SYSTEMATIC REVIEW
DEGENERATIVE
http://dx.doi.org/10.1590/S1808-185120222203270489

USE OF TERIPARATIDE IN SURGICAL PLANNING FOR PATIENTS WITH OSTEOPOROSIS

USO DE TERIPARATIDA NO PLANEJAMENTO CIRÚRGICO DE PACIENTE COM OSTEOPOROSE

USO DE TERIPARATIDA EN LA PLANIFICACIÓN QUIRÚRGICA EN PACIENTES CON OSTEOPOROSIS

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ABSTRACT

Currently, there are no guidelines for treating osteoporosis in spinal surgery. The rate of complications such as screw loosening, proximal junction kyphosis, cage subsidence, and loss of reduction in fractures is high. Objective: To evaluate the use of teriparatide and denosumab in planning spinal surgery in an osteoporotic patient with degenerative pathology, emphasizing the fusion rate, bone mineral density, and decreased complications. Method: A systematic search was performed in medical reference databases for comparative studies of teriparatide and denosumab in spinal surgery to evaluate fusion, screw loosening, bone mineral density, and decrease in the incidence of vertebral fractures. χ^2 was implemented for the statistical analysis, according to PRISMA (2020). Result: Fusion rate with teriparatide was 79.28% in the first six months, 95% CI (OR 2.62) and decreased screw loosening rate 81.9% 95% CI (OR 0.6). Increase in bone mineral density 15.5% OR 1.49 (0.77 - 2.86) and decrease in vertebral fracture rate 85.4% OR 0.5. Conclusions: Teriparatide and denosumab should be considered in perioperative spinal planning due to their effectiveness, synergism, and low adverse effects; to improve bone mineral density and decrease the rate of complications. Clinical, comparative, and statistically significant studies are required to confirm this. ***Level of Evidence II; Systematic Review and Meta-analysis.***

Keywords: Osteoporosis; Surgical Procedures, Operative; Spine; Teriparatide; Denosumab.

RESUMO

Atualmente não existem diretrizes para o tratamento da osteoporose em cirurgia da coluna vertebral. A taxa de complicações como afrouxamento de parafuso, cifose da junção proximal, subsidência da gaiola e perda de redução nas fraturas é alta. Objetivo: Avaliar o uso de teriparatida e/ou denosumabe no planejamento da cirurgia da coluna vertebral em pacientes osteoporóticos com patologia degenerativa, enfatizando a taxa de fusão, densidade mineral óssea e diminuição de complicações. Método: Foi realizada uma busca sistemática em bases de dados de referência médica para estudos comparativos de teriparatida e denosumabe em cirurgia da coluna vertebral, a fim de avaliar fusão, soltura de parafuso, densidade mineral óssea e diminuição da incidência de fraturas vertebrais. O χ^2 foi implementado para a análise estatística, de acordo com PRISMA (2020). Resultado: A taxa de fusão com teriparatida foi de 79,28% nos primeiros 6 meses IC 95% (OR 2,62) e diminuiu a taxa de afrouxamento do parafuso 81,9% IC 95% (OR 0,6). O aumento da densidade mineral óssea foi de 15,5% OR 1,49 (0,77 - 2,86) e a diminuição da taxa de fratura vertebral atingiu 85,4% OR 0,5. Conclusões: A teriparatida e o denosumabe devem ser considerados no planejamento espinhal perioperatório devido à sua efetividade, sinergismo e baixos efeitos adversos, melhorando a densidade mineral óssea e diminuir a taxa de complicações. Estudos clínicos, comparativos e estatisticamente significativos são necessários para confirmar os achados. ***Nível de Evidência II; Revisão Sistemática e Meta-análise.***

Descritores: *Osteoporose; Procedimentos Cirúrgicos Operatórios; Coluna Vertebral; Teriparatida; Denosumab.*

