbond®, LiquiVet®). Interest in developing a typical glue that could be used in humans to repair simple lacerations was significantly hampered by the fact that these glues are all significant skin irritants. However, with the synthesis of a new and much less-irritating compound, 2-octyl cyanoacrylate (2-OCA), steps were taken to obtain approval for use in humans. In 1998, 2-octyl cyanoacrylate resin (Dermabond®, SurgiSeal®) was approved by the United States Food and Drug Administration for use as a topical skin adhesive to repair simple lacerations. Despite its improved safety profile, there have been multiple reports in the literature of contact dermatitis, foreign body reactions, and allergic reactions after its use [2—5].

After great success in topical applications on the skin, its use expanded into research applications involving eye surgery and became used by ophthalmologists during cataract surgery [6—9]. However, true intracorporeal use did not occur until 2004, when a pilot study of 25 patients was performed injecting 2-OCA into gastric varices. The immediate success rate in controlling bleeding from the varices was 100% with no reported toxicity [10]. This was followed by a larger trial in 89 patients and a prospective, randomized trial of 2-OCA injection compared with endoscopic ligation for variceal bleeding [11,12]. In both studies, there were no reports of toxicity and the compound appeared to have an acceptable safety profile, although there have been reports of pulmonary embolism after intravenous injection [11,13].

There has been minimal published research on the use of 2-OCA in thoracic surgery. It has been shown to be effective in use with a pericardial patch for sub-acute left-ventricular-free wall rupture after myocardial infarction [14]. It has also been shown to be effective and safe for bleeding from ventricular pacing wires, perianastomotic bleeding, and epicardial tears [15]. There have been no reports in the literature concerning the use of 2-OCA to control air leaks after lung resection by application directly onto the visceral pleura.

2. Methods

A retrospective study was performed to review and follow the progress of seven patients from a single thoracic surgeon’s
three patients who underwent decortication for empyema. None of the patients developed an air leak later during their hospital stay, either. Postoperatively, none of the patients showed any signs of cyanide or other toxicity. Patients 1–4 in Table 1 recovered uneventfully; however, there were two major complications (patients 6 and 7).

The first patient (patient 6 in Table 1) was 89 years old with severe emphysema and developed acute respiratory distress syndrome (ARDS) and died 24 days after surgery. Autopsy results confirmed that his death was from ARDS and his pathology is shown in Figs. 1 and 2. The 2-OCA was intact and unchanged on the surface of his lung and did not appear to show any signs of degradation or desquamation. In fact, the 2-OCA was easily palpable and still firmly glued to the visceral pleura. Microscopic examination (Fig. 2) showed inflammation and lymphocytic infiltration into the area of visceral pleura in contact with the 2-OCA, although this may have simply been part of the healing response as it was in the area of resection.

A second patient (patient 7 in Table 1) recovered and went home 4 days after his surgery. He followed up in the clinic 2 weeks later, and was found to have a complete collapse of the right lung. He reported developing sharp chest pain after vigorous coughing at home, just 1 day prior to being seen in the clinic (13 days after the operation). A chest tube was placed and a large air leak was found that persisted after admission to the hospital. He was taken back to surgery 15

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3. Results

There were seven patients over a 2-year period from 2007 to 2009 in whom intracorporeal 2-OCA was used to control difficult air leaks that were refractory to standard measures. The patient demographics, indications, and follow-up are listed in Table 1. None of the patients left the operating room with the deliberate intention of using 2-OCA.

In all cases, the deflated lung was submerged under saline or sterile water and then gently insufflated by the anesthetist, while the surgeon looked for air bubbles. When identified, the lung tissue surrounding the air leak was dried with gauze and then the 2-OCA was applied directly onto the visceral pleura or raw lung surface. After use of the 2-OCA, all air leaks sealed within the drying time of the compound (usually less than 60 s) and sealed immediately with a single application. Depending upon the amount of raw surface to cover, one to eight vials (each vial contains 0.5 ml of 2-OCA) were used.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Operation</th>
<th>Rationale for 2-OCA</th>
<th>F/U</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>67</td>
<td>Empyema Emphysema</td>
<td>Decortication</td>
<td>Large raw surface, friable lung, loss of tidal volume</td>
<td>6 months</td>
<td>Full recovery</td>
</tr>
<tr>
<td>Patient 2</td>
<td>22</td>
<td>Empyema Coagulopathy</td>
<td>Decortication</td>
<td>Large raw surface, friable lung, bleeding from decorticated surface</td>
<td>5 months</td>
<td>Full recovery</td>
</tr>
<tr>
<td>Patient 3</td>
<td>42</td>
<td>Empyema Emphysema</td>
<td>Decortication</td>
<td>Large raw surface, friable lung, loss of tidal volume</td>
<td>6 months</td>
<td>Full recovery</td>
</tr>
<tr>
<td>Patient 4</td>
<td>72</td>
<td>Squamous cancer Emphysema</td>
<td>Upper lobectomy</td>
<td>Incomplete fissures, friable lung, intolerance of prolonged air leak</td>
<td>6 months</td>
<td>Full recovery</td>
</tr>
<tr>
<td>Patient 5</td>
<td>53</td>
<td>Single colon cancer metastas to lung, emphysema</td>
<td>Metastasectomy</td>
<td>Tumor deep within major fissure and fissures completely fused, no alternative sealant available</td>
<td>12 months</td>
<td>Full recovery + PET scan</td>
</tr>
<tr>
<td>Patient 6</td>
<td>89</td>
<td>Ruptured bullae Massive air leak Metastases Ewing’s sarcoma</td>
<td>Bullectomy</td>
<td>Lung extremely fragile, no reserve, intolerance of air leak Multiple metastases, large raw surface, no alternative available</td>
<td>24 days</td>
<td>Died, ARDS</td>
</tr>
<tr>
<td>Patient 7</td>
<td>18</td>
<td></td>
<td>Lower lobectomy, metastasectomy</td>
<td></td>
<td>3 months</td>
<td>Developed late pneumothorax</td>
</tr>
</tbody>
</table>

