

Thyroid Surgery Complications High After Age 80

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CHICAGO — Octogenarians undergoing thyroid surgery experience a markedly increased rate of serious perioperative complications, compared with younger patients, according to Dr. Michal Mekel.

Dr. Mekel of Massachusetts General Hospital, Boston, presented a review of 90 consecutive patients over age 80 years and 242 randomly selected 18- to 79-year-olds,

all of whom underwent thyroid surgery at the hospital during the same recent period. Eighty percent of the octogenarians were women, Dr. Mekel reported at the annual meeting of the American Thyroid Association.

The overall 30-day complication rate was 23% in octogenarians and 9% in controls. Moreover, most affected octogenarians had multiple complications. However, no deaths occurred in either group. Mean length of stay was 1.7 days in patients over

age 80 years, compared with 1.2 days in the younger group. The most frequent complications in patients over age 80 years were cardiovascular, with 6.7% of them being affected. Pulmonary complications, occurring in 3.3%, were next most common.

Complications experienced only by the octogenarians included atrial fibrillation, other arrhythmias, heart failure, pneumonia, ischemic colitis, and tracheostomy.

In an analysis, comorbid respiratory conditions proved to be an independent

risk factor for perioperative complications in patients over age 80 years, conferring a 10-fold increased risk. Elderly women had an over threefold increased risk of perioperative complications.

Interestingly, advanced age was not an independent risk factor for serious complications. This finding underscores the point that while careful selection of elderly candidates for thyroid surgery is warranted, advanced age is not a contraindication to surgery, Dr. Mekel emphasized. ■

Table 8
Adverse Events Occurring at ≥2% Incidence in Lovenox-Treated Patients¹ Undergoing Abdominal or Colorectal Surgery

Adverse Event	Dosing Regimen			
	Lovenox 40 mg q.d. SC n = 1228 %		Heparin 5000 U q8h SC n = 1234 %	
	Severe	Total	Severe	Total
Hemorrhage	<1	7	<1	6
Anemia	<1	3	<1	3
Ecchymosis	0	3	0	3

¹ Excluding unrelated adverse events.

Table 9
Adverse Events Occurring at ≥2% Incidence in Lovenox-Treated Patients¹ Undergoing Hip or Knee Replacement Surgery

Adverse Event	Dosing Regimen				
	Lovenox 40 mg q.d. SC		Lovenox 30 mg q12h SC	Heparin 15,000 U/24h SC	Placebo q12h SC
	Peri-operative Period n = 288 ² %	Extended Prophylaxis Period n = 131 ³ %	n = 1080 %	n = 766 %	n = 115 %
	Severe Total	Severe Total	Severe Total	Severe Total	Severe Total
Fever	0 8	0 0	<1 5	<1 4	0 3
Hemorrhage	<1 13	0 5	<1 4	1 4	0 3
Nausea			<1 3	<1 2	0 2
Anemia	0 16	0 <2	<1 2	2 5	<1 7
Edema			<1 2	<1 2	0 2
Peripheral edema	0 6	0 0	<1 3	<1 4	0 3

¹ Excluding unrelated adverse events.

² Data represents Lovenox 40 mg SC once a day initiated up to 12 hours prior to surgery in 288 hip replacement surgery patients who received Lovenox peri-operatively in an unblinded fashion in one clinical trial.

³ Data represents Lovenox 40 mg SC once a day given in a blinded fashion as extended prophylaxis at the end of the peri-operative period in 131 of the original 288 hip replacement surgery patients for up to 21 days in one clinical trial.

Table 10
Adverse Events Occurring at ≥2% Incidence in Lovenox-Treated Medical Patients¹ With Severely Restricted Mobility During Acute Illness

Adverse Event	Dosing Regimen	
	Lovenox 40 mg q.d. SC n = 360 %	Placebo q.d. SC n = 362 %
Dyspnea	3.3	5.2
Thrombocytopenia	2.8	2.8
Confusion	2.2	1.1
Diarrhea	2.2	1.7
Nausea	2.5	1.7

¹ Excluding unrelated and unlikely adverse events.

Table 11
Adverse Events Occurring at ≥2% Incidence in Lovenox-Treated Patients¹ Undergoing Treatment of Deep Vein Thrombosis With or Without Pulmonary Embolism

Adverse Event	Dosing Regimen					
	Lovenox 1.5 mg/kg q.d. SC n = 298 %		Lovenox 1 mg/kg q12h SC n = 559 %		Heparin aPTT Adjusted I.V. Therapy n = 544 %	
	Severe	Total	Severe	Total	Severe	Total
Injection Site Hemorrhage	0	5	0	3	<1	<1
Injection Site Pain	0	2	0	2	0	0
Hematuria	0	2	0	<1	<1	2

¹ Excluding unrelated adverse events.