RESUMEN

Actualmente no existen pautas para el tratamiento de la osteoporosis en cirugía espinal. La tasa de complicaciones como el aflojamiento de los tornillos, la cifosis de la unión proximal, el hundimiento del aparato Ilizarov y la pérdida de reducción de las fracturas es alta. Objetivo: Evaluar el uso de teriparatida y/o denosumab en la planificación de la cirugía de columna en el paciente osteoporótico con patología degenerativa haciendo hincapié en la tasa de fusión, la densidad mineral ósea y la disminución de las complicaciones. Método: Se realizó una búsqueda sistemática en bases de datos de referencia médica para estudios comparativos de teriparatida y denosumab en cirugía espinal con el fin de evaluar la fusión, el aflojamiento de tornillos, la densidad mineral ósea y la disminución de la incidencia de fracturas vertebrales. χ^2 se implementó para el análisis estadístico, según PRISMA (2020). Resultado: La tasa de fusión con teriparatida fue del 79,28% en los primeros 6 meses IC 95% (OR 2,62) y disminuyó la tasa de aflojamiento del tornillo 81,9% IC 95% (OR 0,6). Aumento de la densidad mineral ósea 15,5% O 1,49 (0,77 - 2,86) y disminución de la tasa de fractura vertebral 85,4%

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Received on 12/16/2022 accepted on 07/05/2023
Reviewed by: Erasmo Abreu Zardo

O 0,5. Conclusiones: La teriparatida y el denosumab deben ser considerados en la planificación espinal perioperatoria debido a su efectividad, sinergismo y bajos efectos adversos; con el fin de mejorar la densidad mineral ósea y disminuir la tasa de complicaciones. Se requieren estudios clínicos, comparativos y estadísticamente significativos para confirmarlo. ***Nivel de Evidencia II; Revisión sistemática y metaanálisis.***

Descriptores: *Osteoporosis; Procedimientos Quirúrgicos Operativos; Columna Vertebral; Teriparatida; Denosumab.*

INTRODUCTION

Osteoporosis is currently considered a public health problem, affecting 200 million people worldwide,[1] 10% of the population in the United States, and 50 million over 50 years of age.[2,3]

The interest in its diagnosis and treatment has become more relevant in the last 20 years due to increased life expectancy.[4] In turn, poor bone quality is associated with complications such as loosening of the screws, vertebral fractures, kyphosis of the proximal joint, and pseudarthrosis.[3-7]

Recently, the measurement of Hounsfield Units by tomography predicts outcome and post-surgical complications in planning, thus improving the success rate and greater sensitivity and specificity in diagnosing degenerative spinal pathology, scoliosis, and aortic calcification concerning DEXA.[7] Only 44% of surgeons perform screening before surgery for suspected osteoporosis, and with the diagnosis, only 40% of patients receive pharmacological management.[2]

Several strategies optimize the osteoporotic patient in planning, such as cementation, fenestrated screws, and drugs; however, there is no universally accepted guide to determine the best medicine, dosage, and administration time.[6]

Different drugs are used in the management. Calcium and vitamin D are inexpensive, with few adverse effects but no effect on bone mineral density and fracture risk.[3]

Teriparatide and bisphosphonates have been the most studied drugs in spinal instrumentation. The former, a parathyroid hormone analog, has shown similar fusion but faster (77% vs. 55% six months after) with a decrease in screw loosening compared to bisphosphonates.[1,2,8,9] On the other hand, bisphosphonates present greater adverse effects, such as atypical fractures of the femur, and maxillary necrosis, among others 4. Calcitonin is a regulator of calcium levels. However, it has been associated with cancer 4.6%, and studies are lacking.[3]

Denosumab is a monoclonal antibody considered antiresorptive with promising results in spinal fusion; however, clinical studies on the spine are still lacking. It has been found to have a synergistic effect with teriparatide in enhancing the fusion rate. Tsai et al. found that this combination led to a significant increase in bone cortical thickness two years after treatment ($p<0.002$), and was more effective than monotherapy.[9-11]

Loosening decreases the fusion rate; therefore, it is necessary to improve the bone-implant interface in pharmacological management in cooperation with the endocrinologist[12] and to perform initial studies of alkaline phosphatase, calcium, vitamin D, and parathormone before starting teriparatide.[12]

Our presentation aims to evaluate and describe the different

uses teriparatide and denosumab in the peri-operative planning of the osteoporotic patient with spinal pathology to determine their effectiveness in emphasizing fusion rate, bone mineral density, and decreased complications.

MATERIALS AND METHOD

TYPE OF STUDY: SYSTEMATIC REVIEW and METHOD ANALYSIS, according to "Preferred Reporting Items" (PRISMA 2020).