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Fig. 1. Postmortem photograph of the apex of the right lung still covered with intact 2-OCA 24 days after surgery. The appearance was unchanged as compared to immediately after application.
days after the initial operation for the persistent and large air leak and to rule out a bronchial stump dehiscence. His intraoperative photo is shown in Fig. 3. The 2-OCA was intact and appeared completely unchanged from the time of application 15 days earlier, although the air leak was coming from the base of one of the biopsy cavities, where the 2-OCA had been applied. This was the only treatment failure.

All patients, except one, had follow-up chest radiographs and chest-computed tomography. Nothing of interest was identified at the site of 2-OCA application, and, in fact, the location of the 2-OCA could not be identified by CT scan (no underlying inflammation or parenchymal changes). However, one patient with metastatic colon cancer had a follow-up positron emission tomographic (PET) scan, which did show an increased standard uptake value (SUV) at the periphery of the biopsy cavity. The original metastasectomy was performed to remove a single colon cancer metastasis from the left lung and was a R0 resection. The neoplasm was located deep within a completely fused fissure. The tumor was excised with negative margins. An intra-operative photo of her biopsy cavity is shown in Fig. 4. Due to the size and depth of the cavity creating multiple air leaks, 2-OCA was applied to the cavity and the space was filled with a free pericardial fat pad, as described by Matsumoto and Watanabe [16]. The intracavitary fat density can be seen on her follow-up CT scans, although the 2-OCA cannot. Her PET scan and CT scan 1 month after surgery are shown in Fig. 5, parts A and B. A repeat PET scan and CT scan, 9 months later, are shown in Fig. 5, parts C and D. Her carcinoembryonic antigen (CEA) level remained normal and the SUV decreased from 3.1 to 2.1 over the 9 months. Since the 2-OCA remains as a persistent foreign body, this is likely to be an inflammatory response or giant cell reaction, where the 2-OCA had been applied. This is likely as the microscopic slide (Fig. 2, different patient) did show lymphocytic infiltration and inflammation in the area where the 2-OCA had been applied.

The six surviving patients returned to the office for later evaluation, and all are doing well with no detectable problems. The author plans to continue follow-up on all of them indefinitely.
4. Discussion

These seven patients confirm the utility of using 2-OCA for immediate control of air leaks, as none of the patients left the operating theater with an air leak, even after decortication. The resin dries very fast and is tenaciously adherent to the visceral pleura, making it an ideal sealant. The author was very surprised to find that after 15 days (patient 7) and 24 days (patient 6) in an intracorporeal environment, the 2-OCA remained unchanged. It had not softened nor sloughed off the lung. After the liquid form of the 2-OCA dries, it polymerizes and becomes a very stable and inert compound. This is a two-edged sword. On the one hand, it stays in place and prevents leaks until the underlying parenchyma heals, but on the other hand, it may remain as an inert foreign body within the chest cavity indefinitely. Some very elegant research with nanoparticles composed of 2-OCA has shown that the compound is extremely stable and shows almost no cytotoxicity [17]. In addition, under electron microscopy, 2-OCA shows no inhibition of tissue regeneration and no histotoxicity [18]. Even in amnion cell cultures from fetal membranes, 2-OCA showed no toxicity after bonding and it would appear that theoretical concerns for cyanide elution from the polymer are unjustified [19].

There has been no good research examining the long-term fate of the 2-OCA polymer after being left within the human body. Although it does not appear to have toxicity, the author’s initial clinical results would appear to show that it does not undergo degradation either. This is supported by a rodent model of intracorporeal 2-OCA injection that showed that the polymer persisted within the abdominal cavity out to 12 months, which is when the study ended [20]. The patient with the persistently positive PET scan causes concern. It may represent local recurrence of the tumor or an increased metabolic rate secondary to ongoing inflammation or foreign body reaction. Since her CEA level is normal, the area to show persistent enhancement by PET scan. A larger, prospective study will be necessary to confirm its utility.

There are many surgical sealants that are commercially available and many are hailed as reducing the extent of postoperative air leaks. In randomized trials, only three of the 16 trials have shown a statistically significant reduction in the time until chest drain removal [22]. The author has used many sealants, but one distinguishing feature of the 2-OCA is that it polymerizes and hardens on the pleural surface immediately and seals the leak during the time of observation by the surgeon. This usually occurs within 1 min. By then, inspecting the area under submersion with saline or sterile water, air bubbling, or a persistent leak, can be detected prior to leaving the operating theater. The surgeon does not have to close the chest and ‘hope things seal’. Unlike other sealants, after application, the 2-OCA will not wash off the lung and the chest cavity can be irrigated and the lung tested repeatedly, if needed. In addition, after decortication, the resin also promptly controls bleeding as well. The current report, although unintentional in occurrence, provides significant information about the intrathoracic use of 2-OCA. Although limited by only seven patients, a few firm conclusions can be drawn. First, no adverse events occurred in the three patients with empyema. Second, it is extremely effective in immediately controlling air leaks, with the results being seen instantly. Third, it does not appear to undergo degradation nor disappear from the surgical site, at least not within the first 30 days after surgery. Finally, it may not be a good choice in patients with cancer, as it may instigate a continued inflammatory reaction and allow the area to show persistent enhancement by PET scan. A larger, prospective study will be necessary to confirm its utility.

References