Adverse Events in Lovenox-Treated Patients With Unstable Angina or Non-Q-Wave Myocardial Infarction:

Non-hemorrhagic clinical events reported to be related to Lovenox therapy occurred at an incidence of ≤1%.

Non-major hemorrhagic episodes, primarily injection site ecchymoses and hematomas, were more frequently reported in patients treated with SC Lovenox than in patients treated with IV heparin.

Serious adverse events with Lovenox or heparin in a clinical trial in patients with unstable angina or non-Q-wave myocardial infarction that occurred at a rate of at least 0.5% in the Lovenox group are provided below (irrespective of relationship to drug therapy) [see Table 12].

Table 12
Serious Adverse Events Occurring at ≥0.5% Incidence in Lovenox-Treated Patients With Unstable Angina or Non-Q-Wave Myocardial Infarction

Adverse Event	Dosing Regimen	
	Lovenox 1 mg/kg q12h SC n = 1578 n (%)	Heparin aPTT Adjusted IV Therapy n = 1529 n (%)
Atrial fibrillation	11 (0.70)	3 (0.20)
Heart failure	15 (0.95)	11 (0.72)
Lung edema	11 (0.70)	11 (0.72)
Pneumonia	13 (0.82)	9 (0.59)

Adverse Reactions in Lovenox-Treated Patients With acute ST-segment Elevation Myocardial Infarction:

In a clinical trial in patients with acute ST-segment elevation myocardial infarction, the only additional possibly related adverse reaction that occurred at a rate of at least 0.5% in the Lovenox group was thrombocytopenia (1.5%)

6.2 Postmarketing Experience

There have been reports of epidural or spinal hematoma formation with concurrent use of Lovenox and spinal/epidural anesthesia or spinal puncture. The majority of patients had a postoperative indwelling epidural catheter placed for analgesia or received additional drugs affecting hemostasis such as NSAIDs. Many of the epidural or spinal hematomas caused neurologic injury, including long-term or permanent paralysis.

Local reactions at the injection site (e.g. nodules, inflammation, oozing), systemic allergic reactions (e.g. pruritus, urticaria, anaphylactic/anaphylactoid reactions), vesiculobullous rash, rare cases of hypersensitivity cutaneous vasculitis, purpura, skin necrosis (occurring at either the injection site or distant from the injection site), thrombocytosis, and thrombocytopenia with thrombosis [see *Warnings and Precautions* (5.5)] have been reported. Cases of hyperkalemia have been reported. Most of these reports occurred in patients who also had conditions that tend toward the development of hyperkalemia (e.g., renal dysfunction, concomitant potassium-sparing drugs, administration of potassium, hematoma in body tissues). Very rare cases of hyperlipidemia have also been reported, with one case of hyperlipidemia, with marked hypertriglyceridemia, reported in a diabetic pregnant woman; causality has not been determined.

Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to estimate reliably their frequency or to establish a causal relationship to drug exposure.

7 DRUG INTERACTIONS

Unless really needed, agents which may enhance the risk of hemorrhage should be discontinued prior to initiation of Lovenox therapy. These agents include medications such as: anticoagulants, platelet inhibitors including acetylsalicylic acid, salicylates, NSAIDs (including ketorolac tromethamine), dipyridamole, or sulfipyrazone. If co-administration is essential, conduct close clinical and laboratory monitoring [see *Warnings and Precautions* (5.9)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B

All pregnancies have a background risk of birth defects, loss, or other adverse outcome regardless of drug exposure. The fetal risk summary below describes the potential of Lovenox to increase the risk of developmental abnormalities above background risk.

Fetal Risk Summary

Lovenox is not predicted to increase the risk of developmental abnormalities. Lovenox does not cross the placenta, based on human and animal studies, and shows no evidence of teratogenic effects or fetotoxicity.

Cases of "Gasping Syndrome" have occurred in premature infants when large amounts of benzyl alcohol have been administered (99-405 mg/kg/day). The multiple-dose vial of Lovenox contains 15 mg benzyl alcohol per 1 mL as a preservative [see *Warnings and Precautions* (5.8)].

Clinical Considerations

It is not known if either dose adjustment or monitoring of anti-Xa activity of enoxaparin are necessary during pregnancy.

Pregnancy alone confers an increased risk for thromboembolism that is even higher for women with thromboembolic disease and certain high risk pregnancy conditions. While not adequately studied, pregnant women with mechanical prosthetic heart valves may be at even higher risk for thrombosis [see *Warnings and Precautions* (5.7) and *Use in Specific Populations* (8.6)]. Pregnant women with thromboembolic disease, including those with mechanical prosthetic heart valves and those with inherited or acquired