Data sources and search

A systematic literature search of PubMed, Cochrane, LILACS, and Scielo databases with the MeSH terms: (osteoporosis AND Spine surgery) AND (teriparatide OR denosumab), in English language, results by year, text availability, article attribute, article type, publication date, between January 1990 and March 2022.

Eligibility criteria

Analytical studies, randomized clinical trials, systematic reviews, and meta-analyses were selected within the inclusion criteria; osteoporosis in the context of degenerative spinal pathology (BMD <-2.5 SD by bone DXA or <100 Hounsfield Units by CT scan), articles that compared the use of Teriparatide and/or Denosumab in patients with osteoporosis taken to spinal surgery and finally those that provided a recommendation.

Exclusion criteria

Descriptive articles, case series, letters, laboratory studies without patient data, duplicated, unpublished, and not performed in humans were excluded. Likewise, patients with tumor, infectious and inflammatory pathology.

RESULTS

The initial search showed 231 articles from 1990 to 2022 in Pubmed. On further screening in Pubmed, 204 articles presented full text from 2012 to 2022, of which 140 were in human and English. Forty-seven studies are obtained, and a second review is performed after reading the titles and abstracts, articles associated with rheumatoid arthritis, chronic kidney disease, osteoporosis in postmenopausal women not related to the spine, glucocorticoid osteoporosis, atypical long bone fractures, denosumab in renal transplantation for a total of 24 articles.

After the second review, 14 articles met the inclusion criteria. (Figure 1)

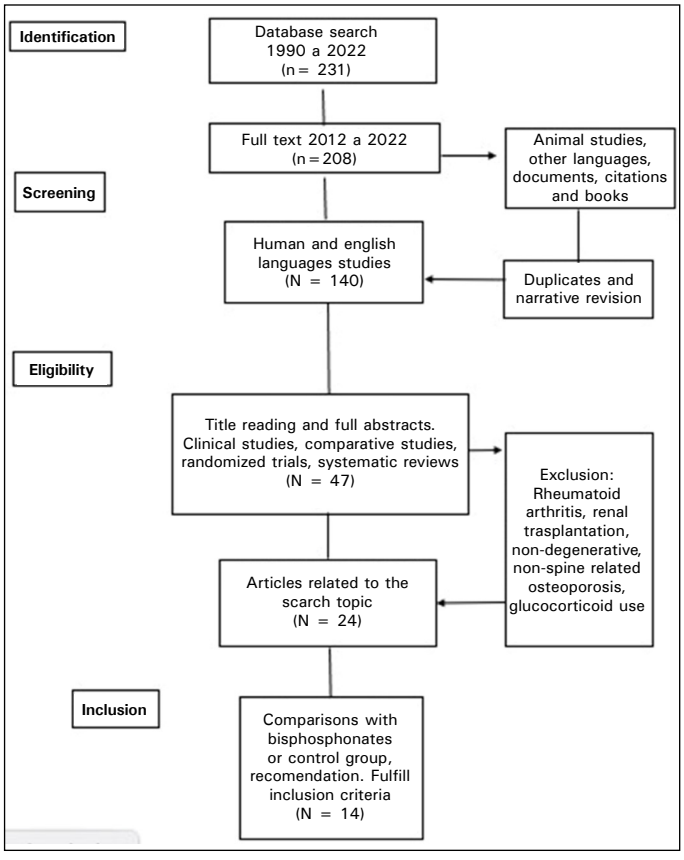

Figure 1. Flowchart visualizing the selection study.

All the 14 articles selected performed a pharmacologic comparison between teriparatide and a control group of bisphosphonates. (Table 1)

Eleven studies related to fusion, of which 6 compared it at six months, four at 12 months, and 1 article at 24 months. Five articles evaluated the rate of screw loosening with pharmacological use, 1 article evaluated torque, three evaluated bone mineral density at 12 months with pharmacological management, and 2 described the presentation of vertebral fractures in osteoporotic patients older than 75 years.

Four tables were made, and using a χ^2 test, the fusion rate, screw loosening in spinal instrumentation, increase in bone mineral density, and decrease in vertebral fractures (in patients older than 75 years) with pharmacological use were analyzed.

The prevalence of pseudarthrosis in osteoporosis was found to be 59.34% (52.94 - 65.54%), a fusion rate of 79.28% with teriparatide in the first six months, 95% CI OR 2.62 (1.79 - 3.84). (Table 2)

Regarding complications associated with osteoporosis, a screw loosening rate of 26.83% (21.5 -32.9%) was evidenced 12 months after surgery, with 18.1% screw loosening with the use of teriparatide,

Table 1. Selected articles meeting the inclusion criteria.

Author (year)	Sample (n)	Synthesis	Conclusions	Type
Cho (2017)[9]	47	Evaluation and comparison of teriparatide vs. PLIF bisphosphonate efficacy	Teriparatide increases the rate of early fusion (6m) and bone formation concerning alendronate. Teriparatide 20 micrograms daily for one-year pop fusion 89%.	Cohort R
Tsai (2016)[11]	94	Bone formation efficacy of teriparatide, denosumab, and their combination in osteoporosis.	Combining teriparatide and denosumab improves bone architecture in osteoporotic patients concerning individual pharmacological management. Teriparatide 20 mcg/day	Randomized controlled clinical trial. R
Inoue (2014)[13]	29	To evaluate the effect of teriparatide on screw torque in fusion surgery patients with osteoporosis.	Administration of teriparatide one month before surgery improves screw torque at fusion.	Cohort . R
Kim (2018)[14]	84	To determine the effect of teriparatide vs. bisphosphonates on screw loosening in spinal surgery in the osteoporotic patient.	Teriparatide significantly decreases screw loosening by 2.3% vs. bisphosphonates 9.2% $p<0.05$. Dose 20 mcg/day for six months pop.	Case study. R
Oba (2020)[15]	104	To compare multilevel fusion in osteoporosis $>$ 50 years teriparatide vs bisphosphonates. Determine the efficacy of teriparatide in posterolateral fusion in osteoporosis.	There is an increasing trend in fusion with teriparatide 46% in the first six months concerning bisphosphonates 32%. No significant differences in multilevel lumbar fusion.	Prospective randomized multicenter clinical trial.
Ohtori (2012)[16]	57		The fusion rate with teriparatide was 82% at eight months vs. 68% at ten months with bisphosphonates in posterolateral fusion.	Prospective R
Ohtori (2013)[17]	62	To evaluate teriparatide efficacy of pedicle screw loosening rate.	Pedicle screw loosening rate 7 to 13% teriparatide vs. 15 to 25% control, one-year $p<0.05$.	Prospective R
Ebata (2017)[18]	66	To evaluate bone fusion and bone formation in PLIF or TLIF with teriparatide in patients with osteoporosis by tomography.	Weekly teriparatide 20 mcg increases bone formation and fusion. Indicated for osteoporosis in patients with degenerative spinal pathology.	Prospective randomized multicenter R
Seki (2017)[19]	58	To evaluate complications in spinal surgery by administering teriparatide and low doses of bisphosphonates.	Perioperative teriparatide decreases complications and maintains the fusion rate more effectively than bisphosphonates in osteoporotic patients with spinal deformity. Screw loosening 0.009, adjacent vertebral fracture 0.00007.	Prospective R
Ide (2018)[10]	16	Evaluating lumbar spinal fusion in osteoporosis with the addition of denosumab to teriparatide.	There is an increase in the rate of spinal fusion and bone formation with the combination of teriparatide and denosumab six months after surgery, $p < 0.05$.	Prospective randomized clinical trial R
Ebina (2017)[20]	78	To evaluate the fusion and increase in bone mineral density of teriparatide associated with denosumab and bisphosphonates.	Denosumab associated with teriparatide increases bone mineral density by 6.2 vs. 2.6% concerning bisphosphonates and teriparatide and decreases the rate of bone resorption.	Observational R
Tseng (2012)[21]	50	To evaluate the use of teriparatide alone vs. vertebroplasty plus bisphosphonates in managing vertebral fractures adjacent to previous vertebroplasty for osteoporosis.	Patients treated with teriparatide had a 78.5% decrease in vertebral fractures (post vertebroplasty) odds ratio=0.21; 95% CI I, 0.02-2.10) with VAS (visual analog scale) decrease at six months $P < 0.05$, concerning the combination of new vertebroplasty and bisphosphonates.	Prospective randomized comparative R
Kaliya-Perumal (2016)[22]	62	To evaluate the effectiveness of teriparatide in multilevel lumbar fusion in patients with osteoporosis concerning placebo.	Teriparatide in posterolateral multilevel fusion increased the fusion rate by 16.7% and decreased loosening by 11% concerning the control group.	Observational, controlled, retrospective R
Ushirozako (2018)[23]	60	To determine the predictors of lumbar fusion after PLIF.	The administration of teriparatide weekly and for six months postoperatively allows a union rate of 61% vs. 27% and bone bridging of 49% vs. 12% concerning those who did not receive it. $p < 0.01$.	Multi-center case-control R

evidencing a decrease in this complication of 81.9% with the use of this drug. OR 0.6 (0.41 - 0.88). (Table 3)

When comparing teriparatide with bisphosphonates, there was evidence of an increase in bone mineral density of 10.71% with a positive predictive value of 15.15% (5.72 - 32.67%), indicating an increase of 4.5% more concerning bisphosphonates OR 1.49 (0.77 - 2.86). (Table 4)

Finally, there is a significant increase in vertebral fractures in patients older than 75 with osteoporosis, with a prevalence of 24.51% in patients who have undergone surgery or vertebroplasty, which was 14.55% with the use of teriparatide, indicating that the use of teriparatide decreased the risk of fractures in this population by 85.4%. OR 0.5 (0.29 - 0.95). (Table 5)

DISCUSSION

The success or failure of spinal surgery in osteoporosis is determined by peri-operative planning, which consists of adequate diagnosis, prevention, and treatment.

Patients with osteoporosis in spinal surgery are prone to failure and poor postoperative results due to early and late complications, such as vertebral fractures, loosening of screws, pseudoarthrosis, and kyphosis of the proximal junction, among others.[24]

A wide spectrum of drugs has been used for the management of osteoporosis. However, teriparatide and bisphosphonates are the drugs with the most publications. Despite contributing to bone fusion in spinal surgery and reducing the risk of fractures, bisphosphonates have been associated with various complications, such as subtrochanteric fractures of the femur, diabetes mellitus, alterations in calcium homeostasis, and necrosis of the maxilla.[25,26]

Different uses of teriparatide have been described in spinal surgery, such as increased fusion, decreased screw loosening, increased bone mineral density, decreased incidence of vertebral fractures in patients older than 70 years, multilevel fusion, increased torque in pedicle screws, and a synergistic effect with the combination of denosumab in cases of severe osteoporosis. It is the duty of the spine surgeon as opposed to the endocrinologist to know its usefulness.[12]

Regarding fusion, Cho[9] in 2017 performed a prospective cohort study with 47 osteoporotic patients in spinal surgery comparing teriparatide with bisphosphonates; they found a similar fusion rate in both groups at 12 and 24 months (92% vs. 96%); however, it was more accelerated with teriparatide in the first six months (77.8 % vs. 53.6% p 0.05), decreasing the presentation of complications described by bisphosphonates when used for a shorter time. Additionally, it found a greater increase in bone mineral density. Other studies[1,6,2,8,11,12,15,16,18,19,27] show that administration of teriparatide vs. bisphosphonates and placebo significantly increases spinal fusion OR 2.12,95% CI 1.45-3.11, p= 0.0001) and placebo (OR 2.23, 95% CI 1.22-4.08, p= 0.009) cohorts, respectively (1,6,9,18). Ebata[18] in 2018 similarly finds increased spinal fusion of 66% in teriparatide vs 35% placebo p0.0035. Current studies found a statistically significant 79% teriparatide fusion rate in the first six months, results that resemble the literature. IC 95% OR 2.62 (1.79 - 3.84).[16,18,19,23]

The decrease in screw loosening has been similarly described in the literature using teriparatide and bisphosphonates. Kaliya - Perumal[22] finds 66.7% vs. 50% multilevel fusion using teriparatide vs. control without statistical significance P 0.2. However, 13.4% vs. 24.4% in screw loosening P 0.001. Kim[14,] in 2018 performed a prospective study in 84 osteoporotic patients taken to elective spinal surgery and fusion, which administered teriparatide and bisphosphonates to the control group and found that loosening rates at six months were 6.9% and 6.8%, respectively, similar; however, the rate decreased markedly at 12 months in the teriparatide group 2.3% vs. 9.2% bisphosphonates without finding statistical significance $P < 0.05$.

In turn, Ohtori[17] in 2013 conducted a study in 62 patients with osteoporosis in elective spinal surgery to evaluate the incidence of screw loosening with the use of teriparatide 20 mcg per day for 12 months, bisphosphonates and placebo; he found loosening of 7 to 13% in teriparatide vs. 13 - 26% in bisphosphonates and 15 - 25% in patients who did not receive drugs $P < 0.05$. Additionally, in contrast to other studies performed in rats, in this study, it was possible to observe an improvement in bone quality with teriparatide and; an improvement of cancellous and cortical bone in the pedicle, which has repercussions on transpedicular fixation. In conclusion, teriparatide had a notable advantage concerning bisphosphonates in reducing screw loosening. Likewise, there were no differences between bisphosphonates and the group that received no drug. In our presentation, a screw loosening of 18.1% was observed using teriparatide without statistical significance.

Another important aspect of using teriparatide is related to increased bone mineral density and quality. Kim evidences a superiority of 14.86% vs. 8.5% in improving bone mineral density at 12 months of pharmacological treatment after surgery.[14] An increase of 15.15% was observed using teriparatide at 12 months postoperatively with statistical significance OR 1.49 (0.77-2.86) and results similar to the literature.[19]

Regarding the presentation of vertebral fractures, they are more frequent in patients over 75. Avoiding these fractures as they increase spinal deformity, worsen balance, produce lumbar pain or irradiation, and gastroesophageal reflux in most geriatric patients,

Table 2. Association of teriparatide and spinal fusion rate at six months.

		Column Fusion Rate		Total
		Appropriate Fusion	Non-union	
Use of Teriparatide	Patients taking teriparatide	88	23	111
	Control. Patients who didn't take teriparatide	55	75	130
Total		143	98	241

Table 3. Association of teriparatide and screw loosening rate at 12 months.

		Loosening rate of column bolts		Total
		With loosening	Without loosening	
Use of Teriparatide	Patients who took teriparatide.	21	95	116
	Control. Patients who didn't take teriparatide	45	85	130
Total		66	180	246

Table 4. Association of teriparatide and increased bone mineral density compared to bisphosphonates.

		Bone mineral density		Total
		With increased bone mineral density	No increase in bone mineral density	
Drug use	Patients who took teriparatide	5	28	33
	Patients who took bisphosphonates	4	47	51
Total		9	75	84

Table 5. Association of teriparatide and decreased vertebral fractures compared to bisphosphonates in patients older than 75.

		Vertebral Fracture Rate		Total
		Presence of vertebral fracture	No vertebral fracture	
Drug use	Patients who took teriparatide	8	47	55
	Patients who took Bifosfonatos	17	30	47
Total		25	77	102

thus worsening functional outcomes and quality of life and increasing the risk of mortality due to associated complications. Seki,[19] in 2017 performed work on 58 patients with osteoporosis to compare the presence of postsurgical vertebral fractures when administering teriparatide vs. bisphosphonates. It finds that teriparatide better avoids complications and fracture incidence and maintains the fusion rate concerning bisphosphonates. Implant rupture or failure was higher in patients over 75 years of age P 0.002. For these reasons, he recommended an administration interval of 3 months before surgery to 12 months postoperatively. Tseng et al[24] found a greater decrease in the presentation of postoperative vertebral fractures with teriparatide compared to low-dose bisphosphonates associated with vertebroplasty.

In our study, we found a prevalence of osteoporotic vertebral fractures of 24.51%, teriparatide showed a decrease of 85.4% in the rate of postoperative vertebral fractures with a 14.55% superiority over bisphosphonates, without statistical significance; OR 0.5 (0.29 - 0.95), similar to the results described in recent literature.[16,17]

Biomechanically, teriparatide increases pedicle screw torque during spinal fusion surgery more efficiently concerning patients without pharmacological treatment (1.28 ± 0.42 Nm) vs control (1.08 ± 0.52).[24]

Other pharmacological lines have played an important role in the management of osteoporosis, such as Denosumab, and despite the existence of scientific evidence in the management of postmenopausal osteoporosis[13] and some pathologies such as giant cell tumor in the sacrum, multiple myeloma, and aneurysmal bone cyst;[28-31] there is still no evidence in the literature of clinical trials, comparative or prospective studies about its usefulness in elective spinal surgery of the osteoporotic patient.[2] Denosumab is the only monoclonal antibody approved by the FDA for the treatment of osteoporosis. Its pharmacological mechanism consists of preventing the binding of RANK to the RANKL receptor,[3] inhibiting early osteoclast differentiation.[5]

Different aspects of denosumab have been studied in spinal surgery. One of the main ones is the synergistic effect with teriparatide, with which an increase in resistance and improvement in bone microarchitecture has been observed. This implies superiority concerning monotherapy with teriparatide. Its effect has been observed with the administration of 60 mg subcutaneously every six months between 1 and 2 years.[28]

Ide[10] in 2018, conducted a study with 16 osteoporotic patients to evaluate spinal fusion with the use e teriparatide and teriparatide associated with denosumab one month before and 12 months after surgery, evidenced a greater fusion in the first six months with the pharmacological association concluding that it could be implemented in the treatment of severe spinal osteoporosis. Other authors have also investigated the synergistic effect of denosumab, even when compared to bisphosphonates, with promising results in spinal fusion (6.2 vs. 2.6 %; $P < 0.01$) in use for one year after surgery.[29]

In a 2-year prospective study, 21 patients with osteoporosis undergoing spinal surgery showed that Denosumab increases screw strength in the pedicle and vertebral body by increasing bone mineral density, being the first study to consider denosumab in spinal instrumentation.[30]

Therefore, teriparatide has different functions in degenerative spinal surgery in osteoporotic patients.[1,5,6,8-12,15,18] Although most of the time the endocrinologist manages it, the spine surgeon should know how to plan the surgery, reducing the number of complications and improving the patients' bone quality and life expectancy. There is still no consensus on the administration interval. However, most studies show that the greatest benefit of teriparatide is obtained when 20 mcg subcutaneous is administered daily before three months after surgery and up to 12 months later, since in this period, it not only increases fusion but also improves bone mineral density and reduces screw loosening.[6,7,14,22]

On reviewing the current literature, most studies show the advantages of teriparatide over bisphosphonates in terms of a faster rate of fusion in the first six months[8], a lower rate of complications, increased torque,[21] improved bone quality[19,22,31] and a better effect in reducing the risk of vertebral fractures.[16,17] We consider that denosumab should be associated with patients with severe osteoporosis due to its effects above.[9,31]

More cost-effective clinical studies with a larger number of patients and a follow-up of more than two years are needed to evaluate new utilities and confirm the synergistic effect of denosumab.

Limitations of the study

1. There is a lack of controlled clinical trials to determine an adequate guideline and interval of teriparatide administration, as well as greater statistical power in the loosening of screws and reduction of vertebral fractures.
2. There are no clinical studies on denosumab to determine its efficacy in osteoporosis of spinal surgery.
3. Small patient samples
4. Heterogeneity of the population
5. Cost-effectiveness of teriparatide needs to be adequately evaluated.
6. Clinical studies are required to evaluate the instrumentation results after 12 months.

CONCLUSIONS

The uses and advantages of teriparatide and denosumab in planning are different. They should be taken into account by the spinal surgeon and endocrinologist. Teriparatide was shown to increase fusion and bone mineral density while decreasing the rate of complications such as screw loosening and the incidence of vertebral fractures more effectively than bisphosphonates.

Denosumab has a synergistic effect with teriparatide in severe osteoporosis by increasing bone mineral density more effectively and, at the same time, decreasing screw loosening during instrumentation. However, clinical and comparative studies are lacking to verify its usefulness and greater statistical significance.

Due to their versatility, advantages over bisphosphonates, and low risk of complications, both drugs should be considered in the peri-operative planning of spinal surgery. Their use does not replace the different surgical methods and techniques that are also part of the planning. Each case should be evaluated individually, analyzing the risks and benefits.

All authors declare no potential conflict of interest related to this article.

CONTRIBUTIONS OF THE AUTHORS: All authors contributed substantially to the production of the article, jointly posing the question and planning. RCJ: analysis of the results with statistical evaluation and draft writing. PLB: Bibliographic search, initial selection of articles, and review of the draft. JCSA: Final selection of articles and translation of the article.

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